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Indian Journal of Tuberculosis

Vol. 57 **New Delhi, January, 2010** **No. 1**

Editorial

MANIFESTATION OF *MYCOBACTERIUM* INFECTION OTHER THAN TUBERCULOSIS

[Indian J Tuberc 2010; 57:1-3]

More than 125 years into its 'known' existence, *Mycobacterium tuberculosis* (MTB) continues to haunt the mankind and tuberculosis (TB) the disease caused by it remains the leading cause of preventable death worldwide. Much is known and written about the pulmonary tuberculosis, its treatment and complications, rightly so as this form of the tuberculosis is the most important from everyone's point of view be it the patient, family, society, physician or the public health administrator. However, as the MTB has adapted itself so well for prolonged survival within the human body, it is inevitable that it invokes several processes within the body that can cause 'non-infectious' complications. Most of these manifestations are believed to be due to hypersensitivity to tubercular proteins.

Perhaps one of the oldest and well recognized non-infectious or para-infectious complications of MTB infection is reactive arthritis (Poncet's disease). It was described way back in 1887 by Poncet who documented small joint arthritis in hands and feet in patients with past or concomitant tuberculosis[1]. However, the term was not properly defined and went into many controversies as all sorts of articular problems associated with TB were being bundled into this category. Currently, the condition is defined as polyarthritis associated with confirmed tuberculosis (mostly extra-pulmonary) and no evidence of direct mycobacterial presence in the involved joints. This is variously called as Poncet's Disease, reactive arthritis, para-infectious arthritis or tuberculous rheumatism[1,2]. The exact pathogenesis is not known, however molecular cross reactivity between tubercular and human antigens (e.g heat-shock proteins) coupled with genetic susceptibility to arthritis are possible explanations[3,4].

Tuberculids are hypersensitive dermatological manifestations of TB. Conditions that are included in this group are lichen scrofulosorum, papulonecrotic tuberculids, erythema induratum and erythema nodosum. By definition, these lesions show granulomatous inflammation that is AFB negative in the presence of a TB focus elsewhere in the body, with strongly positive tuberculin skin test and response to anti tubercular therapy. However, Molecular techniques have shown presence of mycobacterial DNA in the biopsies of some of these patients[5,6]. Similar to skin lesions, ocular tuberculids (Phylectunosis) have also been demonstrated in conjunctiva, most commonly in the limbal region. Sometimes there is extension to the adjacent cornea leading to a more severe form of disease[7].

Other systemic manifestations/complications of TB or its treatment include haematological manifestation (anaemia being the commonest)[8], endocrine manifestations[9], malnutrition[10], amyloidosis[11], and immune reconstitution inflammatory syndrome (IRIS) in patients of tuberculosis with HIV infection[12].

Another disease which has been often linked to MTB is sarcoidosis. Sarcoidosis is a disease of unknown etiology characterized by the presence of non-caseating granulomas in multiple organs. Because sarcoidosis most commonly involves the mediastinal lymph nodes and the lung, the search has centered

on exposure to some airborne antigen, with mycobacteria being a strong contender as an etiologic agent for sarcoidosis[13,14]. In a meta-analysis, it was demonstrated that there is almost 26 percent chance of finding mycobacteria in sarcoidosis using nucleic acid amplification techniques,[14] and in a subsequent study, we found 50 per cent prevalence of mycobacterial DNA in sarcoid samples despite technical limitations with our PCR technique[15]. Recently, a specific mycobacterial protein, the catalase-peroxidase (mKatG) was identified in 55 percent of sarcoid tissues and was the target of circulating IgG in 48 per cent of sarcoid patients[16]. Proteins such as 6-kDa early secreted antigenic target (ESAT-6) and the 10-kDa culture ûltrate protein (CFP-10) encoded by genes located on the region of difference 1 (RD1) are highly speciûc indicators of *M. tuberculosis complex* infection[17]. If indeed mycobacteria are etiologically linked to sarcoidosis, then the humoral responses against RD1 antigens in sarcoid blood samples would be demonstrable, more so in a country with high prevalence of tuberculosis (TB). In a recent study, patients with sarcoidosis showed significant seroreactivity to RD1 antigens[18]. The positive results in patients with pulmonary sarcoidosis not only reinforce the possible pathogenic role of mycobacterial antigens in sarcoidosis, but also limits the clinical value of these antibodies in the differential diagnosis of tuberculosis from sarcoidosis, particularly in a country with high endemicity for TB.

Mycobacterium tuberculosis, is therefore indeed an enigmatic bug. Not only has it defied all our efforts to eradicate it by evolving into multi, extreme and totally drug resistant strains, but also contributes significantly to several other known and unknown diseases.

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The Editor-in-Chief and the members of the Editorial Board of the *Indian Journal of Tuberculosis* wish you all a Very Happy and Prosperous New Year 2010

M.M. SINGH
EDITOR

Original article

CLINICAL PROFILE AND TREATMENT OUTCOME OF TUBERCULOUS LYMPHADENITIS IN CHILDREN USING DOTS STRATEGY

Sangeeta Sharma[1], Rohit Sarin[2], U. K. Khalid[3], N. Singla[4], P. P. Sharma[5] and D. Behera[6]

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Summary

Background: Extra pulmonary TB (EPTB) including tuberculous lymphadenitis is becoming more common probably due to human immuno deficiency virus (HIV) co-infection. While children do experience a high TB related morbidity and mortality, management of TB in children is challenging. The present study was designed to study the treatment outcome of DOTS strategy for pediatric tuberculous lymphadenitis.

Objective: To study the efficacy of DOTS strategy for pediatric lymphhnode tuberculosis.

Methods: Retrospective analysis of 669 children of lymphnode tuberculosis treated with DOTS strategy over 9½ years.

Results: Mean age was 9.8 years with significantly more girls (61.3%) than boys (38.7%) {χ^2=34.08, P< 0.001 (S)}. Most of the patients were in the age group of 11-14 years (48.0%) followed by 6-10 years(34.5%) and 0-5 years(17.5%) respectively. Cervical tuberculous lymphadenitis (88.2%) was the commonest form for all ages followed by axillary lymphadenitis in 3.3%. TB of other sites was seen in only 57 (8.5%) cases. Out of total 622 (93%) cases of lymphnode TB where fine needle aspiration and/ or excisional biopsy was done, it was positive (84.2%) and negative (15.6%) respectively for AFB/ cytology, while it could not be done in 47 patients due to inaccessible sites. Category I, II and III was started on 15.4%, 7.5% and 77.1% patients respectively. Overall, treatment completion rate was 94.9% and the default rate was 2.2% with a failure rate of 2.5%. Death rate was 0.3%.

Conclusion: The study confirms the efficacy of DOTS strategy for pediatric TB lymphadenitis.

[*Indian J Tuberc 2010; 57:4-11*]

Key words: Pediatric tuberculosis, Childhood tuberculosis, Tuberculous lymphadenitis, Directly Observed Treatment Short-course (DOTS), Anti-tuberculosis therapy.

INTRODUCTION

A significant proportion of global tuberculosis (TB) caseload is contributed by children throughout the world [1-3]. With the resurgence of tuberculosis, although pulmonary TB (PTB) contributes to majority of cases, extra pulmonary TB (EPTB) is becoming more common probably due to human immuno-deficiency virus (HIV) co-infection [4,5]. Reliable epidemiological data and complete disease spectrum are not easily available for pediatric TB but children do experience a high TB related morbidity and mortality [6,7].

Management of TB in children is challenging, as a large proportion of cases go unrecognized due to paucibacillary nature of the disease, poor sensitivity of currently available diagnostic modalities and absence of a "gold standard" for diagnosis which is often presumptive[8-10]. Stop TB Strategy highlights the need to promptly identify and effectively manage TB in children in line with the adult TB.[11,12]

Although there are many studies on efficacy of WHO's Directly Observed Treatment Short course (DOTS) strategy for adult TB and pediatric pulmonary TB [10,13-15], there have been very few studies on pediatric EPTB and TB lymphadenitis in the world literature. The present retrospective study was conducted in a tertiary referral centre with the aim to observe the efficacy of DOTS for TB lymphadenitis and also to observe any change in trend over the years.

MATERIAL AND METHODS

The study was conducted over a 9 1/2 year period (January 1995- July 2004) analyzing the data of 669 children diagnosed and treated for TB lymphadenitis at LRS Institute of Tuberculosis and

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Respiratory Diseases, New Delhi, a tertiary referral governmental hospital specializing in the treatment and prevention of TB and also a pilot site for Revised National Tuberculosis Control Programme (RNTCP) of India. Permission of the competent authority (Director) of the institute was taken to review the records and conduct this study. Children with pulmonary TB and non-lymphnode TB were excluded from this study. Diagnostic approach used was based on limited published evidence and rested heavily on expert opinion, an approach recommended by WHO [16-18]. In cases where the diagnosis was doubtful, if there was vague symptomatology or "confounders" and equivocal results on initial baseline tests, specialized investigations like computerized tomography (CT), CT guided fine needle aspiration (FNA) were done and the specimen was sent for cytology, direct smear, conventional and/or BACTEC culture to arrive at the diagnosis. As a policy of the institute at that time, HIV testing was not done for all patients but only for suspected multi-drug resistant (MDR) TB patients due to the cost factor.

All cases diagnosed were categorized, treated and monitored as per W.H.O. and RNTCP guidelines incorporating DOTS strategy [16-18] at the 37 designated DOTS centres covering 1.6 million population of South Delhi. To assist in calculating required dosages of anti-TB drugs for children, the medications were calculated according to the child's weight (R-rifampicin 10mg./kg body weight ; H-isoniazid 10 mg/kg ; Z-pyrazinamide 30-35 mg/kg ; E-ethambutol 30mg/kg ; S-streptomycin 15mg/kg ; for doses given thrice a week) As blister combi-packs in patient-wise boxes for children were not available, medications were given either as syrups, dispersible tablets or by breaking the adult formulation tablets. Compliance was ensured by giving the drugs under direct observation of a health worker. For monitoring treatment, all patients were examined at the end of second month. Wherever patient showed no improvement at the end of second month, that is, there was development of new lymph nodes or enlargement of existing lymph nodes with or without fluctuation and tenderness, review of diagnosis was done. Patients who were found to have some other disease were excluded from the study. But if the diagnosis was certain, intensive phase was extended by one month. After the extended intensive phase (i.e. total three months of $R_3H_3Z_3E_3$ from start of treatment), if they still continued to deteriorate (general ill-health with enlargement / fluctuant lymph nodes; appearance of new nodes), FNA was repeated and the specimen was sent for cytology, direct smear, conventional and / or BACTEC culture to check for bacteriological deterioration. They were declared as failures / non – responders and put on Category II, for cases with / without bacteriological deterioration.

The records were taken out and details of patients, their symptoms, signs, results of various diagnostic investigations, categorization and outcome of treatment were computed. A data collection sheet based on standard protocol and format, using common WHO definitions[16] being followed by RNTCP of India[17] was used in the study. Data entry and record keeping was done by trained staff. Data was analyzed and efficacy of DOTS observed using SPSS 12.0 version (Chicago ,USA) and Epi-info 6.0 (WHO, Geneva and Center for Disease Control, Atlanta, USA). The chi square (χ^2) test was used for test of Homogeneity of proportions. A p value of 0.05 was taken as significance level. Yates correction in chi square was applied where the frequency was less than five in a cell.

RESULTS

Table I shows the demographic profile of patients with TB lymphadenitis. Mean age was 9.8 years with overall significantly more girls (61.3%) than boys (38.7%) {χ_1^2=34.08, P< 0.001 (S)} except 0-5 year age group where sex ratio was reversed (χ_1^2 = 6.23,p=0.013). In the age group of 0-5, 6-10 and 11-14 years, there were 17.5%, 34.5% and 48% patients respectively. Out of total 941 cases of EPTB during the study period, lymph node TB was the commonest type of EPTB responsible for total 669 (669/941; 71.1%) cases. Cervical lymphadenitis was the commonest type of lymph node affection seen in 590 cases (88.2%) followed by axillary TB lymphadenitis in 22 (3.3%) and TB lymphadenitis of other sites like inguinal, mediastinal, mesenteric, retroperitoneal, etc., only in 57 (8.5%) cases respectively.

Table 1: Demographic Profile of Pediatric Tuberculous Lymphadenitis (0-14 yrs) (N=669)

	EPT SITE Lymphnode	0-5 Years			6-10 Years			11-14 Years			Total		Grand Total
		M	F	Total (%)	M	F	Total (%)	M	F	Total (%)	M(%)	F(%)	
1	Cervical	67	40	107	84	118	202	79	202	281	230	360	590(88.2)
	Axilliary	2	3	5	4	7	11	1	5	6	7	15	22(3.3)
	Other Sites	3	2	5	7	11	18	12	22	34	22	35	57(8.5)
	Total	72	45	117 (17.5)	95	136	231 (34.5)	92	229	321 (48.0)	259 (38.7)	410 (61.3)	669(100)
M vs F PValue		χ_1^2=6.23 P = 0.013 (S)			χ_1^2=7.23 P < 0.007 (S)			χ_1^2=58.47 P < 0.001 (S)			χ_1^2=34.08 P < 0.001 (S)		

S=Significant
NS=Not Significant

Table 2: Age & sexwise distribution of various investigations performed*

Investigations	0-5 Yrs.			6-10 Yrs.			11-14 Yrs.			Total		Grand Total
	M	F	Total	M	F	Total	M	F	Total	M	F	
X-Ray	60	42	102	58	59	117	70	120	190	188	221	409
Mx	72	45	117	95	136	231	92	229	321	259	410	669
H/O Contact	12	11	23	10	15	25	7	13	20	29	39	68
FNA	62	40	102	81	121	202	83	204	287	226	365	591
Excision	7	3	10	7	6	13	3	5	8	17	14	31
USG	15	8	23	9	9	18	10	34	44	34	51	85
CT	1	2	3	0	1	1	2	4	6	3	7	10
Total	228	151	379	260	347	607	267	609	876	756	1107	1863

* This data was calculated manually from the registers and is within the 37% error range of N=2203 as calculated from the records in the computer, which is acceptable.
* More than one investigation was performed in some cases

Table 3: Age and Sexwise distribution of categorization

	EPT SITE	0-5 Years			6-10 Years			11-14 Years			Total			Grand Total	Percentage (%)
		M	F	Total	M	F	Total	M	F	Total	M %	F %	M Vs F P Value		
CAT-1	Lymphnode	8	10	18	15	23	38	12	35	47	35 (34)	68 (66)	χ_1^2=10.57 P=0.0017 (S)	103	15.4%
CAT-II	Lymphnode	4	1	5	3	11	14	8	23	31	15 (30)	35 (70)	χ_1^2=8.0 P=0.0047 (S)	50	7.5%
CAT-III	Lymphnode	60	34	94	77	102	179	72	171	243	209	307	χ_1^2=18.61 P<0.001 (S)	516	77.1%

Table 4: Comparison of Outcome of treatment for different categories of treatment in children

EPT sites	Categories	Treatment completed (%)	Default (%)	Died (%)	Failure (%)	Total (%)	Total/ Grand Total (%)	Grand Total
Lymphnode	Cat 1	93 (90.3)	4 (3.9)	1 (1)	5 (4.8)	103 (100)	15.4	669
	Cat II	44 (88)	3 (6)	1 (2)	2 (4)	50 (100)	7.5	
	Cat III	498 (96.5)	8 (1.6)	0 (0)	10 (1.9)	516 (100)	77.1	
	Total	635 (94.9)	15 (2.2)	2 (0.3)	17 (2.5)	669(100)		

	Lymphnode
CAT I Vs II	χ_1^2=0.19 P= 0.669 (NS)
CAT II Vs III	χ_{yates}^2=6.17 P= 0.03 (S)
CAT I Vs III	χ_{yates}^2=6.32 P= 0.012 (S)

S=Significant
NS=Not Significant
$\chi_Y^2 = \chi_{yates}^2$

The details of investigations performed to diagnose TB lymphadenitis is shown in Table 2. Diagnosis of lymphnode involvement was primarily made on the basis of fine needle aspiration (FNA) and excision biopsy specimen, which was examined for cytology, direct smear and culture, if required. CT guided FNA was possible in 10 cases of inaccessible sites like intra-thoracic (hilar, paratracheal, mediastinal) and extra-thoracic (mesenteric, retroperitoneal) lymphnodes while it could not be done in 47 cases. Out of the total 622(93%) cases of lymphnode tuberculosis where FNA and excision were done, 524(84.2%) and 98 (15.6%) were positive and negative respectively for cytology, direct smear or culture alone or in combination.

Age and sex-wise distribution of categorization is shown in Table 3. Category I, II and III was started in 103 (15.4%), 50 (7.5%) and 516 (77.1%) patients respectively, with significantly more females than males for all categories. Out of

Table 5: Sex-wise Comparison of Outcome for different categories of treatment in children

Categories	Treatment Outcome	Male		Female		Total		M Vs F P Value
	Types of outcome	No. (%)		No.	%	No.	%	
Cat 1	Treatment completed (TC)	30 (85.7)		63	92.6	93	90	χ_Y^2=0.60 P= 0.439 (NS)
	Default	2		2		4		
	Died	0		1		1		
	Failure	3		2		5		
	Total	35	100	68	100	103	100	
Cat 1I	Treatment completed (TC)	11	73.3	33	94.3	44		χ_Y^2=2.61 P= 0.106 (NS)
	Default	1		2		3		
	Died	1		0		1		
	Failure	2		0		2		
	Total	15	100	35	100	50	100	
Cat 1II	Treatment completed (TC)	202	96.7	296	96.4	498	96.1	χ_1^2=0.02 P= 0.887 (NS)
	Default	3		5		8		
	Died	0		0		0		
	Failure	4		6		10		
	Total	209	100	307	100	516	100	
Grand Total		259		410		669		χ_1^2=1.84 P= 0.175 (NS)
Overall TC		243/259	93.8	392/410	95.6	635/669	94.9	

TC New Cases 591/619 = 95.5%
TC Re-treatment Cases 44/50 = 88.0 %
S=Significant
NS=Not Significant
$\chi^2_Y = \chi^2_{yates}$

50 patients treated with Cat II, 28(56%) were smear positive, three were culture positive smear negative and 20 were diagnosed by cytology along with history of prior ATT and clinical deterioration. Out of 28 smear positive patients, 12(42.8%) had positive culture. Thus out of 50 patients treated with Cat II, 15 (30%) culture positive patients, with 12 and 3 being smear positive and negative respectively.

Table 4 shows the comparison of outcome of treatment for different Categories of TB lymphadenitis of EPTB and different Category of treatment in children. Overall treatment completion rate was observed in 635 (94.9%) cases, default in 15 (2.2%) cases and failure in 17 (2.5%) cases. There were two deaths (0.3%) reported with one being each in Category I and Category II respectively. Although, Category I showed better treatment completion (90.3%) as compared to Category II (88%) but this was not significant (χ_1^2=0.19, P = 0.669, not significant) while Category III showed significantly better treatment completion (96.5%) as compared to Category II (88%) {χ^2_{yates}=6.17, P = 0.03, significant} and Category I {χ^2_{yates}=6.32, P = 0.012, significant} respectively. Paradoxical deterioration (PR defined as clinical enlargement/fluctuant lymph nodes; appearance of new nodes in a patient who had received anti-TB therapy for at least two weeks) occurred in 67 (10%; 95% confidence interval 18-28%) patients, at a median onset time of seven weeks (range 4-18 weeks) after starting anti-TB medication with development of new nodes in anatomical sites other than those observed at initial presentation was observed in 31 (4.6%) cases. While only 45 cases (6.7%) reported persistence of lymphadenitis after completion of therapy.

DISCUSSION

Lymph node tuberculosis has increased over last two decades [19]. In a retrospective study of 459 children of tuberculosis started on anti-tubercular drugs from a tertiary referral institute of Delhi, pulmonary tuberculosis was the commonest followed by lymph node tuberculosis. The mean age of the children was 93 months and sex distribution was almost equal [20]. The present study also confirms the high prevalence of EPTB in children with significantly increased contribution by girls (60.9%) than boys (39.1%) (χ_1^2 = 44.6, p=0) except very young children (0-5 year age group) where significantly more males were affected than females (χ_1^2 = 9.3, p=0.002) . During the same period we conducted the study and published our experience on pulmonary TB in 1098 children from our hospital[10]. Hence, the proportion of TB in children caused by EPTB during the same study period was 46.2% which is much higher than in adult population confirming that children are affected by EPTB more often [15]. Marais *et al*[7] also observed disease to be more common in girls (50.5%) than boys (49.5%) and a high proportion of TB in children less than 3 years of age and in HIV positive cases. They observed spectrum of both pulmonary and extra pulmonary TB in children from a highly endemic area of South Africa and concluded that children suffered significant morbidity with most severe disease recorded very young and / or HIV-infected children. They looked for all types of TB in children and found intrathoracic TB in 86.7% children, extrathoracic in 20.3% children with 5.7% with co-existing intrathoracic disease.

Short-course chemotherapy for childhood tuberculosis is well established [19,20]. In the retrospective study of 459 children of tuberculosis started on anti-tubercular drugs from a tertiary referral institute of Delhi, treatment with intermittent regimens was comparable to daily regimens. Directly observed treatment strategy had shown encouraging results for all forms of TB including lymph node tuberculosis. 323 patients were in Category I, 12 in Category II, 120 in Category III and 4 in Category IV. 365 (80 percent) children completed the treatment. Of these, 302 (82.7 percent) were cured with the primary regimen assigned to them in the beginning, 54 (14.8 percent) required extension of treatment for three months and nine (2.5 percent) patients required change in the treatment regimen. [20] However, our study was only on TB lymphadenitis and we observed a high treatment completion rate (94.9%) with two deaths out of 669 children (0.3% death rate), 15 defaults (2.2% default rate) and 17 failures (2.5% failure rate) in our study. For pulmonary TB, we observed a cure rate of 92.4%

(302/327), treatment completion rate of 97% (636/656), default rate of 3%, failure rate of 1.9% and death rate of 1% for new cases under DOTS strategy[10]. This has been made possible due to strict adherence to DOTS strategy under the Revised National TB Control Programme (RNTCP) of India in which the onus of treatment falls on the health providers and not on the patient. All the children were treated in one of the DOTS centres depending on their address, where quality assured drugs were swallowed by the patients in the presence of health care providers. Help of family members and teachers was sought to ensure compliance[21]. Our study confirms that all categories of treatment were effective for treatment of EPTB and that though the disease was more prevalent in female children (61.3%) than in male children (38.7%), the treatment completion rate was equally good in both sexes and in all three categories being 85.7%, 73.3% and 96.7% in male children and 92.6%, 94.3% and 96.4% in female children for Category I, II and III respectively. There were total 2 (0.3%) deaths with 1 deaths in Category I treatment and 1death in Category II and no death in Category III treatment, confirming the efficacy of DOTS strategy for TB lymphadenitis in both boys and girls. Higher incidence of TB in female children is probably due to better social status of boys in the Indian society where they are given preferential treatment, better nutrition, vaccination, education and early treatment for any disease due to cultural beliefs as boys are supposed to look after parents in their old age and carry on with the profession of their parents [10]. The higher prevalence of TB in female children can have a long lasting effect on their menstrual function and future fertility status, as has been demonstrated by our previous study on adolescent girls in which we observed a high prevalence of oligohypomenorrhoea and amenorrhoea in girls with pulmonary and extra-pulmonary tuberculosis[10,22]. The limitations of our study are its retrospective nature, multiple DOTS centres and lack of data on the HIV status as it was not done on all TB patients due to financial constraints. In India, HIV sero-prevalence in tuberculosis patients varies from as low as 0.7% in Delhi[23], 2% in Aligarh[24] and as high as 5.89% in Mumbai[25] and 20.1% in Pune [26]. A prevalence rate of 18% is reported in children with miliary and neuro tuberculosis.[27] As the study was conducted in Delhi with low seroprevalence of HIV (reported 0.7% in TB patients), we presume it not to be a major contributing factor. Also , since all the 37 DOTS centres were following the same standardized WHO protocol for diagnosis and treatment of EPTB included under India's RNTCP programme, our excellent results are the major strengths of this study, results comparable with the best centres in the world [13-15,19,20] highlighting the need of access to accurate diagnosis, prompt effective treatment and adherence particularly in resource poor endemic areas with greater burden of the disease, a finding reported by others also [3,10,28-31].

CONCLUSION

DOTS strategy is an effective treatment modality for TB achieving a high treatment completion rate (94.9%), low default rate (2.2%), low failure rate (2.5%), and low death rate (0.3%) and thus, is strongly recommended for pediatric TB lymphadenitis, especially in developing countries for better results.

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Original Article

A SOCIOLOGICAL STUDY ON STIGMA AMONG TB PATIENTS IN DELHI*

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Summary

Setting **:** The study was carried out at Delhi State, New Delhi.

Objectives **:** 1. To assess the effect of social stigma in TB patient's treatment, their personality, emotions, feelings, changes in their thinking process and behaviour of their family members, friends.

2. To study the relationship of gender and to what extent social stigma affects their lives.

Design **:** It was a prospective study. A total of 1977 newly diagnosed and registered cases under Revised National TB Control Programme for treatment during the period of March 2009 to May 2009 were included in the study. Out of a total population of 170 lacs, a proportion of 31 lacs of Delhi, distributed among five chest clinics of Delhi, comprised the study population. All the patients were interviewed according to a pre-designed & pre-tested questionnaire after taking informed consent of the patients. The data was collected and analysed after processing into MS excel sheets for statistical analysis.

Results **:** There was an immense stigma observed at society level with 60% of the patients hiding their disease ($p<0.05$) from friends and neighbours. Stigma was observed more among middle and upper middle class when compared to lower middle class and lower class ($p<0.05$). Gender-wise further it was observed that stigma was more among females ($p<0.05$) than in males.

Conclusion **:** The study has demonstrated that despite good performance of Revised National TB Control Programme the stigma in tuberculosis still remains a problem and we need to supplement the efforts in advocacy, communication and social mobalization for reducing the stigma problem among TB patients in effective control of tuberculosis.

[Indian J Tuberc 2010; 57:12-18]

Key words : Stigma, tuberculosis, gender.

INTRODUCTION

Tuberculosis (TB) is one of India's most important public health problems. India accounts for nearly one fifth of the global TB burden. Every day in India more than 20,000 people develop the disease, and more than 1000 die from TB[1]. TB is a classical example of a disease with both medical and social dimensions, characterized by its close relation to poor socio-economic conditions[2]. TB patients experience psychological and social sufferings and their basic rights may be negated. Amongst problems met by TB patients, social stigma has been increasingly recognized. Social stigma is "an undesirable or discrediting attribute that an individual possesses, thus reducing that individual's status in the eyes of society[3]" India lags far behind developed countries in managing tuberculosis (TB) because of social stigma attached to it. The stigma attached to TB adds to the burden of disease for both men and women, and even more so if they are of marriageable age. While men have to deal with the stigma at their work place and at the community level, women are faced with ostracism within the household and in the immediate neighbourhood. They are also inhibited in discussing their illness and participating in social functions due to fear of becoming an outcast[4].

Implementation of Directly Observed Treatment Short Course (DOTS) under Revised National TB Control Programme, improved IEC activities, ACSM, continuing medical education programmes, community meetings, public health messages and increased dissemination of knowledge about the transmission of tuberculosis has certainly

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made a considerable difference in overcoming the stigma among TB patients. Nevertheless in India the stigma to TB is still rampant and is an important factor which not only delays the initiation of treatment but is also a major factor in hinderness to adherence to treatment.

A study was carried out at New Delhi Tuberculosis Centre to define the problem of social stigma among TB patients in the domiciliary area covered under Revised National TB Control Programme in Delhi.

OBJECTIVES

1. To assess the effect of social stigma in patient's treatment, their personality, emotions, feelings, changes in their thinking process and behaviour of their family members, friends etc.

2. To study the relationship of gender and to what extent social stigma affects their lives.

MATERIAL AND METHODS

Study population comprised 31 lacs population of Delhi out of a total population of 170 lacs distributed among five chest clinics of Delhi namely Gulabi Bagh, R.K. Mission, LNJP, Jhandewalan and Pili Kothi. Almost all chest clinics had representation of slum population as well.

A total of 2196 patients diagnosed and registered under the Revised National TB Control Programme for treatment during the period of three months i.e. March 2009 to May 2009 were included in the study. All these patients were subjected to personal detailed interview according to a pre-designed semi-structured questionnaire after taking informed consent of the patients. The questionnaire contained various questions formed to elicit requisite information about the knowledge of tuberculosis action taken by the patients, their experience at work place and their family response. Before conducting the study, the proforma was pre-tested and evaluated for proper conduct of the study. The interviews were conducted by two properly trained health visitors having diploma in TB Health Visitor's course and who had been specially trained for the purpose. The investigators had taken special interest and supervision during these interviews. The interviews were conducted in the intensive phase of treatment.

The information was elicited from TB patients regarding 'problems faced in their homes, attitudes of neighbours, friends and co-workers. Interview included questions regarding data on socio-economic and awareness of TB and the nature of their disclosure of their disease to family members, relatives, neighbours, friends and employers. The information was also elicited regarding behavioural changes such as maintaining appropriate personal distance and avoiding close contact activities with family members neighbours, friends and other fellow employees.

The data was scrutinized and analysed after processing into MS excel sheets in computer for statistical analysis and chi square test and proportion tests were used to assess significance. A value of $p<0.05$ was taken as significant.

RESULTS

Out of a total of 2196 patients registered for treatment in the three months period, 20 had expired and 53 children below 14 years of age were excluded, leaving 2123 for interview. Out of these remaining 2123 patients, 1977 (93.1%) could be interviewed. The various reasons of those who could not be interviewed (6.9%) were patients on non-DOTS treatment (49), defaulters (38), left locality (9) or taking treatment from covered services like ESI (11) and therefore not available for personal interview at the DOT Centres.

Five chest clinics which were selected for the study are Gulabi Bagh where 478 patients interviewed formed 24.2% of total study length, R.K. Mission 527 patients had 26.6% representation, Jhandewalan had 385 patients 19.5% representation, LNJP had 286 patients 14.5% representation and Pili Kothi had 15.2% representation 301 patients who were interviewed in the study.

Table 1: The stigma at family level

S.No.		No.	Percentage	Significance
1.	Total No. of patients interviewed. Disclosure of their disease in their family. • Male • Female	1977 1961/1977 1131/1144 830/833	100.00 99.2 98.9 99.6	---- No Stigma No Stigma (P>0.05)
2.	Disclosure of their disease with diagnosis as • Pulmonary TB(+) • Pulmonary TB(-) • EP TB	 904/914 287/291 770/772	 98.9 98.6 99.7	 No Stigma (P>0.05)
3.	Number of patients who were unmarried and between age 18-38 years. • Male • Female	456/888 330/456 126/456	51.3 72.4 27.6	
4.	The patients who were unmarried and not worried about marriage after having disease • Male • Female	 241/330 80/126	 73.0 63.5	 No Stigma P>0.05
5.	First reaction of the family members after disclosure of disease. • Supportive • Shocked • No reaction	 1870 47 41	 94.6* 2.4 2.0	 Significant P<0.05
6.	No any change in the behavior of spouse in married patients. • Male • Female	 1002 599/634 403/455	 92.0 94.5 88.6	 Significant Z=5, P<0.05
7.	The sharing of information about disease with the family members. • Male • Female	 1178/1977 743/1144 435/833	 59.6 64.9 52.2	 Significant Z=5.93 P<0.05

Table 2: The stigma at work level

S.No.			No.	Percentage	Significance
1.	Total number of patients interviewed. Employed. • Males • Females		1977 773 723/773 50/773	100.00 39.1 93.5 6.5	----
2.	Disclosure of their disease among				
	Males	Colleagues Employers	595/723 576/723	82.3* 79.6**	Z=3.93 P<0.05* Z=4.6 P<0.05**
	Females	Colleagues Employers	30/50 26/50	60.0* 52.0**	Significant
	Total	Colleagues Employers	625/773 602/773	80.8 77.9	No Stigma
3.	No change in behaviour. • Males • Females		 573/723 28/50	 79.9 56.0	Significant Z=2.76 P<0.05
4.	Continuing with the same jobs. • Males • Females		 679/723 42/50	 93.9 84.0	Significant Z=2.76 P<0.05
5.	Allowed to attend the clinic for treatment of disease • Yes • N.A.		 35 738	 4.5 95.5	

If we see the sex wise distribution, then we can say that males were more than females, 1144 (57.8%) / 833 (42.2%) females formed the ration 1:1.37. Out of total number, 1413 (71.3%) were literate and 567 (28.7%) were illiterate. As far as marital status is concerned, 1089 patients were married and 888 were unmarried. Further we have bifurcated total strength in six different heads of occupation i.e. Employed (773), Unemployed (185), Students (422), Retired (47), Housewives (412) and others (138).

Out of total 1977 patients who were interviewed, 1144 were newly diagnosed males and 833 were females. They were further categorised in three categories as per the RNTCP recommendations, 914 were pulmonary smear positive, 219 were pulmonary smear negative and 772 were extra-pulmonary. Most of the patients belonged to Category I (1237) rest of 424 belonged to Category II and 316 in Category III. 79.3% (1568) patients had no history of ATT, 81.6% (1613) did not have any TB patients in the family. Almost every patient was given initial motivation.

No stigma at family level was observed in the present study and the family members by large were found supportive to the patients (P<0.5). This

Table 3: The stigma at society level

S.No.			No.	Percentage	Significance
1.	Number of interviewed patients belonged				
	1. Upper Class Upper Middle Class		203	10.3	
	2. Lower Middle Class Upper Lower		905	45.8	
	3. Lower		869	43.9	
2.	Number disclosed their disease among Friends – F, Neighbourers - N				
	♦ 1 Upper Class Upper Middle Class	F	120/203	59.1*	Significant Z= 5.97 P<0.05
		N	121/203	59.6	
	♦ 2 Lower Middle Class	F	583/905	64.4	
		N	602/905	66.5	
	♦ 3 Upper Lower Class	F	688/869	76.8*	
		N	666/869	76.6	
3.	Patients disclosed their disease at society level.				Significant P<0.05
	• Yes • No		788 1189	39.9 60.1	
4.	Number disclosed their disease among				Significant Z=8.5 P<0.05 Significant Z=7.0 P<0.05
	Male	Friends	876/1144	76.5	
		Colleagues	869/1144	75.9	
	Female	Friends	495/833	59.4*	
		Colleagues	520/833	64.4**	
5.	Number of patients who have been invited for social ceremonies after disclosure of their disease				
	Male	Friends	534/876	60.9*	
		Colleagues	524/869	60.2**	No Stigma
	Female	Friends	338/495	68.2*	
		Colleagues	338/520	63.7**	No Stigma

♦ *Classification based on Socio economic criterion of Kuppuswamy's socio-economic status scale modified for 2007.*

could have been the result of efficiently running DOTS programme in the area for over 10 years. Sharing of information with family however was significantly less among female patients (P<0.5) as compared to males.

At the work level also, the study did not find any significant stigma with 80.8% having disclosed their disease to their colleagues and 77.9% to their employers. However when analysed according to sex, less female patients shared their disease with colleagues as well as their employers as compared to males and this was found significant statistically (Z=3.93, P<0.5 and Z=4.6, P<0.5). Patients were allowed by their employees to attend the chest clinic for treatment and 93% were continuing the same jobs and continuing treatment.

There was an immense stigma observed at society level with 60% of the patients hiding their disease (P<0.5) from the friends or neighbours and this was found to have statistically significant difference with more stigma among middle and upper middle class when compared to lower middle class and lower class. Moreover the stigma was observed to be more among females (P<0.5).

DISCUSSION

The consequences of stigma can be seen affecting care-seeking behaviours, as patients have been known to hesitate or choose not to disclose their TB status to family or friends out of fear of being socially avoided. Stigma has also been shown to hinder adherence to treatment. Research has demonstrated that in some cases personal rejection occurs as a result of the strong stigma surrounding TB. Understanding patient's perception about tuberculosis will enable better design of a client-oriented comprehensive programme for tuberculosis[5]. By identifying both the sources and consequences of stigma, social science research has illustrated the need for effective intervention strategies[6].

Stigma in tuberculosis patients is usually of two types[7] – one i.e. a fear of the patient about other's behaviour to him and a sense of inferiority due to development of tuberculosis i.e. **perceived stigma**; and other due to actual discrimination or being actually avoided by the people since the patient has now tuberculosis i.e. **enacted stigma**. Patient often tries to hide his/her disease from others due to stigma resulting in further delay in diagnosis and treatment and thus increase chances of transmission to healthy community.

In a study by K. Jaggarajamma[2] *et al*, among both male and female TB patients enrolled under Revised National TB Control Programme, perceived stigma was more than enacted stigma in the context of personal, family, community and work place interactions. One third of the TB patients were reluctant to attend social functions due to their illness. About 10-25% of the patients experienced negative reactions from the family members. Problems related to marriage prospects were expressed by 63% of unmarried patients from this study. Uplekar *et al*[8] also reported that parents of the young women don't want to reveal their daughter's illness or don't want to send them to DOTS due to difficulties that may arise in marrying them. However the present study did not substantiate this. Compared to the study by Jaggarajamma *et al*[7], the present study revealed more supportive attitudes of the family for the patients & more tolerance by the colleagues at the work place. But at society level 60% of patients preferred to hide their disease (P<0.5) from friends & neighbours & this stigma at society level was observed to be significantly higher among females and also among high middle and upper class. However, it may be mentioned here that the number of patients in their study was 350 and only 79% (276) of the patient included could be interviewed whereas in the present study 1977 (i.e. 93.1%) could be interviewed.

Though the RNTCP has improved the stigma situation regarding tuberculosis, but still enough needs to be done to change the mind set of the patients and the society. Reducing stigma about TB can only break the barrier of having undisclosed TB patients who keep on spreading the disease. Once stigma is removed, these patients will volunteer themselves at the TB Centre for DOTS treatment and once effective treatment is started these patients

will turn non-infectious within two weeks of start of DOTS therapy. Fear of infection had been identified as the main reason for the stigmatization attitudes and behaviour of both health professionals and community members towards those with TB. A study conducted in Ghana[9] found that the activities of health professionals could be a basis of stigmatization of those suffering from TB in society. The use of isolation wards by most hospitals, and the observation that some doctors and nurses use mask and gloves when dealing with TB patients can lead to stigmatization of TB in the eyes of the community members. Besides, the humiliating attitudes and behaviour of health professionals and open avoidance of TB patients could send a message to the community members that TB is a shameful disease.

Another study was conducted in Thailand[10] to assess social stigma, knowledge and belief about TB/HIV co-infected patients. Out of 769 enrolled, 500 (65%) reported high TB stigma, 177 (23%) low TB knowledge and 379 (49%) low HIV knowledge. Patients with low TB knowledge were more likely to have severe TB disease.

DOTS programme has been in operation in Delhi since 1997 and total coverage had been achieved in March 2006 and a desirable change in the stigma against TB has been felt. Macq Jean *et al* from rural Nicaragua[11] also demonstrated that perceived stigma among TB patients is significantly reduced when a package of interventions including TB clubs, patient's centered home visits is successfully implemented.

To conclude, the study has demonstrated that despite the excellent performance of Revised National TB Control Programme for over more than a decade in Delhi and the excellent results of success rates over 82% and case detection of over 70%, the stigma in TB still remains a problem and we need to supplement our efforts in Advocacy, Communication and Social Mobilization for reducing the stigma problem among TB patients which will pay dividends towards effective TB control and to achieve millennium development goal.

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11 Macq J, Soils A, Martinez G, Martiny P. Tackling tuberculosis patients internalized social stigma through patients' centered care: An intervention study in rural Nicaragua. *BMC Public Health* 2008; **8**: 154.

Original article

EVALUATION OF THE DIAGNOSTIC YIELD AND SAFETY OF CLOSED PLEURAL BIOPSY IN THE DIAGNOSIS OF PLEURAL EFFUSION

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Summary

Aim: To assess the diagnostic yield and safety of closed pleural biopsy in patients with pleural effusion.

Methods: In all, 48 consecutive cases of pleural effusion were evaluated with complete pleural fluid biochemical and microbiological analysis, cytology, routine bacterial and mycobacterial cultures. In all these 48 cases of pleural effusion closed pleural biopsy was done with tru-cut biopsy needle and biopsy samples were sent for histopathology and mycobacterial culture.

Results: Out of 48 cases, main causes of pleural effusion were Tuberculosis in 21(43.8%) cases, Malignancy in 14(29.2%) cases, paramalignant effusion in six (12.5%) cases, Empyema in three (6.3%) cases, transudative effusion in three (6.3%) cases and parapneumonic effusion in one (1.9%) case. Diagnostic yield of closed pleural biopsy was 62.2% in cases of all exudative pleural effusion, 76.2% in cases of tubercular pleural effusion and 85.7% in cases of malignant pleural effusion. There was no incidence of post pleural biopsy pneumothorax or hemothorax, underlining the safety of pleural biopsy procedure.

Conclusion: Closed pleural biopsy provides the highest diagnostic yield in cases of pleural tuberculosis and malignancy, the two most important causes of exudative pleural effusion. In view of low cost, easy availability and very low complication rates, it is a very important diagnostic tool in the hands of a trained pulmonary physician in India. **[*Indian J Tuberc 2010; 57:19-24*]**

***Key words*:** Closed pleural biopsy, Pleural effusion

INTRODUCTION

Pleural effusion is one of most common problems, with which a patient presents to the pulmonary physician. Most common causes of pleural effusion in India are tuberculosis, parapneumonic effusion, malignancy, congestive heart failure, renal failure, connective tissue disorders and pulmonary embolism. To find out the cause of pleural effusion, thoracocentesis and biochemical and microbiological analysis of pleural fluid is a common practice. It broadly differentiates exudates from transudates and provides the diagnostic evidence for para-pneumonic effusion. However, this initial analysis has low sensitivity to detect tuberculosis and malignancy, the two most important causes of pleural effusion in India. Pleural biopsy provides diagnostic evidence for both tuberculosis and malignancy[1,2]. In 1955, De Francis *et al* first described use of closed pleural biopsy in the diagnosis of pleural effusion[3]. Tape *et al* in their paper on procedural skills of practising pulmonologists, reported that 98% of practising pulmonologists in US routinely performed pleural biopsy[4]. Though there is no study available on Indian Pulmonologists, very few pulmonary physicians in India do pleural biopsy as a routine procedure in the diagnostic work up of pleural effusion.

AIM

This study was planned to study the diagnostic yield and safety of blind pleural biopsy (Closed pleural biopsy) in the evaluation of pleural effusion.

MATERIAL AND METHODS

The study was conducted at Christian Medical College Hospital, Vellore (Tamil Nadu) a

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tertiary care super-speciality teaching hospital. All consecutive patients with pleural effusion attending Pulmonary Medicine OPD over a period of six months and who signed informed consent, were included in the study. Under local anesthesia, an expert Pulmonologist did the Thoracocentesis and closed pleural biopsy. Five to six pieces of parietal pleura were obtained with true cut biopsy needle (Fig. 1). Post procedure, patients were kept under close monitoring of vital signs for six hours. Pleural fluid was sent for complete biochemical, microbiological analysis and cytology. Both pleural fluid and pleural biopsy specimens were sent for AFB smear and culture for mycobacteria. Pleural biopsy specimens were sent for histopathological examination. Adverse events related to the procedure were recorded.

All data was collected and analyzed with SPSS 11 software.

RESULTS

A total of consecutive 48 cases of pleural effusion, were included in the study. Most of the effusion were exudates (45 (93.7%) cases). Among 45 exudative pleural effusion, predominant cells in pleural fluid were lymphocytes in 36 (80%) cases (Fig. 2).

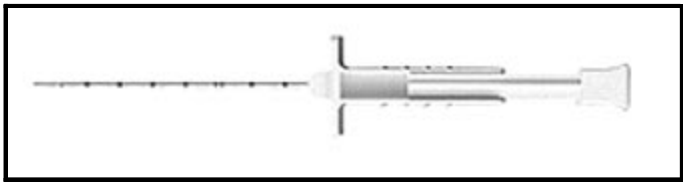

Figure 1: Tru cut biopsy needle used for closed pleural biopsy

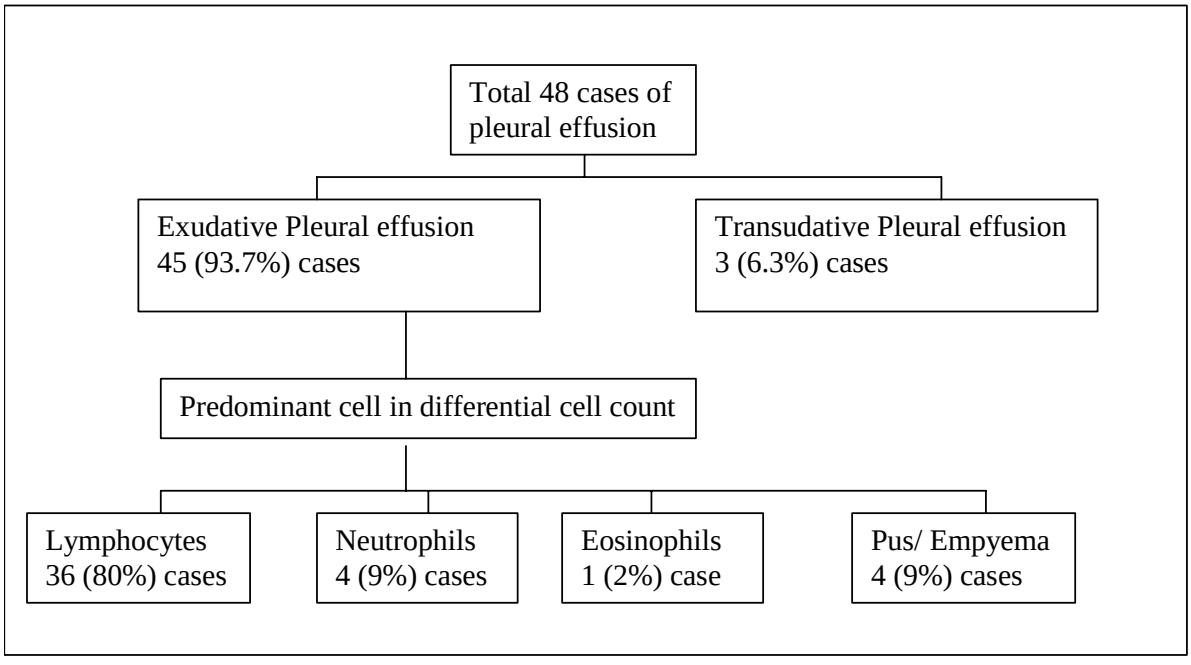

Figure 2: Distribution of total 48 cases according to type of pleural effusion.

Most common diagnosis was tubercular pleural effusion (43.8%), followed by malignancy (29.2%) (Table 1).

All 21 cases (43.8%) of tubercular pleural effusion were exudates. Yield of closed pleural biopsy was 76% in cases of tuberculosis (Table 2). In 14 (66.7%) cases of tubercular pleural effusion, pleural biopsy was the only diagnostic test.

Pleural fluid culture did not grow mycobacterium in any case. In only two cases of tubercular pleural effusion, pleural biopsy culture grew mycobacterium, but in both these cases, pleural biopsy histopathology also showed granulomas. However on follow up, all these cases of biopsy proven tubercular pleural effusion improved with Anti TB treatment.

In three cases of tubercular pleural effusion, there was no evidence of tuberculosis in the pleural fluid and pleural biopsy samples. Out of these three cases, one case was sputum smear positive for AFB and remaining two cases were tuberculin skin test positive and improved with empirical Anti- tubercular therapy (Table 2).

Distribution of cases of malignant pleural effusion is given in Table 3. Diagnostic yield of pleural fluid cytology and pleural biopsy was 50 and 86% respectively (Table 4). Pleural fluid cytology alone was diagnostic of malignancy in only two

Table 1: Final diagnosis of 48 cases of Pleural effusion

Final diagnosis	Number (%) of cases of pleural effusion
Tuberculosis	21 (43.8%)
Malignant pleural effusion	14 (29.2%)
Paramalignant effusions	6 (12.5%)
Pyogenic Empyema	3 (6.2%)
Parapneumonic effusion	1 (2.1)
Transudates	3 (6.2%)
Total cases	48 (100)

Table 2: Diagnostic yield of various procedures in 21 cases of tubercular pleural effusion

Diagnostic test	Number of cases (%)
Pleural biopsy showed granuloma	16 (76.1%)
Pleural fluid smear positive for AFB	1 (4.8%)
Sputum smear positive for AFB	1 (4.8%)
Lung biopsy showed granuloma	1 (4.8%)
Improvement with Empirical ATT	2 (9.5%)
Total	21 (100%)

Table 3: Final diagnosis of 14 cases of Malignant pleural effusion

Type of Malignancy	Number of cases (%)
Bronchogenic carcinoma	4(28.6%)
Mesothelioma	2 (14.3%)
Papillary carcinoma	1 (7.1%)
Malignant effusion with unknown primary	5 (35.7%)
Lymphoma	2 (14.3%)
Total cases	14 (100%)

Table 4: Diagnostic yield of various procedures in 14 cases of Malignant pleural effusion

Diagnostic test	Number of cases (%)
Pleural biopsy showed Malignancy	12 (86%)
Pleural fluid Cytology positive for malignant cells	7 (50%)

(14.3%) cases, while pleural biopsy alone was diagnostic of malignancy in seven (50%) cases.

There were no serious adverse events with any of the thoracocentesis and pleural biopsy procedure. Few patients complained of mild transient chest pain at biopsy site, which subsided with analgesics.

DISCUSSION

Pleural effusion is one of the most common problems with which patients come to the Pulmonary Physician. In the diagnostic work up of pleural effusion, biochemical and microbiological analysis can provide the diagnosis in all cases of empyema, parapneumonic effusion and transudative effusion. In our study also, all seven cases of pyogenic empyema (three cases), transudative pleural effusion (three cases) and parapneumonic effusion (one case) were identified by biochemical and microbiological analysis. But in cases of empyema also, tuberculosis needs to be ruled out with the help of smear, culture and pleural biopsy.

In this study, one case of tubercular Empyema was diagnosed only with the help of pleural biopsy showing necrotizing granulomas, as all pleural fluid and pleural biopsy smears for AFB and mycobacterial cultures were negative.

Tuberculosis and malignant pleural effusion are first two most important causes of pleural effusion with which a patient presents to a tertiary care hospital. In cases of tubercular pleural effusion, pleural fluid AFB smear is found positive in zero to 20 % cases.[5,6] Because of which it cannot be used to diagnose all the cases of tubercular pleural effusion. In our study, out of 48 patients, only one patient had pleural fluid smear positive for AFB.

Pleural fluid mycobacterial culture is found positive in only up to 30% cases of tubercular pleural effusion[5]. Mycobacterial culture with LJ media also take six to eight weeks to confirm the diagnosis. Rapid culture media like BACTAC and MGIT are costly and not available everywhere.

In our study, Pleural fluid culture did not show growth of *Mycobacterium tuberculosis*. In any case, though pleural biopsy culture grew Mycobacterium in two cases (9.5%) of tubercular pleural effusion, reflecting the very poor sensitivity of this time consuming test in diagnosing tubercular pleural effusion[7]. Moreover, in both these cases, pleural biopsy showed necrotizing granulomas and yielded the diagnosis within three days.

According to various studies, diagnostic yield of pleural biopsy in all cases of pleural effusion is about 60 to 80%[8,9]. In our study, diagnostic yield of pleural biopsy in all cases of exudative pleural effusion was 62.2%. One of the reasons of this low diagnostic yield in our study was that in all the cases, pleural biopsy was done only once. While our experience and available literature show that repeat pleural biopsy increases the diagnostic yield of pleural biopsy up to 89 to 100%[9-11].

According to various studies, diagnostic yield of closed pleural biopsy in tubercular pleural effusion ranges from 60 to 95%[12]. In one of the largest reviews of over 2500 pleural biopsies, Tomolson *et al* reported a diagnostic yield of 75% for Pleural tuberculosis[13]. In an Indian study, Christopher *et al* reported that the diagnostic yield of pleural biopsy was 75% for pleural tuberculosis[1]. In our study, closed pleural biopsy yielded the diagnosis in 76.2% cases of tubercular pleural effusion, and in 66.7% cases, pleural biopsy was the only diagnostic test. This 76.2% yield was with single pleural biopsy. In an Indian study on role of serial pleural biopsies in the diagnosis of pleural effusion, J. C. Suri *et al* showed that in case of tubercular pleural effusion, three serial pleural biopsies increase the yield from 60% to 93%[9].

Though Pleural fluid ADA and Interferon Gamma levels are good indirect markers to diagnose pleural tuberculosis, but in India, further studies are still required to standardize the cut off values of these tests. High cost and less availability of IFN gamma assay are other problems.

This study shows that pleural biopsy is a very important instrument in the diagnostic

armament of pulmonary physician to diagnose pleural tuberculosis effectively and quickly. Missing the diagnosis and opportunity to treat pleural tuberculosis may lead to pulmonary and extrapulmonary involvement in up to 65% of cases over subsequent five years[14].

In cases of malignant pleural effusion, literature review shows that the diagnostic yield of pleural biopsy is less than the pleural cytology. Pleural cytology diagnostic yield in malignant pleural effusion ranges from 40 to 87 %[9,15]. Loddenkemper *et al* reported a diagnostic yield of 44% for closed pleural biopsy and 62% for pleural fluid cytology in cases of malignant pleural effusion[16]. Tomilson *et al* in their review of more than 2500 pleural biopsy reported a diagnostic yield of 57% for pleural biopsy in cases of malignant pleural effusion[13]. In an Indian study, Christopher *et al* reported that the diagnostic yield of pleural biopsy was 71% for pleural malignancy.[1] In our study, diagnostic yield of pleural cytology and pleural biopsy was 50% and 85.7% respectively in the cases of malignant pleural effusion. Pleural biopsy was the only diagnostic test in 50% cases of malignant pleural effusion.

One reason for only 50% diagnostic yield of pleural fluid cytology in malignant pleural effusion in our study can be submission of only one pleural fluid sample for cytology. Repeated submission of pleural fluid sample for cytology examination increases the diagnostic yield[17]. Another reason for high sensitivity of pleural fluid cytology in western countries can be availability of good pulmonary cytologist services, which is still awaited in India.

However, a high diagnostic yield of pleural biopsy (85.7%) in malignant pleural effusion in this study further underlines the profound utility of this procedure in the diagnostic workup of pleural effusion in India.

Another advantage of pleural biopsy over pleural fluid cytology is that pleural fluid cytology sometimes fails to subclassify the malignant cell types, which is essential for further management of chemosensitive malignancies.

Thoracoscopy provides a direct visualization of parietal and visceral pleura, and thus the diagnostic yield of thoracoscopic guided pleural biopsy increases up to 95 %[16,18]. But it involves a high instrument cost and intenstive training, which makes it a rare entity in India. Thoracoscopic procedure also requires chest tube drainage, which further increases the hospital stay as well as the health care cost. In comparison to thoracoscopy, closed pleural biopsy can be done as a day care procedure and does not require chest tube placement and cost (Rs.600/true cut biopsy needle) is nothing in comparison to cost of thoracoscope and thoracoscopic guided biopsy.

So closed pleural biopsy should be offered to all the patients with exudative pleural effusion and thoracoscopic procedures should be reserved for cases of undiagnosed pleural effusion and for talc pleurodesis.

Pneumothorax and hemothorax are known complications of closed pleural biopsy. Various studies show about 4 to 11 % incidence rate of pneumothorax because of pleural biopsy[8,19]. But there was not a single incident of pneumothorax or hemothorax in our study, underlining the safety of this procedure.

Limitation of this study was that only 48 cases of pleural effusion were studied. But this was an initial study and its results are quite promising. A bigger study has been planned and data is being collected.

CONCLUSION

In the diagnostic work up of pleural effusion, closed pleural biopsy provides a very high diagnostic yield in the diagnosis of pleural tuberculosis and malignancy, the two most important causes of exudative pleural effusion. In view of low cost, easy availability and very low complication rates, closed pleural biopsy is a very important diagnostic tool in the hands of a trained pulmonary physician in India.

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TUBERCULOSIS SEAL CAMPAIGN - UTTARAKHAND

Tuberculosis Association of Uttarakhand, the newly formed State TB Association affiliated to the Tuberculosis Association of India, organized a function on 2nd October, 2009 on the occasion of the inauguration of the 60th TB Seal Campaign. The function was held in Jilla Panchayat Sabhagar Hotel Gaurav, Dehradun and inaugurated by former Chief Minister of Uttarakhand Rt. Maj Gen Shri B.C. Khanduri. The function was attended by about 200 persons.

The function had very good coverage by the media and they carried out a very good and useful awareness programme about the tuberculosis problem, its prevention, control and treatment.

Original Article

CLINICAL PROFILE OF PATIENTS HAVING SPLENIC INVOLVEMENT IN TUBERCULOSIS

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Summary

Background: Tuberculosis of spleen is very rare, usually seen in disseminated or miliary form of the disease and in patients having HIV infection. Splenic tuberculosis is currently described poorly in available literature.

Objectives: In this series, we analyzed the clinical profile of patients having splenic involvement in tuberculosis.

Methods: Patients of tuberculosis (pulmonary and/or extra-pulmonary) with abnormal splenic parenchymal lesion on ultrasound were scanned in the light of demographic, clinical, radiological features, response to treatment and co-morbid illnesses. In selected eligible cases, CT scan abdomen and ultrasound guided FNAC of spelnic lesion was also done.

Results: Most of the patients (62%) were in the age group of 25-50 years with male/female ratio of 3:1. Constitutional symptoms such as fever (75%), anorexia (50%), and weight loss (10%) were common presentations apart from other symptoms such as pain abdomen (62%) and distention (12%). Half of these patients also had HIV infection. 62% patients had associated pulmonary tuberculosis. Other body sites involved were ascites (50%), intraabdominal lymph nodes (37%), pleural effusion (37%), cervical lymph nodes (12%), intestine (12.5%), etc. Ultrasonographic findings were multiple splenic abscess (62%), multiple diffuse, hypo-echoic foci (25%), solitary abscess and calcified granuloma (6%). About 44% patients became asymptomatic after receiving Category I treatment under RNTCP with complete clearance of initial sonographic abnormality in splenic parenchyma.

Conclusion: The splenic involvement in tuberculosis seems to be more frequent in patients with HIV infection and in disseminated form of disease. Ultrasonography of the spleen is simple, easily available, affordable, non-invasive, imaging technique highly useful for the diagnosis of splenic involvement in tuberculosis. The sonographic findings should be correlated with overall clinical presentation with demonstration of tuberculosis at other body sites and image guided FNAC may be considered in cases with isolated splenic involvement. ***[Indian J Tuberc 2010; 57:25-30]***

Key words: Spleen, Tuberculosis, HIV infection, USG abdomen, Splenic abscess

INTRODUCTION

Tuberculosis continues to be a major health problem despite recent advances in its diagnosis and management. There are diverse manifestations of this disease with increasing trend of presentation as extra-pulmonary tuberculosis in the era of HIV infection[1]. Among the extra pulmonary tuberculosis, splenic tuberculosis is exceptionally rare and poorly described in the available literature[2].

Splenic tuberculosis is an important manifestation of tuberculosis and should always be included in differential diagnosis of patients presenting with pyrexia of unknown origin[3]. The splenic involvement is more common in patients with disseminated tuberculosis, however, there are reports of isolated splenic involvement also[4].

Most of the reports on splenic involvement in tuberculosis are in the form of single case report or small case series and only few reports[5] have described the specific clinico-radiological manifestations of this disease. This series on splenic involvement in tuberculosis analyzes clinico-radiological manifestations of this form of disease from the western part of our country for the first time.

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MATERIAL AND METHODS

This study retrospectively analyzes clinical record of patients having splenic involvement in tuberculosis attending our institute during last four years. The diagnosis of tuberculosis was established by demonstration of *Mycobacterium tuberculosis* on smear and/or culture in clinical specimens or histological demonstration of caseating granulomas/ acid-fast bacilli (AFB) in tissue specimens and with highly suggestive clinico-radiological features of tuberculosis with response to anti-tuberculosis drugs.

The clinical record reviewed included age and sex of patients with duration of illness and clinical symptoms with special attention on abdominal symptoms and presence or absence of co-morbid illnesses. We also analyzed the other body parts involved in patients having splenic tuberculosis. The ultrasonography images of all these patients were reviewed with radiological description of the lesion. HIV status of these patients was also noted. In selected patients, CT scan of abdomen and

Table 1: Demographic and Clinical Characteristics of Patients having Splenic Tuberculosis (n=16)

Characteristics		No. of Patients	Percentage
Age	< 25 years	6	37.5%
	26 – 50 years	10	62.5%
Sex	Male	12	75%
	Female	4	25%
Duration of illness	1-3 months	9	56.3%
	3-6 months	6	37.5%
	> 6 months	1	6.3%
Constutional symptoms	▪ Fever	12	75%
	▪ Anorexia	8	50%
	▪ Weight loss	8	50%
	▪ NIL	2	12.5%
Abdominal symptoms	▪ Pain	10	62.5%
	▪ Distension	2	12.5%
	▪ NIL	6	37.5%
Cornorbid illness	▪ HIV infection	8	50%
	▪ Myelodysplastic syndrome	1	6.3%
	▪ Diabetes mellitus	-	
	▪ Hepatic / Renal dysfunction	-	
	▪ None	7	43.8%

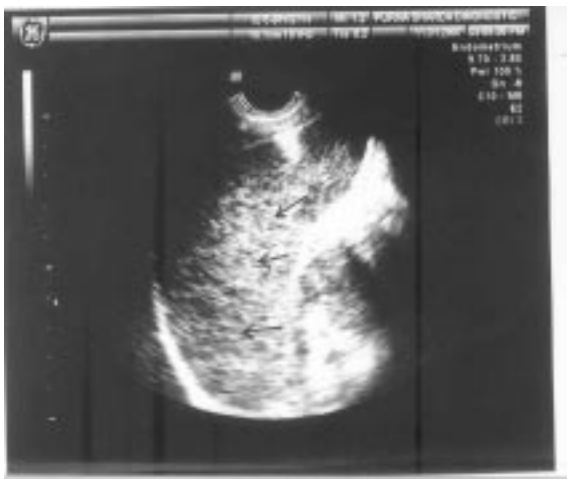

Fig. 1: USG spleen showing diffuse multiple ill defined hype echoic lesions, suggestive of granulomatous disease

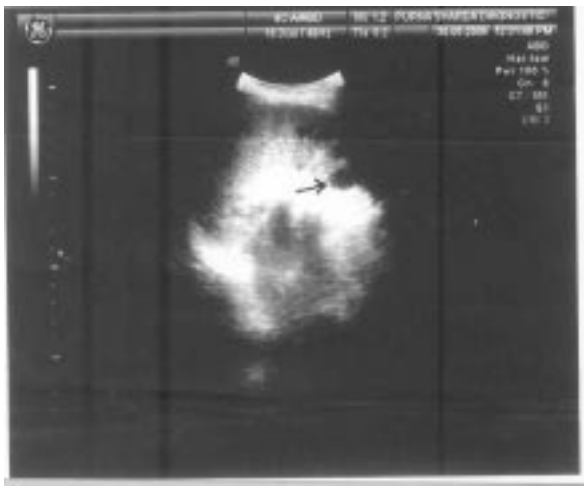

Fig. 2: USG spleen showing well defined intraparenchymal splenic abscesses

ultrasonography guided FNAC of splenic lesion was done and respective reports were analyzed. Patients having portal hypertension, chronic liver disease, hematological and other malignancies or any other long standing infection (Kala Azar, infiltrative disorder, etc.) were excluded from final analysis.

RESULTS

During 2005 to 2008, 9205 patients of tuberculosis were diagnosed and in only 16 (0.01%) patients we found splenic involvement in tuberculosis. Demographic and clinical profile of these patients is summarized in Table 1.

Table 2: Sites of Tuberculosis other than Spleen

Site of Tuberculosis	No. of Patients	Percentage
Pulmonary	10	62.5%
Ascites	8	50.0%
Pleural	6	37.5%
Abdominal lymph nodes	6	37.5%
Cervical lymph nodes	2	12.5%
Intestinal	2	12.5%
Pericardial effusion	1	6.3%

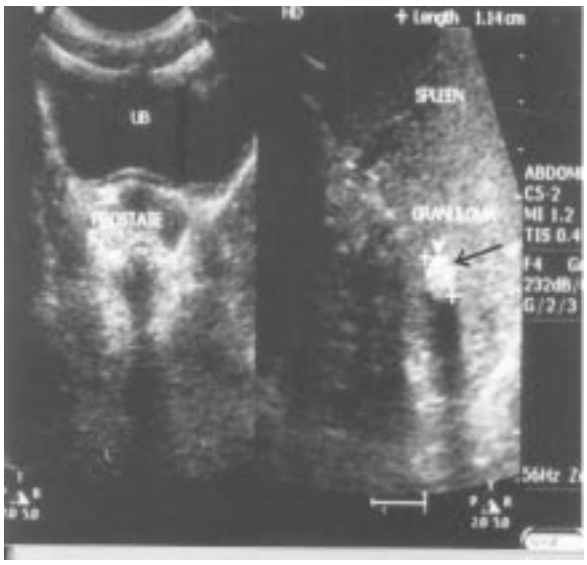

Fig. 3: USG spleen showing intraparenchymal calcified granuloma in spleen

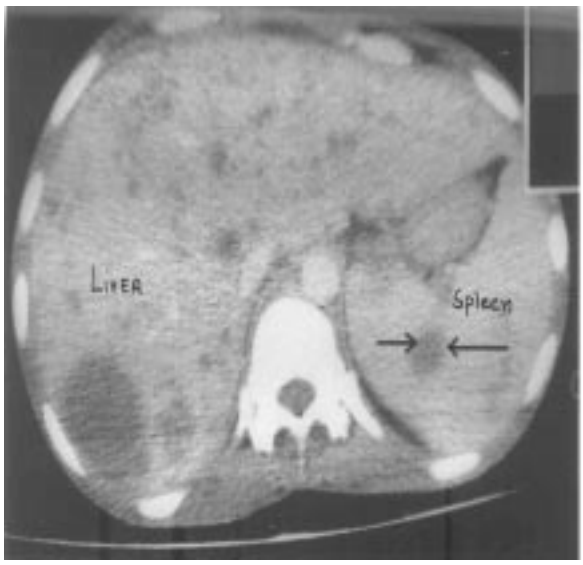

Fig. 4: CT scan abdoman showing hypo-dense areas in spleen and liver

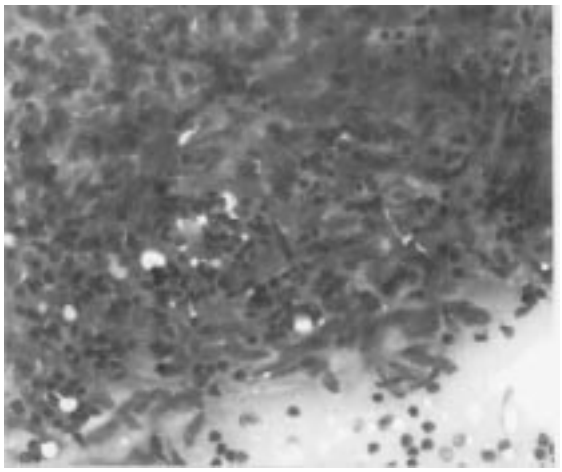

Fig. 5: Photomicrograph of FNAC from splenic lesion showing cluster of epithelioid cells, lymphocytes and macrophages with area of caseous necrosis suggestive of tuberculous etiology (H &E x 400)

Most of the patients (62%) were in the age group of 26-50 years. The males were three times more commonly affected than females. About half of the patients had short duration of clinical illness varying from one to three months. 75% of the patients had fever as a presenting symptom followed by anorexia and weight loss in 50% cases. Pain abdomen was the major abdominal symptom seen in 62% cases followed by abdominal distension in 12% cases. Among co-morbid illnesses, HIV infection was seen in 50% cases and one case had myelodysplastic syndrome.

The pulmonary tuberculosis was associated in 62% cases. The other extra pulmonary sites affected in patients with splenic tuberculosis were abdominal lymph nodes in 37%, ascites in 50%, pleural effusion in 37%, intestinal involvement and cervical lymph nodes in 12% cases each. In one case, there was associated pericardial effusion. Ultrasound abdomen detected various patterns of splenic involvement in tuberculosis. The commonest was multiple well-defined splenic abscesses in 62%, followed by multiple diffuse ill-defined hypo echoic foci in 25%, solitary abscess and calcified granuloma in 6% cases each (Figs. 1, 2 and 3). CT scan study of abdomen also showed hypo dense areas in splenic parenchyma with few cystic lesions (Fig. 4). In three patients, USG guided FNAC of splenic lesion was also done and caseating granulomatous lesion was detected in two cases while AFB in one case (Fig. 5).

All patients received anti-tuberculosis treatment with Category I regimen under RNTCP.

Ten patients completed the six months' treatment, of whom seven patients turned asymptomatic with resolution of sonographic abnormality and in three patients re-treatment regimen (Category II) was initiated in view of persistent symptoms and sonographic lesions in spleen. Four patients died during treatment due to extensive disease and concurrent illness (three HIV-seropositive and one myelodysplastic syndrome) while two patients were lost to follow up.

DISCUSSION

Tuberculous involvement of spleen is very rare, especially in immunocompetent host and usually seen in disseminated or miliary form of the disease and in patients infected with HIV[6,7].

Splenic tuberculosis commonly manifests as fever, left upper quadrant abdominal pain, weight loss, diarrhoea and sometimes with ascitis[8]. Since splenic involvement is much more common in patients with disseminated tuberculosis, the clinical presentation may overlap with other symptoms according to other sites of involvement. Very rarely, splenic involvement is totally asymptomatic[9]. In the present series, patients presented predominantly with constitutional and abdominal symptoms. However, in 37% cases, there were no abdominal symptoms despite sonographic demonstration of splenic lesion. A predominant constitutional symptom at presentation was also observed by Sharma *et al*[5] in a combined 23 patient case series from Delhi and Trupati. Presentation with weight loss and fever with no pain abdomen was also noted by Ho PL *et al*[10]. Diagnosis of isolated splenic tuberculosis is therefore difficult and often delayed because of vague clinical manifestations.

Most of the reported cases of splenic tuberculosis were found to have underlying HIV infection also[11]. Splenic involvement was initially thought to be seen only in the immuno-compromised stage. However, there are sporadic reports of splenic tuberculosis mainly in the form of splenic abscess, in immunocompetent host also[12]. In the present series, half of the patients had underlying HIV infection. On the other hand, Sharma *et al*[5] observed HIV infection in only two among 23 cases (8%) of splenic tuberculosis. Adil *et al*[13] reported a series of ten individuals with splenic tuberculosis but did not found HIV infection in any of them. Valencia ME *et al*[7] specifically analyzed 23 patients with tuberculosis and splenic abscess with HIV infection and found multi-drug resistant tuberculosis in 60% cases, suggesting serious form of the illness.

Involvement of spleen in tuberculosis usually occurs in miliary or disseminated form of the disease; however, spleen may also be involved as an isolated organ. Patients may have solitary tuberculosis or multiple tubercular abscesses. Splenic abscess is comparatively a common stage than the solitary or nodular stage, when patients seek medical advice. On sonography, splenic lesion commonly presents as multiple regular hypo-echoic nodule representing tuberculoma and sometimes irregular hypo-echoic lesion representing splenic abscess, especially in presence of HIV infection[14]. These findings were similarly observed in this cohort also, where most of the patients were HIV positive having splenic abscess as predominant sonographic findings. On Sonography, multiple hypo-echoic intrasplenic lesions may also be seen in other conditions including myeloproliferative disorder such as leukemia, lymphoma, Hodgkin's disease and metastasis[15]. Similar sonographic pattern is also being reported in AIDS related lymphomatous involvement of spleen[16]. However, the diagnosis may be confirmed by FNAC performed under sonographic guidance and in the presence of evidence of tuberculosis at other body sites in the same patient. This practice was followed in our case series.

Anti-tuberculosis treatment is the mainstay of the therapy for splenic involvement in tuberculosis and splenctomy is rarely required[17]. In this series also, most patients responded by short course anti-tuberculosis chemotherapy. However, the outcome is also influenced by the co-morbid illnesses and the extent of the disease process.

It is concluded that high degree of suspicion should be observed for splenic

involvement in tuberculosis cases, because of vague clinical manifestations. We could not find any specific symptoms that can be attributed to splenic tuberculosis; however, presence of tuberculosis (pulmonary and/or extra pulmonary) with fever, pain abdomen and abnormal splenic parenchymal lesion on ultrasound abdomen is a strong indication of splenic involvement in tuberculosis, especially in immuno-compromised host. Radiological examination and if possible FNAC should be done for diagnosis in all such cases. With the increasing cases of HIV infection/AIDS, abdominal tuberculosis with splenic involvement is likely to be detected frequently now-a-days. The clinical response of treatment with anti-tuberculosis therapy should be closely observed in view of high incidence of drug resistant tuberculosis in patients having associated HIV infections[7].

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STATUS REPORT ON RNTCP*

RNTCP has continued to achieve the twin objectives of NSP case detection and treatment success rate at the national level during the third quarter, 2009.

RNTCP performance during third quarter 2009

During the quarter, over 1.83 million suspects were examined, 234,282 sputum positive cases were diagnosed, and 390,420 TB cases were registered for treatment. The annualized total case detection rate is 142 cases per 100,000 populations. With a total of 158,002 new smear positive cases being registered for treatment, the new smear positive TB case detection rate (annualized) for the third quarter 2009 is 72%. In addition to this, 97,853 new smear negative cases, 58,751 new extra pulmonary cases, 52,729 smear positive re-treatment cases and 22,703 re-treatment Others' were also registered for treatment in this quarter. The treatment success rate amongst the new smear positive PTB cases registered in the third quarter 2008 is 87% and the sputum conversion rate of patients registered during second quarter 2009 is 89%. The default rates among NSP (5.7%), NSN (6.9%) and re-treatment cases (14%) continue to show the declining trend over the past several quarters.

Major activities during the quarter

Progress in accreditation of Intermediate Reference Laboratories (IRL)

The programme is in the process of establishing a network of about 27 Intermediate Reference Laboratories (IRL), and 16 other labs across the country in a phased manner for diagnosis and follow up of MDR TB patients. The IRLs at Andhra Pradesh, Delhi, Gujarat, Kerala, Maharashtra, Orissa, Rajasthan, Tamil Nadu, and

Population in India covered under DOTS and total tuberculosis patients put on treatent eac uarter

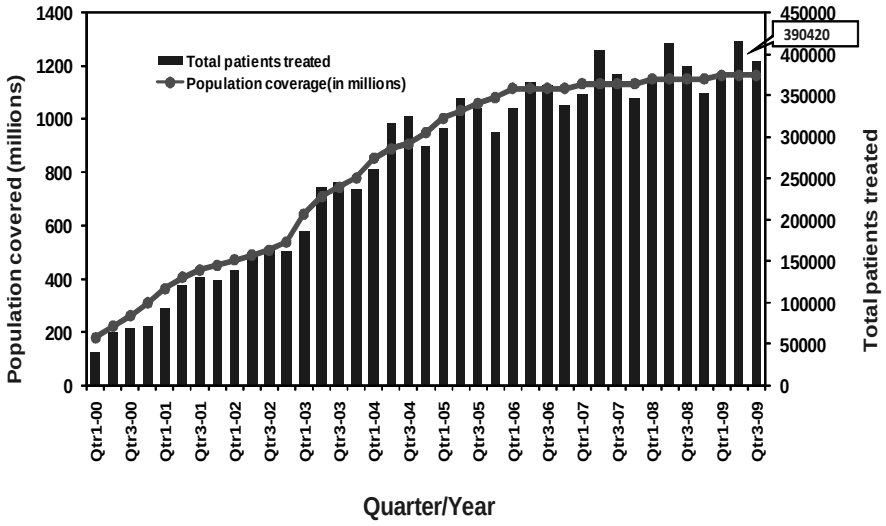

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Table: Performance of RNTCP Case Detection (2009, third quarter), Smear Conversion (2009, second quarter), and Treatment Outcomes (2008, third quarter)

State	Population (in lakh) covered by RNTCP[1]	Suspects examined per lakh population	No of Smear positive patients diagnosed[2]	Total patients registered for treatment[3]	Annualized total case detection rate	New smear positive patients registered for treatment	Annualized new smear positive case detection rate (%)		No of new smear negative cases registered for treatment	No of new EP cases registered for treatment	No. of smear positive re-treatment cases registered for treatment	3 month conversion rate of new smear positive patients	Cure rate of new smear positive patients	Success rate of new smear positive patients
Andaman & Nicobar	4	225	76	170	162	49	47	62%	44	49	22	94%	88%	90%
Andhra Pradesh	830	164	19370	28509	137	12605	61	81%	7157	3070	4251	92%	87%	89%
Arunachal Pradesh	12	260	321	675	222	235	77	103%	169	117	86	89%	88%	88%
Assam	304	126	6046	10287	135	4541	60	80%	2828	1218	976	90%	85%	87%
Bihar	953	98	12388	22516	95	9494	40	53%	7383	1625	1977	88%	82%	90%
Chandigarh	11	347	553	742	273	264	97	102%	105	226	96	94%	87%	87%
Chhatisgarh	240	111	3239	6837	114	2703	45	56%	2535	903	401	89%	82%	88%
D & N Haveli	3	168	69	102	151	37	55	68%	15	25	13	90%	86%	86%
Daman & Diu	2	342	54	81	168	28	58	73%	21	4	9	91%	83%	92%
Delhi	176	235	6230	12596	286	3490	79	83%	2213	3937	1810	88%	87%	87%
Goa	17	189	337	463	111	156	37	47%	85	129	58	92%	87%	87%
Gujarat	572	190	15042	20382	143	8754	61	77%	2657	2752	4564	92%	87%	88%
Haryana	241	166	6361	10132	168	3601	60	63%	2031	1750	2061	90%	85%	86%
Himachal Pradesh	66	256	1995	3503	212	1295	78	82%	611	817	548	93%	88%	90%
Jammu & Kashmir	128	161	1938	3237	101	1454	46	48%	513	741	421	91%	86%	89%
Jharkhand	304	128	5774	10895	143	4670	61	82%	3735	917	756	90%	85%	89%
Karnataka	580	198	10614	16976	117	6737	46	62%	3737	3141	2291	86%	80%	81%
Kerala	346	210	3829	6716	78	2918	34	68%	1440	1504	655	83%	82%	84%
Lakshadweep	1	70	1	9	51	4	23	30%	4	1	0	100%	100%	100%
Madhya Pradesh	705	112	12277	21301	121	7694	44	55%	6884	2510	2869	88%	83%	87%
Maharashtra	1083	156	18354	32872	121	12457	46	58%	7729	5954	3875	90%	83%	85%
Manipur	27	141	385	1124	169	276	42	55%	430	221	86	82%	85%	86%
Meghalaya	26	223	698	1283	200	447	70	93%	264	305	148	87%	85%	86%
Mizoram	10	224	182	612	247	129	52	69%	183	193	47	90%	91%	93%
Nagaland	22	175	449	952	172	339	61	82%	198	202	131	93%	89%	89%
Orissa	403	137	7516	13212	131	5732	57	67%	3337	2386	1100	88%	82%	86%
Puducherry	11	420	599	357	131	172	63	84%	59	77	42	90%	88%	88%
Punjab	269	163	5996	9926	148	3968	59	62%	1807	2003	1678	89%	85%	88%
Rajasthan	657	147	18155	28508	174	10249	62	78%	7752	3691	5671	91%	87%	89%
Sikkim	6	344	169	434	289	121	81	107%	106	116	54	86%	89%	89%
Tamil Nadu	669	221	11125	20560	123	8315	50	66%	5281	4082	2248	90%	85%	86%
Tripura	36	137	489	750	84	381	43	57%	164	123	65	90%	87%	90%
Uttar Pradesh	1944	159	44749	73191	151	31122	64	67%	20385	8903	9713	90%	85%	89%
Uttarakhand	96	197	2744	4083	169	1439	60	63%	998	640	784	88%	81%	85%
West Bengal	889	147	16158	26427	119	12126	55	73%	4993	4419	3223	88%	84%	85%
Grand Total	11641	158	234282	390420	134	158002	54	72%	97853	58751	52729	89%	85%	87%

1 Projected population based on census population of 2001 is used for calculation of case-detection rate. 1 lakh = 100,000 population

2 Smear positive patients diagnosed, include new smear positive cases and smear positive retreatment cases

3 Total patients registered for treatment, include new sputum smear positive cases, new smear negative cases, new extra-pulmonary cases, new others ,relapse,failure,TAD and retreatment others

West Bengal have been accredited. Besides three labs in other sectors, i.e. CMC Vellore, BPRC-Hyderabad and Hinduja Mumbai are also accredited.

Progress in the DOTS- Plus services for MDR TB cases.

DOTS Plus services for management of MDR TB have been rolled out in the states of Gujarat, Maharashtra, Andhra Pradesh, Haryana, Delhi, Kerala, West Bengal, Tamil Nadu and Rajasthan. In this quarter, 330 MDR TB patients have been initiated on DOTS Plus treatment bringing the total number of MDR TB patients on treatment to 969 in these states.

Progress in the involvement of NGOs and PPs

A National review of NTPC project sites was done in August 2009. NTPC is providing ambulance, binocular microscope and laboratory technicians at these sites. At 10 project sites, NTPC is running DMC-cum-DOT centres.

The "Partnership for Tuberculosis Care and Control in India" (the Partnership) brings together civil society across the country on a common platform to support and strengthen India's national TB control efforts. A consultation meeting was held in New Delhi on 30 September 2009 where, besides partners, corporate, media and government representatives participated. The objective of the meeting was to share progress, cross-learning and experience in the Partnership; develop a common understanding and agreement among the key stakeholders like government, international agencies, donors, civil societies, corporate bodies, and media on TB care and control in India, and advocacy towards the government and international donor community for increased investment in the wider TB care and control activities in India, including civil society support to TB care and control activities.

Progress in procurement and drug logistics management

In this quarter, drug logistic management of workshops was organized in the states of West Bengal and Jharkhand for the state and district level staff.

Progress in TB-HIV Collaborative Activities

Implementation of intensified package for TB-HIV in the states of Gujarat and Delhi has been started in this quarter.

Progress in ACSM

Communication material for community level activities for awareness generation and for use by the DOT providers for patient counselling has been finalized by the media agency, and will be available on RNTCP website by next quarter.

Process of hiring of media agency at the national level is in progress. Technical evaluation of the proposal has been done in this quarter.

Case Report

PRIMARY TUBERCULOUS PYOMYOSITIS OF FOREARM MUSCLES

Ramesh Kumar Sen[1], Sujit Kumar Tripathy[2], Sarvdeep Dhatt[3], Raghav Saini[4], Sameer Aggarwal[4] and Amit Agarwal*

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***Summary*:** Tuberculosis involving the soft tissue from adjacent bone or joint is well recognized. However, primary tuberculous pyomyositis is rare. Their atypical presentations in unusual sites lead to delay in diagnosis. We report three cases of primary tubercular pyomyositis of the forearm muscles in immuno-competent patients. The presentation was subacute with a swelling and vague pain over forearm. Their diagnostic dilemma and response to chemotherapy has been discussed in the present literature. A high grade of suspicion is required to diagnose tubercular myositis, particularly in patients presenting with unexplained soft tissue swelling in an endemic area. However if an early diagnosis and treatment is instituted, morbidity is decreased significantly. **[*Indian J Tuberc 2010; 57:*34-40]**

Key words: Tuberculosis, Pyomyositis, Forearm muscles, Soft tissue tuberculosis

INTRODUCTION

Tuberculosis is considered as a 're-emerging disease', because of its resurgence and increased incidence in the twenty-first century particularly in immuno-compromised patients[1-3]. About one-fifth of diagnosed new cases of tuberculosis have an extrapulmonary lesion, of which about one-tenth involve the musculoskeletal system[2]. Tuberculosis of soft tissue without underlying bony pathology is rare and the pathogenesis is still confusing[4,5]. Their unusual presentations in atypical sites lead to delay in diagnosis and treatment in many patients. Tubercular pyomyositis is the least frequent extraspinal musculoskeletal tuberculosis reported in the literature[6]. We report three cases of tubercular pyomyositis of forearm. The unique feature of this article is that tuberculous pyomyositis in all cases is primary and confined to the forearm muscles of immuno-competent individuals.

MATERIAL AND METHODS

Case 1: A 23 year active female patient presented with aching pain and swelling on the lateral aspect of left forearm (Fig. 1A) for six months. She had been treated with nonsteroidal anti-inflammatory drugs and physiotherapy by the local physician. The patient reported with progressive increase in size of the swelling associated with pain and restriction of movement of the elbow joint. She had loss of appetite and evening rise of temperature in preceding four weeks and had no other systemic complaints. The swelling was soft, nonmobile, nonpulsatile and mild tender with range of elbow joint movement possible from 0 to 90 degree of flexion. Laboratory data revealed normal blood parameters except a raised erythrocyte sedimentation rate (ESR=50 mm/hr). Radiograph of local part did not show any pathology in the bone. Magnetic Resonance Imaging revealed well-defined oval heterogenous T1W isointense to subtle hypointense and T2W hyperintense space occupying lesion of size 5.33 x 3.38 x 2.21 cms at ventro-lateral aspect of proximal forearm in intramuscular location involving the belly of Brachioradialis muscle with associated diffuse muscle edema (Fig. 1B and 1C). It was suggestive of an inflammatory / neoplastic pathology. On aspiration with a needle frank pus came out, but no organisms were isolated from the culture. Gram stain and AFB (Acid Fast Bacilli) stain

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were negative. Further investigations were carried out for tuberculosis. Chest X-ray and sputum test were normal. Tuberculin test showed induration of 15 x 12 mms. It was suspected to be an acute myofascial infection (pyomyositis) and decided to proceed for incision and drainage. Brachioradialis muscle was found to be thickened, oedematous and on probing with a stab knife, gush of pus came out (Fig. 1D). All the dead, necrosed muscles were debrided and purulent material were drained out. The material was sent for biopsy, culture sensitivity, gram stain and AFB stain. The wound was closed with two drainage tubes and was attached to a negative suction. Biopsy revealed it to be a chronic granulomatous lesion with epitheloid cells and multinucleated giant cells. Though AFB stain was negative, MTB DNA (*Mycobacterium tuberculosis* DNA) quantitative assay by polymerase chain reaction (PCR) was positive at 2,500,000 copies/ml. Culture media could not isolate any organism. No primary focus of tuberculosis was identified after thorough systemic and laboratory investigations. The patient was put on multidrug

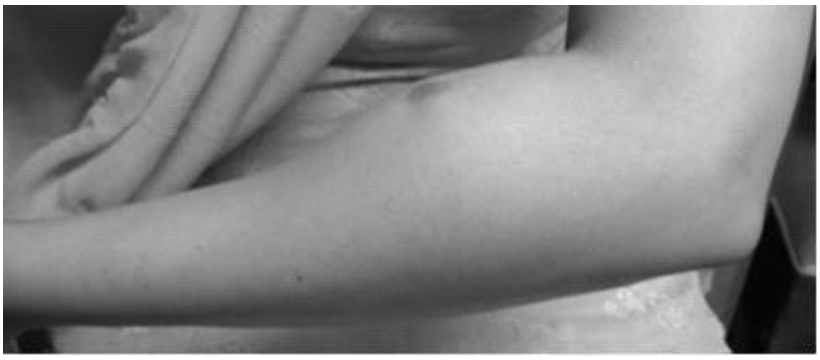

Fig.1A: Lateral aspect of left proximal forearm showing a soft tissue swelling of size 10 x 5 cms (case 1)

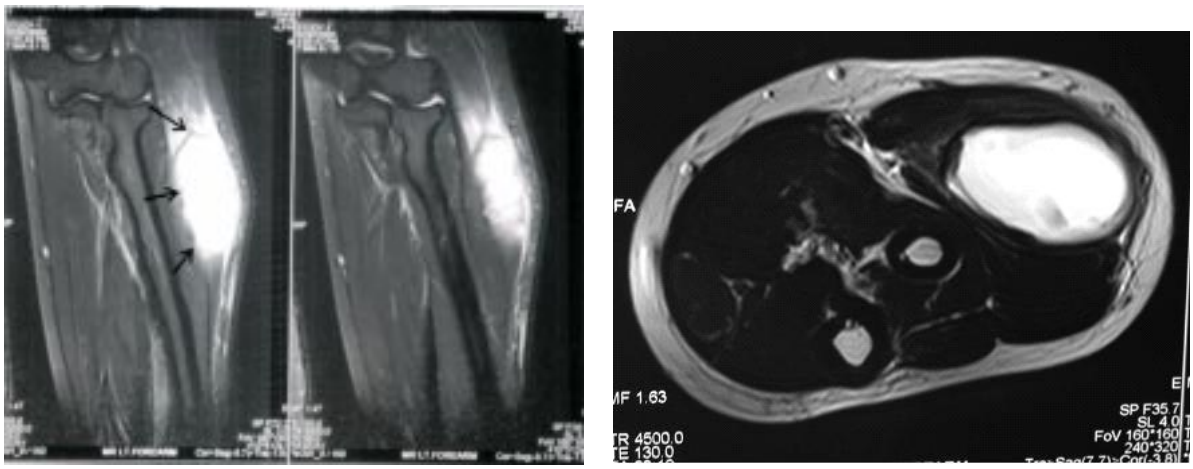

Fig.1B and 1C: Coronal and axial cut section of magnetic resonance imaging (T2W image) of forearm showing a well defined oval intramuscular lesion in the ventro-lateral aspect of proximal forearm involving the belly of Brachioradialis muscle with associated diffuse muscle edema

antitubercular chemotherapy for 12 months which includes four drugs (Isoniazide 300 mg, Rifampicin 600 mg, Pyrazinamide 1500 mg and Ethambutol 800 mg) for three months and two drugs (Isoniazide 300 mg, Rifampicin 600 mg) for further nine months. The wound discharge persisted for one month in the postoperative period and complete healing was noticed at the end of one and half month. There was atrophy and contracture of the forearm muscles with slight restriction of dorsiflexion of wrist joint and extension of elbow joint at the completion of treatment. Complete remission of the disease was noticed at the end of treatment but the footprint of the disease remained in the form of a scar healed by secondary intention.

Case 2: A thirty-eight years old female patient presented with a small swelling on the anterior aspect of proximal forearm (Fig. 2A) with history of occasional mild aching pain for last three months following a trauma. At present she was not having any constitutional symptoms and systemic problems. The swelling was nontender and nonmobile. There was no restriction of movement of elbow joint. We advised her analgesic and physiotherapy, with the impression of a localized

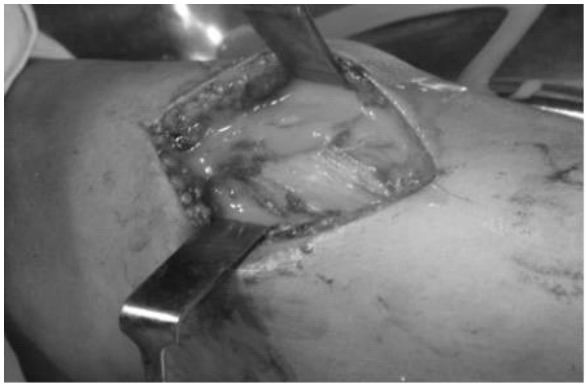

Fig.1D: On probing with a stab knife gush of pus came out from the belly of Brachioradialis muscle, which clinches the diagnosis of pyomyositis.

Fig. 2A: Soft tissue swelling on the proximal aspect of right fore arm in a 38 years' lady (case 2)

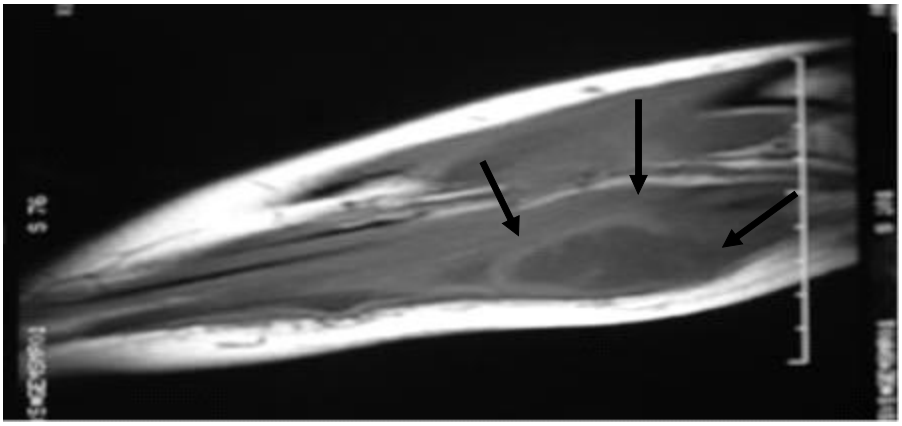

Fig. 2B: Coronal plane MRI (T1W image) of forearm showing a large oval abscess with multiple septa and debris inside. Adjoining fat plane is effaced with thickening of the overlying skin.

organized hematoma in the forearm. Again she came back to us after one month with similar symptoms as that of before. But this time the lesion was found to be little bigger and tender. MRI of the lesion revealed an oval shaped abscess of size 55 x 28 x 26 mms in the flexor compartment of right forearm in its proximal extent and more towards radial side. The collection shows thick wall with multiple septa and shows fluid and debris inside (Fig. 2B). On FNAC, few milliliters of thick purulent, creamy material were aspirated. It was subjected to Gram stain, Ziehl Neelsen stain and bacterial culture. No organisms were isolated. Tuberculin test was found to be positive. But it was not conclusive of tuberculous infection. Open biopsy revealed the deep flexor compartment muscle of forearm was found to be involved. It was whitish in colour and was getting easily separated from the healthy tissue. Surgical procedure was completed after thorough debridement of nonviable muscle tissues. Histopathological report revealed it to be a chronic granulomatous lesion with multinucleated giant cells and occasional epitheloid cell granulomas. No fungal profiles are seen. AFB and PAS stain was negative. Similar to the previous case polymerase chain reaction for mycobacterium tuberculosis DNA was positive. But no primary focus of tuberculosis could be identified. Postoperatively she was treated with multidrug anti-tubercular therapy for 12 months and complete disease remission was noticed.

Case 3: A 32 year old lady presented with a small swelling over the proximal aspect of forearm with a history of trauma 2 months back. She was afebrile and no other clinical symptoms were present. Hematological investigations revealed raised ESR (ESR= 65mm/hr). X-ray of the local part was normal. MR scan revealed extensive, diffuse, irregular, nonencapsulated heterogenous mixed signal intensity of soft tissue suggesting an infiltrative pathology in the form of localized fluid collection (T1W hypointensity and T2W hyperintensity) in intramuscular plane of the flexor compartment of forearm. There was associated diffuse edema with loss of inter-muscular fascial plane. No marrow edema or periosteal reaction was seen in the underlying bone. Three phase MDP bone scan showed increased tracer uptake in perfusion, blood pool phase and delayed phase. This increased abnormal activity of the right fore arm bone and soft tissue revealed it to be an infective or inflammatory pathology. Fine needle aspiration of the affected muscles demonstrated necrotic tissue and occasional leucocytes; but stains and cultures for bacteria, fungi and mycobacteria were negative. The lesion was debrided and histopathological report revealed it to be an epithelioid granulomatous lesion with mixed inflammatory infiltrate in the background of dead necrotic muscle fiber. Culture from the lesion site further confirmed the organism to be *Mycobacterium tuberculosis*. PCR for *Mycobacterium tuberculosis* was positive. Twelve months of anti-tubercular therapy was given postoperatively and the lesion was completely healed at the end of treatment.

DISCUSSION

'Pyomyositis' is the term used to describe a bacterial infection of skeletal muscle with formation of abscess with in it. The exact etiology is still unknown, but factors like trauma, nutritional deficiencies, viral infections, septic load and parasitic infestations have been implicated as the predisposing factors[7]. Infection by *Mycobacterium tuberculosis* is an extremely rare cause for pyomyositis, particularly in an immunocompetent person[8]. There are few case reports in the literature about tubercular pyomyositis, but it has been described frequently in association with immunodeficient individuals as in HIV infected patients, renal failure patients, patients on chemotherapy or corticosteroid and chronic drug abusers[9-11]. However as in the present cases, it can be seen in immunocompetent patients also[2,5,12].

Pathogenesis of tubercular pyomyositis is still confusing. Most of the authors believe the involvement of skeletal muscle to be secondary to underlying bones, synovial sheaths of nearby joints, by direct inoculation (trauma, syringe) or hematogenous dissemination[13]. As noted in the third case, the patient had underlying bone involvement with tuberculosis of brachioradialis muscle, which was evident only in bone scan. But the involvement of the bone in this case was primary or secondary from the overlying soft tissue, is not clear. There

was no marrow edema and periosteal reaction in MRI and radiographs, which is more indicative of absence of the primary pathology in the bone. However the soft tissue lesion in this case was more evident clinically. Just reverse to this concept, Derkash *et al*[13], Baylon *et al*[8], Versheney *et al*[5] and many authors have reported soft tissue tuberculosis as the primary focus of infection. Tubercular pyomyositis, in the absence of a direct spread from an adjacent primary focus, may be found in three circumstances: immunocompromised patients[14], inoculation through needles and syringes contaminated with mycobacterium[15] and idiopathically in an immunocompetent host, as in our cases[2,5,12,16,17]. We could not find any local or distant source of infection in all of these cases. Skeletal muscle is considered as the 'forbidden tissue' for tuberculosis. The reasons hypothesized for this resistance include poor oxygen content, high lactic acid concentration, and a paucity of reticuloendothelial tissue[18]. However with increasing reports about the primary involvement of the striated muscles by *Mycobacterium tuberculosis*, it is no longer considered as immune to the bacilli. Tubercular bacilli never produce any proteolytic enzymes and hence TB is not a pyogenic infection. If the disease is allowed to progress without treatment, however, abscesses may develop in the surrounding tissue[19].

The basic step in the diagnosis of a tubercular pyomyositis is clinical suspicion[4]. With the increased reports of tuberculosis in HIV infected patients and increased frequency of MDR TB (multidrug resistant tuberculosis), typical clinical presentation is lacking. Constitutional symptoms like fever, weight loss, loss of appetite is not seen in many cases. Two of the cases in our report were not having any clinical symptoms other than a vague swelling and intermittent mild aching pain.

Tubercular myositis is frequently misdiagnosed as sarcoma, or perhaps a benign soft-tissue tumor[1,13]. Parasitic infections like cysticercosis or hydatid cyst, fungal infection, hematoma with secondary infection can present with similar soft tissue mass[7,8]. Sometimes it is treated with physiotherapy and analgesic for a prolonged period of time, suspecting it to be a post traumatic muscle contusion[12]. The delay in diagnosis is because of lack of awareness about this disease, unfamiliarity with this entity, atypical presentations, lack of early specific signs and a wide range of differential diagnosis. Because of late presentation and treatment a large group of muscle fibers get affected and results in atrophy and contractures. However all muscular swellings are not tuberculosis and hence all other disease pathology should be excluded before thinking of this entity. Blood parameters may not be indicative of any infectious pathology. Sometimes, raised erythrocyte sedimentation rate may be the only consistence finding. Diagnostic techniques like ultrasound and computed tomography/ magnetic resonance imaging are very useful in diagnosis[1,8,20]. Local part X-ray is the initial radiographic investigation, which can detect the underlying bony pathology if any. CT scan shows areas of low attenuation with loss of muscle planes and surrounding rim enhancement. MRI detects hypointense lesions with hyperintense rim on T1W, which enhances on contrast injection. These are hyperintense on T2W image. But unlike pyogenic myositis, there was neither venous thrombosis nor signs of cellulitis surrounding the infected muscle[20]. MR scan is superior to CT and USG in detection and characterization of the lesions[1,16]. Fat suppressed STIR MRI should be performed if there is doubt about the soft tissue inflammation secondary to infection or tumours[1]. A muscle biopsy or aspiration of pus with culture and sensitivity, clinches the diagnosis[8]. An inconclusive FNAC report should not be relied upon, as sometimes the necrotic material (shreds of muscle fiber) may be aspirated. However a positive report can establish the diagnosis obviating further invasive open biopsy. We do not agree with Shahla masood[19], as FNAC in none of our cases was conclusive. The biopsy specimen or fluid aspirated should be subjected to staining and culture sensitivity for bacteria, fungi and mycobacteria. The treatments in all of the cases were instituted on the basis of histopathological findings, irrespective of the culture report. We do believe that treatment of antitubercular multidrug therapy should be started as early as possible, if histology or culture proves the diagnosis and other noninfectious pathology has been excluded

by clinical examination, imaging or laboratory investigations. We found sensitivity of PCR is quite high, as it was found to be positive in all of our cases. The advent of DNA detection by PCR may increase sensitivity of mycobacterial detection and allow for the exclusion of non-tuberculous mycobacteria that also cause soft tissue infections[3]. Once soft tissue tuberculosis is identified, a thorough systemic clinical examination as well as laboratory and radiological investigations should be performed to diagnose primary focus of infection.

The infection by tubercular bacilli involves a single large muscle, most commonly the quadriceps femoris, either by direct extension or by hematogenous spread[21]. Involvement of forearm muscle is very rare and only two cases have been reported in the literature as per our knowledge. The case reported by Baylon *et al*[8] had different presentation. The patient in their case was immunocompetent and having persistent discharge from forearm with a soft tissue mass. But in their case, the primary focus was lung with another secondary focus in submandibular lymph node. The success of their treatment was their ability to diagnose the primary focus and the secondary lymph node, which were treated appropriately. Sagar Narang[12] from India reported a case of TB pyomyositis of forearm as the primary focus in an immunocompetent individual, but having constitutional symptoms. The present cases reported in this article are unique in that they are found in the forearm muscles of immunocompetent individuals without any identifiable local or distant primary source of infection. Hence it is not unusual to find TB pyomyositis in immunocompetent persons particularly in developing countries like India where tuberculosis is endemic[5,12,20]. The presentation may be variable: subacute with a soft tissue mass or chronic discharge from a wound. The lesion may be nontender or mild tender.

In any muscular swelling tuberculosis may be considered as the etiology once other pathology has been excluded. In all secondary TB myositis, a search should be made to identify the primary focus. Both the primary and secondary lesion should be treated simultaneously under the cover of multidrug chemotherapy which is clearly evident from Baylon's report[8]. In the present study, the outcome was excellent after the abscess was drained, the surrounding tissue was debrided, and the patient was managed with twelve months of antituberculous chemotherapy. With no evidence of coexistent active skeletal or extraskeletal tuberculosis, the pathogenesis of this intramuscular tuberculous abscess is still not clear.

In conclusion, tubercular pyomyositis is rare and a high clinical suspicion is required for diagnosis. However, an early diagnosis and treatment with chemotherapy and surgical drainage lead to good prognosis.

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TUBERCULOSIS HEALTH VISITORS' COURSE

The 2010-2011 Tuberculosis Health Visitors' Course of 9 months' duration will be conducted at the New Delhi Tuberculosis Centre. The minimum qualification for admission to this course is 10 + 2 with science and/or hygiene. Science education up to class 10 is essential. Application forms for admission to the course can be obtained from the Secretary General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110 001. The last date for receipt of applications is 30th April, 2010.

Case Report

TUBERCULOSIS PNEUMONIA AS A PRIMARY CAUSE OF RESPIRATORY FAILURE-REPORT OF TWO CASES

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Summary*:** Tuberculosis (TB) is one of the treatable diseases rarely causing Acute Respiratory Failure (ARF). Hypoxic respiratory failure is often fatal in miliary tuberculosis and acute tuberculous bronchopneumonia. We describe two patients of tuberculous pneumonia with ARF who were successfully treated with early appropriate anti-tuberculosis therapy. ***[Indian J Tuberc 2010; 57: 41-47]

Key words: Tuberculosis, Pneumonia, Acute Respiratory Failure, Miliary Tuberculosis

INTRODUCTION

Tuberculosis as a primary cause of respiratory failure is an uncommon occurrence[1] with an incidence of 1.5% in patients hospitalized with pulmonary TB[2]. Patients with miliary or disseminated disease are especially prone to develop respiratory failure. Tuberculous Pneumonia has rarely been identified as a cause of ARF[3-4]. Acute tuberculous pneumonia presents as parenchymal consolidation with or without endobronchial spread mimicking bacterial pneumonia. It probably represents an exudative hypersensitivity reaction to tuberculoprotein, rather than actual inflammation caused by the *Mycobacterium tuberculosis* organism *per se*. These infiltrates can appear within a matter of days and can clinically simulate acute bacterial pneumonia. Anti-tubercular treatment has been considered to be an important factor affecting patient's outcome. In this report, we describe two patients with tuberculosis who developed ARF and were successfully treated with early appropriate anti-tuberculosis therapy. The experience with these cases serves to re-emphasize the importance of quality sputum examination routinely for AFB in patients at risk of TB with respiratory failure and pneumonic infiltrates, particularly in endemic areas since specific and effective therapy for tuberculosis is available in contrast to most other conditions associated with respiratory failure.

Case-1. Mr. "S" 18 years' old, young male, non-smoker, unmarried, student, resident of Delhi was admitted on 17 May 2008 with complaints of haemoptysis, fever and shortness of breath for one week's duration. A year ago, he had haemoptysis and for which he had taken 6 month Category-I anti-tuberculosis treatment from a DOTS centre, as a case of smear positive pulmonary tuberculosis. He improved with the treatment except for some residual early morning cough with expectoration and was declared cured after sputum examination for AFB. He remained well for two months, when in May, 2008 he developed cough, expectoration, fever and haemoptysis. Fever was insidious in onset, high grade, and more in the evening. Cough was productive with yellow colour sputum and sometimes mixed with blood. There were 2-3 episodes of haemoptysis in one week with 150-200 ml of blood loss in each episode. He was admitted at a peripheral hospital and received two units of whole blood transfusion. There was no history of

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alcohol abuse or smoking. During his hospitalization, his breathlessness progressively increased and he was referred to our institute on 17th May, 2008. On admission, examination revealed a lethargic young man in respiratory distress; blood pressure was 100/70 mm Hg, pulse rate was 136 beats per minute, temperature was 102^{O} F and respiratory rate was 42 per minute. Abnormal findings were limited to coarse crackles all over the chest. There was no pallor, cyanosis, lymphadenopathy, or pedal edema. Laboratory data revealed the following values: hemoglobin 13.0g%; total leucocytes count 10,800/cu.mm (90 per cent polymorphonuclear leukocytes, 9 per cent lymphocytes and 1 percent monocytes); serum protein, 5.8 g/dl; serum albumin 3.0 g/dl total bilirubin levels, 0.51mg/dl; SGOT levels 52U/L; SGPT levels 50U/L; and alkaline phosphatase level, 261U/L. Serum electrolytes were: Na^+ 140 mmol/L; K^+ 4.2mmol/L; Cl^- 106 m mol/L and the result of urine analysis were normal. A chest X-ray film (Fig. 1A) showed multiple ill-defined confluent nodular opacities widely distributed throughout both the lungs. The nodules were larger than those of miliary shadows. Multiple small cavities were present in left upper zone. Initial therapy with ceftriaxone 1 gm intravenously 12 hourly, Hydrocortisone 100 mg intravenously 8 hourly was begun. Gram stain of sputum revealed scanty leukocytes and no pathogens. A culture of sputum grew normal oral flora. Sputum smear examination was positive for acid-fast bacilli. Anti-tuberculosis treatment (Cat II) thrice a week with injection streptomycin 0.75 gram intramuscular, capsule rifampicin 450 mg., tablet isoniazid 600 mg., tablet pyrazinamide 1500 mg. and tablet ethambutol 1200 mg was started. On admission oxygen saturation (SaO_2) at room air was 74%. The SaO_2 rose to 87.5% with oxygen delivered by venturi mask (FIO_2 =32%). Arterial blood gas analysis at FIO_2 of 32 % showed the following values: pH, 7.409; $PaCO_2$: 50.8mm Hg; and PaO_2:53.3 mm Hg. PaO_2 / FiO_2 ratio was 167. With FiO_2 of 50 percent he was able to maintain SaO_2 above 90 per cent. His breathlessness gradually improved and on 3rd day respiratory rate settled to 28 per minute with pulse rate of 100 beats per minute. Repeat chest X-ray on 5th day did not reveal any marked change, however patient was able to maintain SaO_2 above 90 % at room air and his fever also responded. Within two weeks, he was doing his routine activity and oxygen therapy was stopped. Anti-tuberculosis therapy was continued and Corticosteroids were tapered and stopped. At three weeks he was maintaining oxygen saturation (SaO_2) of 96% at room air. After a week, he had high grade fever and found to have urinary tract infection and cholelithiasis. He was treated for urinary tract

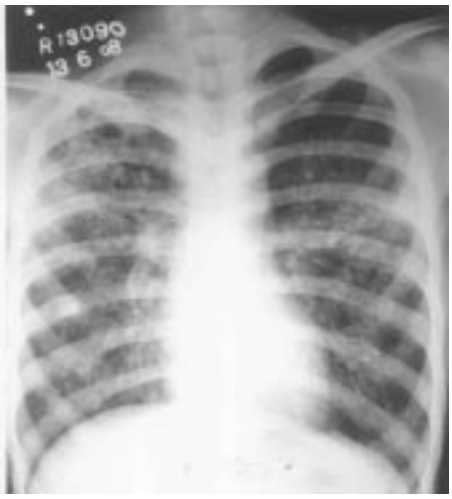

Fig. 1a: CXR-PA view on admission revealing poorly defined nodules in upper and lower lung fields of both lungs. The nodules are larger than those of miliary shadows. A cavity is seen in right upper lung field.

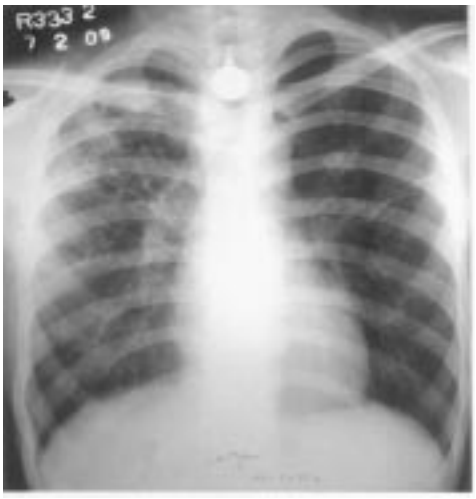

Fig. 1b: After 8 months, chest X-ray PA view revealing healing of cavity and fibrotic lesions in upper and middle lung fields of both lungs with complete resolution of nodular densities.

infection. He was discharged and referred to DOTS centre for completion of Anti tuberculosis treatment. His hospital stay was 57 days. Chest X-ray after completion of eight months of Cat II anti-tuberculosis treatment revealed significant resolution of opacities (Fig. 1 B).

Case- 2. Mr. "M S" a 25-year-young male, rickshaw-puller, non smoker attended Chest OPD of LRS Institute of Tuberculosis and respiratory Diseases on 14 February, 2009 with symptoms of cough, expectoration, fever, breathlessness on exertion, loss of weight and appetite for three weeks. Ten days ago he had haemoptysis with loss of 10-15 ml of blood followed by blood mixed in sputum for three days. In the past, ten years ago he had inadequate unsupervised daily anti-tuberculosis treatment for three months. In last three years he had history of abuse of 250 ml alcohol per day. His sputum smear examination was found to be positive for AFB. He was referred to DOTS centre for Category-II anti-tuberculosis treatment. After four days, before the initiation of ATT, he was hospitalized on 23 February 2009 with high grade fever and respiratory distress. Examination revealed a cachectic man with BMI of 14.7 Kg/ m^2 in respiratory distress, with blood pressure of 130/76 mm Hg, pulse rate of 116 per minute, temperature of 101° F, and respiratory rate of 36 per minute. Pertinent findings included coarse crackles all over the chest and hepatomegaly. Laboratory data revealed the following values: hemoglobin 10.7g%; total leucocytes count 22,900/cu mm (80 per cent polymorphonuclear leucocytes and 20 per cent lymphocytes); blood urea nitrogen (BUN) level, 23.8 mg/100 ml; bilirubin level, 0.77 mg/100 ml; alkaline phosphatase level, 1134 international units (IU)/L; and serum glutamic-oxaloacetic transaminase (SGOT) level, 964 IU/L and serum glutamic-Pyruvic transaminase (SGPT) level, 737 IU/L. The findings from urine analysis were normal. Six weeks into treatment sputum culture grew *Mycobacterium tuberculosis*. The chest X-ray film taken on admission (Fig. 2a) showed widespread poorly defined opacities in upper and lower lung fields of both lungs with air bronchogram. Analysis of arterial blood gases while the patient breathing oxygen 4 liter per minute by nasal canulae revealed a pH of 7.406, an arterial oxygen pressure (PaO_2) of 45.3 mm Hg; and arterial carbon dioxide tension ($PaCO_2$), 56.6 mm Hg. PaO_2 / FiO_2 ratio of 142. Gradually, he was able to maintain oxygen saturation(SaO_2) above 90% with 0.50 FiO_2 with venturi mask and arterial blood gas levels revealed : pH, 7.421; PaO_2 of 85.1 mm Hg; $PaCO_2$ of 58.0 mm Hg. Initial therapy included Injection Ceftriaxone 2 gram

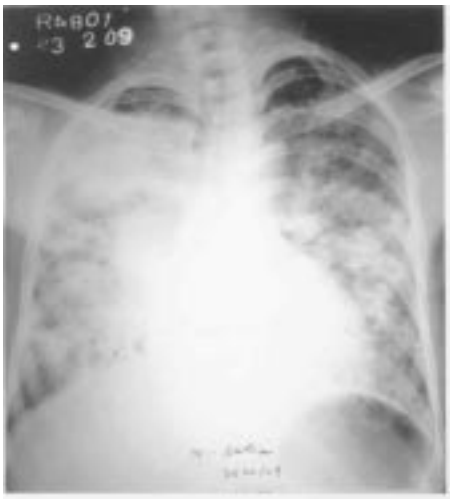

Fig. 2a: Chest X-ray P.A. view on admission revealing widespread poorly defined opacities in upper and lower lung fields of both lungs. Note the air bronchogram.

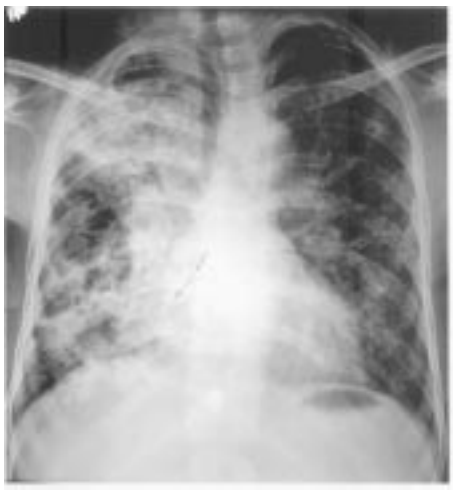

Fig. 2b: Chest X-ray PA view after one week revealing partial resolution of opacities. Note air bronchogram is more prominent.

intravenously 12 hourly, Hydrocortisone 100 mg intravenously 12 hourly along with anti-tuberculosis treatment (ATT) . Gram stain of sputum revealed scanty leukocytes and no pathogens. A culture of sputum grew normal oral flora. Therapy with ceftriaxone was stopped. In view of deranged liver functions, modified daily ATT with injection streptomycin 0.75 gram intramuscular, tablet ethambuol 1000 mg and levofloxacin 750 mg was started. Repeat X-ray chest after a week showed radiological improvement with partial resolution of opacities (Fig. 2b). Corticosteroids were tapered and stopped in two weeks' time. With the improvement of liver functions thrice a week, Category-II ATT was initiated on 16th March 2009 with injection streptomycin 0.75 gram intramuscular, capsule rifampicin 450 mg., tablet isoniazid 600 mg., tablet pyrazinamide 1500 mg. and tablet ethambutol 1200 mg. Gradually in 8 weeks he was able to maintain 90% oxygen saturation (SaO_2) at room air. Anti-tuberculosis therapy was continued and at 12 weeks he was maintaining oxygen saturation (SaO_2) of 94% at room air. He was discharged and referred to DOTS centre for completion of Anti tuberculosis treatment. On discharge, arterial blood gas levels revealed: pH, 7.471; PaO_2 of 67.5 mm Hg; $PaCO_2$ of 37.1 mm Hg. His hospital stay was 111 days.

DISCUSSION

Identification of the primary cause of respiratory distress is vital for the initiation of appropriate therapy. Active pulmonary TB is a rare primary cause of ARF and is associated with very high mortality[1]. Important factors contributing to ARF in TB patients included Gram-negative pneumonia and/or sepsis, chronic obstructive pulmonary disease, prior TB with anti-TB medication non-compliance, and malignancy[5]. Tuberculosis occurring initially as an acute, rapidly progressive pneumonia is unusual because tubercle bacilli multiply only once every 18 to 24 hours as opposed to most pathogenic bacteria, which can multiply every 20 to 30 minutes. It is suggested that for this to occur, either a massive number of tubercle bacilli or, more likely tuberculoprotein must be aspirated causing an acute exudative hypersensitivity reaction into new areas of the lung[6]. This is usually due to liquefaction of a caseous lesion and its erosion into a bronchus. Perforation of a lymph node into a bronchus may be a factor in this reaction[7]. Acute exudative consolidation was experimentally induced by intratracheal injection of acid-fast organisms into rabbits[8] and the importance of a hypersensitivity reaction associated with tuberculoprotein was confirmed by intratracheal injections of tuberculin into normal and tuberculous guinea pigs[9]. In human tuberculosis, Rich[6] found areas of fresh pneumonic exudates surrounding caseous foci in which few or no acid-fast bacilli were seen and attributed this peripheral reaction to a hypersensitivity response to tuberculoprotein. The pathogenesis of ARDS in both pulmonary and miliary tuberculosis is not well understood. It has been speculated that lipoarabinomannan, a component of mycobacterial cell wall has been shown to induce the production of tumor necrosis factor in human macrophages, which might contribute to the development of ARDS.

Acute tuberculous pneumonia is characterized by fever, productive cough, and high temperature with signs of severe toxicity and of consolidation, presence of large confluent dense shadows on the chest x-ray film involving at least one lobe; and tubercle bacilli in the sputum[7]. The rapidly progressive course of acute tuberculous pneumonia can mimic bacterial pneumonia. The longer duration of symptoms before admission is the most important factor differentiating TB from other infectious causes [3]. In acute tuberculous pneumonia symptoms are usually less than one month[10]. The reported mean duration of symptoms before admission was 29 ± 28 days in various studies[3, 12 - 13]. Patients with acute massive tuberculous pneumonia are subjectively better than those with a bacterial pneumonia of equal extent with less pleuritic pain, toxemia, and dyspnea. It is difficult to differentiate radiologically between TBP and severe bacterial pneumonia as causes of ARF, meaning accurate diagnosis can be delayed. The white blood cell count is rarely greater than 15,000/cu mm, and the temperature is usually between 37.8 ^{0}C and 38.9^{0}C (100^{0}F and 102^{0}F)[11].

The hospital mortality for tuberculosis patients mechanically ventilated compared with that for non-tuberculous pneumonia with similar APACHE II scores was significantly worse (69% VS 36%, $p < 0.025$)[14]. In tuberculous pneumonia patients (TBP) advanced age, longer duration of symptoms before hospital admission, the presence of shock unrelated to sepsis and non-use of steroids influence patient survival[12]. Advanced age and presence of shock unrelated to sepsis were independently associated with poor outcomes; however, the use of corticosteroids was a favourable prognostic factor for patients with TBP[12]. Acute respiratory distress syndrome (ARDS) is the most common reasons for ICU admission of patients with TB[13, 15]. ARDS is characterized by[16-17] : (a) acute onset , (b) bilateral infiltrates on chest radiograph ,(c) pulmonary artery wedge pressure < 18 mmHg (obtained by pulmonary artery catheterization), if this information is available; if unavailable, then lack of clinical evidence of left ventricular failure suffices (d) if PaO_2:FiO_2 < 300 mmHg acute ling injury (ALI) is considered to be present (e) if PaO_2:FiO_2 < 200 mmHg acute respiratory distress syndrome (ARDS) is considered to be present. Sharma *et al* reported ARDS in 1.06% hospitalized adult patients with active TB[18]. Presence of duration of illness beyond 30 days at presentation, absolute lymphocyte count < 1625/ mm^3 and serum ALT > 100 IU were independent predictors of ARDS development. Patients with APACHE II score >18; those with APACHE II score <18 in the presence of hyponatraemia and PaO_2/ FIO_2 ratio <108.5 were likely to have more mortality[18].

ARF is more common in miliary tuberculosis than in tuberculous bronchopneumonia and also has a worse prognosis[19]. ARDS caused by miliary TB is associated with a high fatality rate[20]. The mortality rate in the patients with pulmonary tuberculosis requiring mechanical ventilation is very high, with multiple organ failure and consolidation on chest radiographs[21]. Concomitant extra pulmonary TB, ARDS or DIC were more common in the MTB group than in the TBP group ($p<0.05$). However, there were no significant differences in hospital mortality rates between the two groups (68.2 *vs* 58.3%, $p = 0.385$)[12]. Treatment has been considered to be an important factor affecting patient's outcome[14, 22-23]. Higher mortality is present in patients who did not receive an optimal treatment with a triple combination including INH and RMP. Impaired liver function being a major reason to withdraw the INH and RMP; however, other causes have been also described [24]. With anti tuberculosis treatment, diffusing capacities may improve rapidly. Usually it returns to normal in three weeks, however sometimes defect persists for months. In three weeks, our patient with tuberculous bronchopneumonia, was able to maintain oxygen saturation (SaO_2) of 96% at room air, while patient with tuberculous pneumonia in case 2 was able to maintain SaO_2 of 90% at room air at six weeks.

Organ dysfunction in critically ill patients is another cause for changes in the treatment regimen. Although the duration from exhibition of first symptoms to treatment onset was outlined as a crucial factor to mortality[25]. HIV status and longer history of symptoms such as fever or haemoptysis did not show a significantly worse outcome in study reported by Kim *et al*[12]. Nosocomial infection during ICU stay has significant impact on the mortality of critically ill TB patients[26]. Interestingly, some of the predictive factors for mortality, such as nosocomial infections, were actually related to the intensive care procedures.

The beneficial effects of corticosteroids in the management of TBP with ARF are suggested by several reports. Mycobacterial antigen can induce release of pyrogens from monocytes, lymphokines from specifically sensitised lymphocytes and cytokines, such as tumor necrosis factor, from macrophages and peripheral blood mononuclear cells, which may be responsible for constitutional symptoms and tissue damage[27]. Corticosteroids can inhibit the release and activities of lymphokines and cytokines. The granulomatous host response to TB may paradoxically protect sequestered *M. tuberculosis* from anti-TB therapy. The adjuvant corticosteroids may be beneficial in permitting anti-TB drugs to penetrate into granulomas, by disrupting granuloma formation[28]. Tuberculous pneumonia patients with ARF receiving corticosteroid therapy showed a lower mortality rate than those not receiving corticosteroid therapy (56.7% *vs* 77.8%; $p = 0.046$)[12]. The use of systemic corticosteroid

was based entirely on the attending physician's decision and/or the patient's underlying condition; and the corticosteroids did not affect either the duration of mechanical ventilation (p = 0.603) or arterial oxygenation *i.e.* arterial oxygen tension/ inspiratory oxygen fraction (p = 0.182)[12]. Further randomised controlled trials are necessary to clarify the role of corticosteroids in the management of tuberculous pneumonia with ARF. Any benefit of adjuvant corticosteroids in patients with miliary Tuberculosis with ARF is not clear, since only limited evidence with conflicting results are available. A beneficial response was observed in one study[29], but such benefit was not documented in another[30].

CONCLUSION

Identification of the primary cause of respiratory distress is vital for the initiation of appropriate therapy. Active pulmonary TB is a rare primary cause of ARF and is associated with very high mortality. Acute pneumonia probably represents an exudative hypersensitivity reaction to tuberculoprotein, rather than actual inflammation caused by the *Mycobacterium tuberculosis* organism *per se*. These infiltrates can appear within a matter of days and can clinically simulate acute bacterial pneumonia. Tuberculosis should be considered in the differential diagnosis of acute pneumonic infiltrates with respiratory failure.

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Case Report

DISSEMINATED TUBERCULOSIS WITH INVOLVEMENT OF PROSTATE - A CASE REPORT

Rashmi Mittal[1], R. Sudha[1], Mahalakshmi Veeraraghavan[1], S. Murugan[2], S. Adikrishnan [2], M. Krishnakanth [2], S. Shobana[3], S. Anandan[4] and S. Pandey[5]

(Received on 1.4.2009; Accepted after revision on 2.11.2009)

***Summary*:** We present a 55-year-old male who presented with painful non-healing ulcers on the lower lip and scrotum associated with productive cough, fever, anorexia and dysuria. Erythrocyte sedimentation rate was raised, sputum was positive for acid fast bacilli. Chest X-ray was suggestive of pulmonary tuberculosis. A prostate biopsy was also suggestive of tuberculosis. A diagnosis of disseminated tuberculosis was made and the patient showed a good response in two weeks.

[Indian J Tuberc 2010; 57:48-52]

***Key words* :** Tuberculosis, Skin, Orificial

INTRODUCTION

Tuberculosis is one of the most important infections and is likely to be as old as the human race. It has been estimated that the genus 'mycobacteria' causes more suffering for the humans than all the other bacterial genera combined. With the advent of anti-tubercular drugs, tuberculosis has been on the decline. However, in 1993, it was declared as a 'global emergency' by WHO because of a sharp increase due largely to the HIV pandemic. Cutaneous tuberculosis is becoming a rare disease in developed countries except in certain high risk patients like immuno-suppression with HIV or those on immuno-suppressive drugs. However, it is not uncommon in developing countries and exhibits considerable variability.

CASE REPORT

A 55-year-old heterosexual, married male presented to the Dermatology out patient department with painful non-healing ulcers over the lower lip and scrotum of four months' duration.He complained of cough with expectoration since four months. He had been having low grade fever, anorexia and dysuria since six months. He complained of occasionally straining to void urine since four months. There was no history of haematuria, chyluria, pyuria. There was no hesitancy, incomplete evacuation, urgency or intermittency. The lesions on both the lip and scrotum started as painful papules which ulcerated in a week. The ulcers rapidly increased in size discharging pus and blood. None of his family members had evidence of tuberculosis. He was an alcoholic and had a history of multiple, unprotected, extra-marital, heterosexual exposures.

Cutaneous examination revealed a tender, non-indurated ulcer on the lower lip of size 1cmx2cm oval in shape with dried adherent haemorrhagic crusts. The edges were undermined (Fig. 1). The ulcer on the penoscrotal junction on the left side was similar except that there were no crusts (Fig. 2). It was of size 1cm x 1cm. Base was healthy with granulation tissue. Rest of the genitalia was normal. Perianal area was normal. There was no evidence of a BCG vaccination scar.

General examination revealed a thin build and poor nourishment. Bilateral inguinal lymph nodes,

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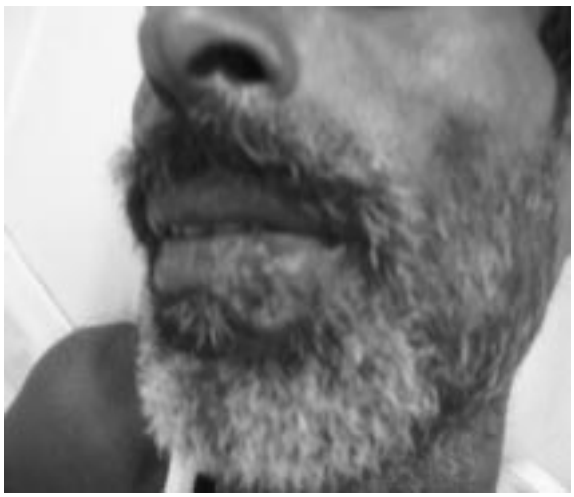

Fig. 1: Ulcer on the lower lip, before treatment

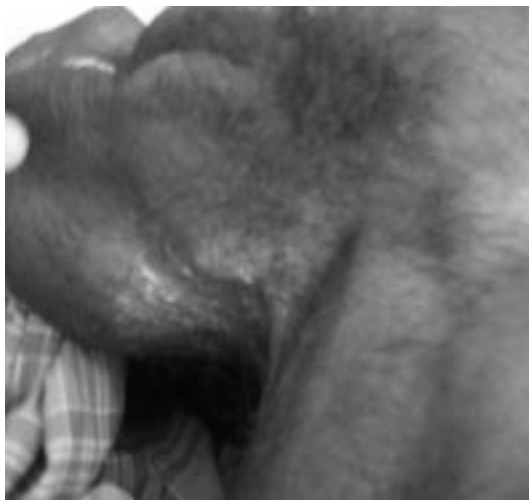

Fig. 2: Ulcer on the ventral aspect of scrotum, before treatment

left more than right were enlarged, non-tender, discrete and firm in consistency. On auscultation of the chest, basal crepitations were heard. Rest of the systems were normal. On per rectal examination, a hard, fixed and irregular prostate was palpated.

Laboratory examination revealed a normocytic, normochromic anaemia with a haemoglobin of 9.9gm% and a total leucocyte count of 4900/cmm.Erythrocyte Sedimentation Rate (ESR) was 60mm in ½ hour and 120mm in 1st hour. Liver and renal function tests were normal. Serology for HIV, HBs antigen, VDRL was negative. Serum prostate specific antigen was also normal. Routine urine examination was normal. Urine culture grew no organism. Sputum was positive for acid fast bacilli and culture grew *Mycobacterium tuberculosis*. Urine examination for acid fast bacilli on three consecutive days was negative. A Fine Needle Aspiration Cytology

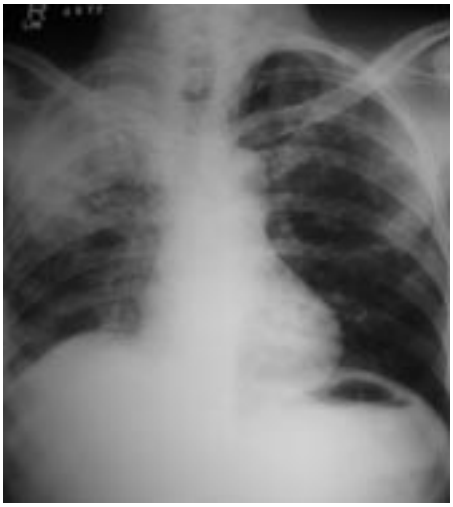

Fig. 3: Chest radiography (posterior anterier view) showing bilateral infiltrates

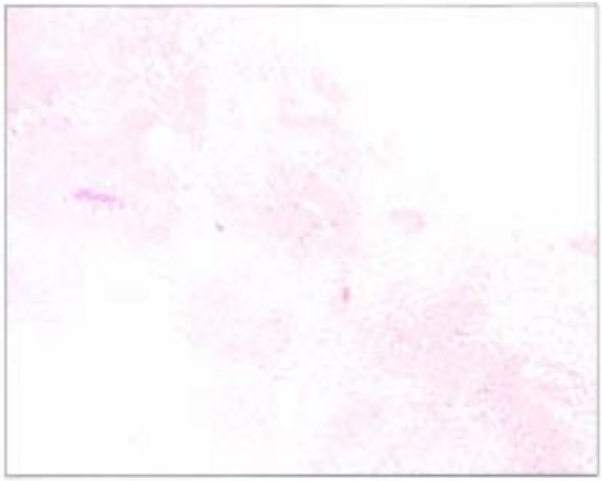

Fig. 4: 10 x H & E. Prostatic tissue showing granuloma

Fig. 5: Ulcer on the lower lip, after treatment

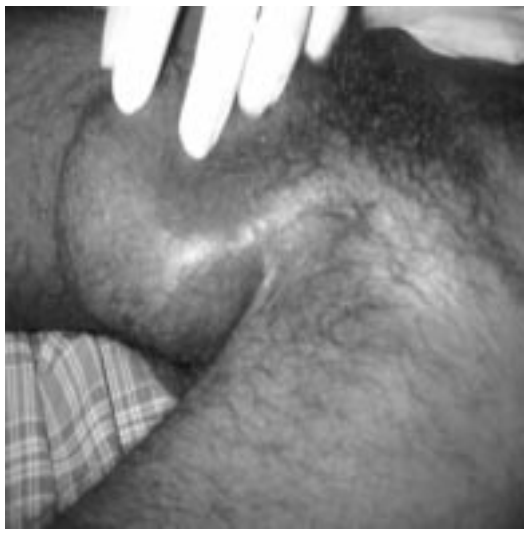

Fig. 6: Penoscrotal ulcer, after treatment

(FNAC) from the inguinal lymph node showed a granulomatous reaction with positive staining for *Mycobacterium tuberculosis*. Mantoux test was negative. Chest X-ray showed bilateral infiltrates in the right upper mid zone which was suggestive of pulmonary tuberculosis (Fig. 3). Ultrasonogram of the abdomen revealed mild hepatomegaly with bilateral renal cortical calyces. Right simple renal cyst 2.8x2.0cm. Right renal calculus of 8mm size at the lower pole. Histopathological examination of skin could not be done as the patient was hesitant to undergo biopsy from the lip. A transrectal ultrasound guided prostate biopsy was done . It showed cores of prostatic tissue with large areas of amorphous eosinophilic necrotic material (caseation) with multiple epithelioid granulomas and Langhan's type of giant cells (Fig. 4). Large number of acid fast bacilli were seen.

On the basis of clinical, histopathological and laboratory findings, a diagnosis of disseminated tuberculosis was made. The patient was started on Isoniazid (5mg/kg) – 300 mg, Rifampicin – 450mg, Pyrazinamide (15-30mg/kg) – 1.5 gm and Ethambutol – 20 mg/kg. After two weeks of treatment, there was significant healing in the skin lesions (Figs. 5, 6). The patient had no urinary complaints so improvement was assessed on the basis of healing skin lesions.

DISCUSSION

HIV infection renders the host immune response impoverished, thus resulting in an inability to locally contain any infection. In the case of tuberculosis, it can disseminate and cause an overwhelming infection. Ross and Somasundaram[1] reported forty two out of fifty one HIV infected patients developed disseminated tuberculosis. In a retrospective case series[2], Andres SC defined "disseminated tuberculosis" as active haematogenous spread of bacilli in two or more organs/systems in the body leading to a generalized systemic illness. Patients fulfilling more than one of the following criteria were considered to have disseminated tuberculosis:

1) Demonstration of acid fast bacilli or culture of *Mycobacterium tuberculosis* in more than one source.
2) Biopsy specimen revealing caseating granulomas with or without acid fast bacilli on histopathological study on one or more organs.
3) Chest X-ray revealing a military pattern.
4) Patients with a clinical illness presenting with fever, night sweat, anorexia, cough with no other cause and a positive skin reaction (8 mm induration after 48-72

hours) when tested with five international tuberculin units of purified protein derivative of tuberculin[2].

Tuberculosis can involve any organ system in the body. While pulmonary tuberculosis is the most common presentation, extrapulmonary tuberculosis is also an important clinical problem[3]. The term 'extrapulmonary tuberculosis' has been used to describe isolated occurrence of TB at body sites other than the lung. The most common extrapulmonary site in HIV positive individuals is the lymph node. However, neurological, pleural, pericardial, abdominal involvement has been seen commonly in HIV positive patients[4].

Genitourinary tuberculosis (GUTB) may involve the kidneys, ureter, bladder, or genital organs. Clinical symptoms usually develop 10-15 years after the primary infection. Only about a quarter of patients with GUTB have a known history of TB; about half of these patients have normal chest radiography findings. Genitourinary tuberculosis complicates 3-4% with pulmonary tuberculosis. Haematogenous dissemination from an active site of infection results in genitourinary tuberculosis. Active GUTB usually develops 5 – 25 years after the primary pulmonary infection and is usually encountered between the second and third decades of life[5]. *Mycobacterium tuberculosis* bacilli are inhaled through the lungs to the alveoli, where they are phagocytosed by polymorphonuclear leukocytes and macrophages. Although most bacilli are initially contained, some are carried to the region's lymph nodes. Eventually, the thoracic duct may deliver mycobacteria to the venous blood; this may result in seeding of different organs, including the kidneys. Multiple granulomas form at the site of metastatic foci. In the kidneys, they are typically bilateral, cortical, and adjacent to the glomeruli and may remain inactive for decades.

Growing granuloma may erode into the calyceal system, spreading the bacilli to the renal pelvis, ureters, bladder, and other genitourinary organs. Depending on the status of the patient's defense mechanisms, fibrosis and strictures may develop with chronic abscess formation. Ureteral TB is an extension of the disease from the kidneys, generally to the ureterovesical junction. The higher frequency of isolated epididymal TB lesions in children favors the possibility of hematological spread of infection, while adults seem to develop tuberculous epididymoorchitis caused by direct spread from the urinary tract[6]. The formation of a draining sinus is uncommon in developed countries, but epididymal induration and beading of the vas are common.

Involvement of the testis is usually due to direct extension. Infertility may result from bilateral vasal obstruction. Nodular beading of the vas is a characteristic physical finding. Orchitis and the resulting testicular swelling can be difficult to differentiate from other mass lesions of the testes. Prostatic TB is also spread hematogenously, but involvement is rare. The affected prostate is nodular and not tender to palpation. Eighty-five percent of patients also have renal TB. Severe cases may cavitate and form a perineal sinus, although this development is rare. Decreased semen volume may indicate extensive prostatic disease or ejaculatory duct obstruction[7].

Patients with genital and urethral TB present with a superficial tuberculous ulcer on the penis or in the female genital tract secondary to mycobacteria exposure during intercourse. The penile ulcer may cause cavernositis that extends to the urethra. Acute urethritis manifests as mycobacterial discharge and often results in chronic stricture formation.

The most common symptoms of GUTB are increased frequency of urination, dysuria, painful testicular swelling, perianal sinus or genital ulcer. Asymptomatic patients are not uncommon. Most of the case reports described so far have presented as scrotal swelling, nodules, testicular enlargement. There has been a report of a patient who developed a scrotal fistula five months after receiving intravesical BCG therapy for bladder cancer[8]. **We present this case for its rare disseminated involvement of lung, prostate and skin. Our case fulfills the criteria of having disseminated tuberculosis. Very rarely fulminant prostatic involvement can cause abscess formation and**

subsequent perineal fistulization which could be the explanation in our patient.

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Case Report

EXFOLIATIVE DERMATITIS TO ALL FOUR FIRST LINE ORAL ANTI-TUBERCULAR DRUGS

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(Received on 13.10.2009; Accepted afer revision on 15.11.2009)

***Summary*:** Exfoliative dermatitis to all four first line drugs singly or rarely in combination has been reported. Here we report a rare case of pulmonary tuberculosis with exfoliative dermatitis to all four oral first line antitubercular drugs. (Rifampicin, Isoniazid, Ethambutol, Pyrazinamide). To the best of our knowledge, this is the first such case.
[Indian J Tuberc 2010; 57: 53-56]

***Key words*:** Exfoliative dermatitis, Antitubercular drugs.

INTRODUCTION

Exfoliative dermatitis also known as erythroderma is an uncommon but serious skin disorder which results in generalized scaling eruption of the skin. It is usually drug induced, idiopathic, or secondary to underlying cutaneous or systemic disease. Theoretically, any drug may cause exfoliative dermatitis. Among antitubercular drugs, exfoliative dermatitis has been reported with rifampicin, isoniazid, ethambutol, pyrazinamide, streptomycin, PAS either singly or combination of two drugs in some case reports.[1-6] It usually presents by six to eight weeks of initiation of antitubercular treatment. Early recognition, prompt withdrawal of antitubercular therapy and institution of steroids, if reaction is severe, are cornerstones of its management. Here we report a rare case of pulmonary tuberculosis with exfoliative dermatitis to all four oral first line antitubercular drugs (rifampicin, isoniazid, ethambutol, pyrazinamide).

CASE REPORT

A 73-year-old male patient, a diagnosed case of smear positive pulmonary tuberculosis, on CAT -I antitubercular treatment for eight weeks, presented to us with complaints of itching and generalized rash all over the body. On examination, he was febrile and there was generalized scaling eruption involving the scalp, trunk, extremities and palms (Figs. 1-3). A diagnosis of exfoliative dermatitis due to antitubercular treatment was made because he was not taking other medicines. Anti-tubercular treatment was then withheld and he was started on corticosteroids (initially 1mg/kg).

Further workup revealed a normal Total Leukocyte Count (TLC-12,000), normal liver and kidney function tests, Elisa for HIV negative, sputum smear examination negative for AFB and sequential CXRs showed radiological improvement.

Once his rash completely resolved, drugs were reintroduced according to WHO recommendations[7]. On reintroduction of Isoniazid (50 mg), he developed increase in itching and rash. Isoniazid was then withdrawn. After subsidence of rash, rifampicin 150 mg was reintroduced, following which, patient again developed scaling eruption. Rifampicin was also stopped. He responded in a similar way to both ethambutol and pyrazinamide, while he tolerated streptomycin and Ofloxacin well and his rash completely disappeared (Figs. 4-6). He has been continued on streptomycin, ofloxacin in continuation phase(daily regimen). Steroids were gradually tapered and stopped. After five months of ATT, patient showed clinical and radiological improvement.

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Fig. 1

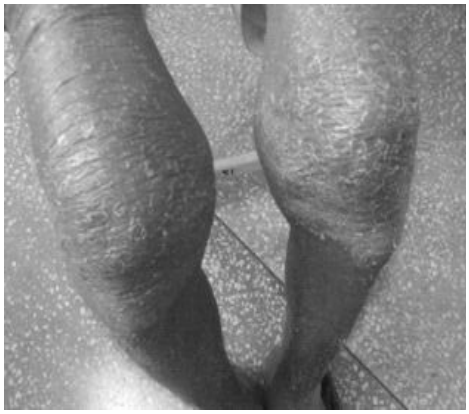

Fig. 2

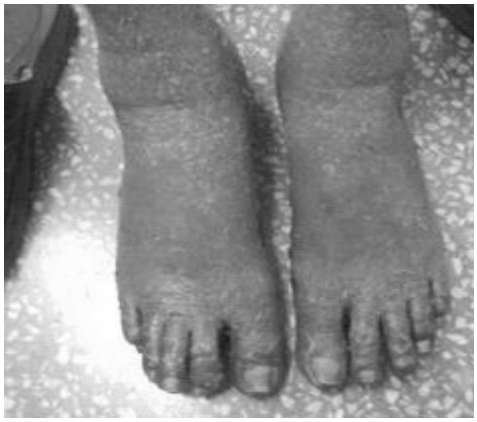

Fig. 3

Figs. 1-3: Scaly eruptions involving palms and extremities

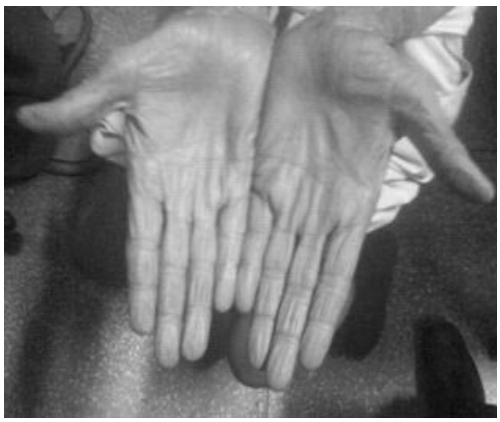

Fig. 4

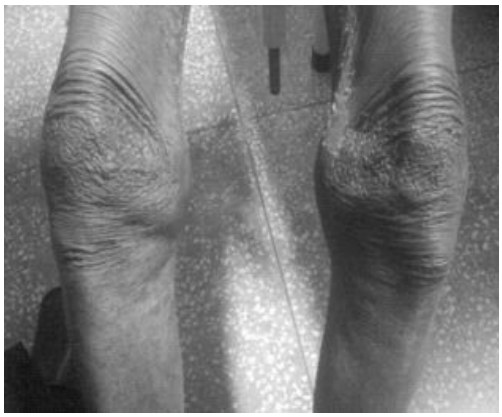

Fig. 5

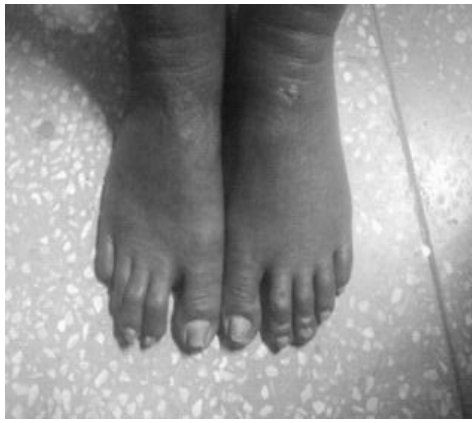

Fig. 6

Figs. 4-6: Resolution of lesions after stopping incriminating drugs

DISCUSSION

Cutaneous adverse drug reactions (CADR) are one of the commonly observed major adverse effects of first line antitubercular therapy being reported in 5.7% of tubercular patients.[8] CADR associated with antitubercular treatment include morbiliform rash, erythema multiforme syndrome, urticaria, lichenoid eruption and other more serious ones like SJ syndrome and exfoliative dermatitis.

SJ syndrome is a rare but potentially fatal complication of anti-tubercular therapy. In a review of 9,111 hospitalized patients of pulmonary tuberculosis, 25 or 0.27% developed SJ syndrome[9]. Thiacetazone was the possible causative agent in most of the cases but definitely not in all cases. In another report, anti-tubercular drugs, particularly thiacetazone, were causative agents for SJ syndrome and toxic epidermal necrosis[10].

Exfoliative dermatitis or erythroderma is an erythematous, scaly dermatitis involving most, if not all, of the skin and results in massive scaling.

In a large tertiary care centre study on CADR with antitubercular drugs, pyrazinamide was the commonest offending drug (2.38%), followed by streptomycin (1.45%), ethambutol (1.44%), rifampicin (1.23%) and isoniazid (0.98%)[8].

Majority of cutaneous hypersensivity reactions occurred within two months after the initial dose. In our case, patient developed exfoliative dermatitis by end of second month of treatment. Surprisingly, he tolerated streptomycin well while he developed reaction to Isoniazid, Rifampicin, pyrazinamide and ethambutol introduced sequentially, which is in contrast to the findings of above mentioned study.

There have been several case reports of exfoliative dermatitis with single antitubercular drugs[1-6] but to the best of our knowledge no case of cutaneous hypersensitivity to all four first line drugs has been reported.

Human Immunodeficiency Virus (HIV) infection[11], polypharmacy, advanced age, autoimmune disorders, and pre-existing renal or liver impairment were common predisposing conditions for developing cutaneous hypersensitivity reactions to antitubercular treatment. Workup of our patient revealed no other risk factor apart from elderly age.

If the cutaneous reaction is not serious, desensitization can be attempted, but in case of serious reactions, reinstitution of drug is not to be attempted. So in our case he was put on a modified regimen of streptomycin and Ofloxacin during continuation phase, which he is tolerating well.

Severe hypersensitivity reactions to standard antitubercular drugs are rare but they may be fatal. They usually commence after four to six weeks of therapy and must be recognized early to reduce associated morbidity and mortality.

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The Union Karel Styblo Public Health Prize - 2009

Dr. Behera receiving the 'The Karel Styblo Prize for Public Health - 2009' by the Union (IUATLD) at Cancun Mexico on 4.12.2009 for his contribution in the field of Tuberculosis.

Dr D. Behera, Director of the LRS Institute of Tuberculosis and Respiratory Diseases, New Delhi has been selected as the recipient of The Union Karel Styblo Public Health Prize – 2009 by the Union in recognition of his contributions in tuberculosis. He has received ICMR Awards thrice and Dr. BC Roy award twice given by the Medical council of India. Besides these, he has to his credit many more National and International awards. He has authored a Text book on Pulmonary diseases released recently. Dr Behera received the Award on 4th of December at Cancun, Mexico during the 40th Annual meeting of the International Union against Tuberculosis and Lung Diseases (the Union). He also took over as the Chairman of the Tuberculosis section of the Union.

Congratulations Dr Behera!

FORUM

The study "Long term status of TB patients" by V. V. Banu Rekha *et al* from Tuberculosis Research Centre, Chennai published in the IJT July 2009 issue, recognizes and highlights the need to widen the scope of the TB Control Programme.

The study confirms our observations in day-to-day clinical practice. We encounter patients who have persistence of symptoms after completing the full course of anti- tuberculosis treatment. Their activities are restricted due to severe impairment in pulmonary functions, thus reducing their quality of life. This is also true for patients who have musculoskeletal TB where deformities severely compromise mobility of the limbs affecting day-to-day functions and job performance which may lead to loss of income.

It is time, as the authors have aptly concluded and recommended, that programme mangers recognize and address these issues and introduce rehabilitation programmes for both Pulmonary and Extra-Pulmonary TB. In the implement of this, we should learn from the Leprosy Programme where Prevention of Disability (POD) and Rehabilitation are integral part of the NLEP.

We need to document such long term effects on a larger scale to advocate the recommendations made by the authors.

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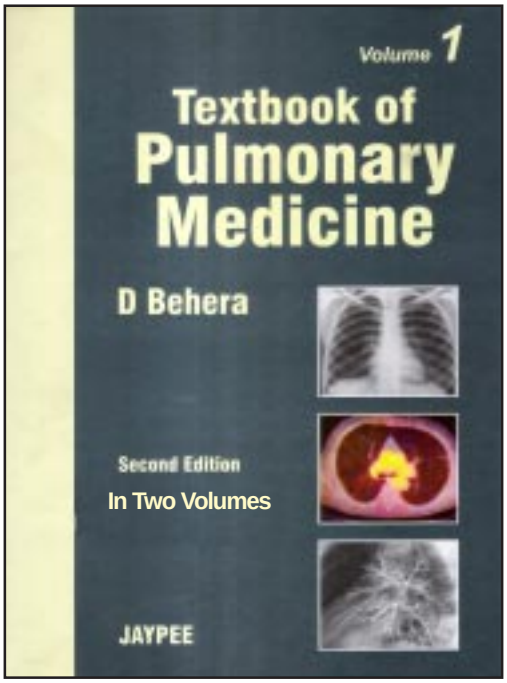
BOOK REVIEW

Textbook of Pulmonary Medicine – Second Edition, 2010; (Author) D Behera; Published by Jaypee Brothers Medical Publishers (P) Ltd., B-3, EMCA House, 23/23B, Ansari Road, Daryaganj, New Delhi-110 002; 1787 pages, 34 chapters with black and white and multi-coloured figures, tables, X-rays, etc; ISBN 978-81-8448-749-7; Price Rs. 2,995/-.



Prof. D. Behera is one of the senior-most pulmonologists. Currently, he is the Professor of Pulmonary Medicine in PGI, Chandigarh and at present he is working in LRS Institute of TB & Respiratory Diseases, New Delhi as its Director.

Authored by Dr. Behera, the publication of second edition of the Textbook of Pulmonary Medicine is a comprehensive book covering about 1787 pages in two volumes. The book includes 34 different subjects starting from "Physical Examination of the Respiratory System" and concluding with "Critical Care in Pulmonary Medicine". The publication of this book is a very good addition and shall help both undergraduate and postgraduate students of pulmonary medicine.

These two volumes contain valuable literature on Chest Medicine. This comprehensive book has been thoroughly updated with the latest available researches on different subjects. This book is well comprehended with the latest references and rich illustrations of medical and pathology sections. The various subjects on pulmonary medicine include a perfect amalgamation between laboratory diagnosis and pathogenesis. The book has tables and photographs in colour. There is extensive and vivid display of photographs (number 631) and Tables being 269 besides a number of appendices and Annexures. The chapter on Tuberculosis has a welcome inclusion of RNTCP and various guidelines of the programme. The printing quality is excellent and gives a feeling of pleasant reading.

Prof. Behera has, to his credit, several other books written by him, as for example, Bronchial asthma and Lung Cancer. This second edition of the Textbook of Pulmonary Medicine has covered almost all aspects of pulmonary medicine. The book includes all the recent developments and details of various chest diseases and various aspects of chest medicine which is now-a-days a growing speciality.

This second edition indeed covers all aspects and has a vivid coverage of all sorts of practical utility information.

I wish to recommend this book for all the persons involved in the Chest Medicine.

M.M. SINGH
EDITOR, IJT

ABSTRACTS

Comparison of Lumin™ LED fluorescent attachment, fluorescent microscopy and Ziehl-Neelsen for AFB diagnosis

A. Trusov, R.Bumgarner, R. Valijev, *et al*. *Int J Tuberc Lung Dis* 2009; **13(7)**: 836-41

This is a cross-sectional study done in Russia (*n* = 502) and Macedonia (*n* = 205), with fluorochrome-stained sputum examined by 1) the new Lumin™ light emitting diode (LED) fluorescent attachment on a light microscope, and 2) conventional fluorescent microscope (CFM) available in each laboratory, and compared to 3) Ziehl-Neelsen (ZN) restaining/reading of the same smears. Poor readings of ZN-restained smears in Russia stimulated a retrospective laboratory registry analysis for sensitivity and specificity of directly ZN-stained smears (*n* = 791) from a previous period. In Macedonia, the sensitivity of the Lumin and CFM were 87.8%, and that of restained ZN smears with conventional light microscope was 78.0%. In Russia, sensitivity was as follows: Lumin 72.8%, CFM 52.5%; re-stained ZN smears 28.5% and directly ZN stained smears 55.6%. Fluorescence microscopy is more sensitive than conventional microscopy. The Lumin attachment to conventional light microscopes provided results equal to or better than the CFMs. Smear re-staining for ZN showed a 12% advantage for Lumin and CFM in Macedonia, in line with other meta-analyses. Re-staining for ZN gave poor results in Russia for unknown reasons. Retrospective analysis of directly ZN-stained smears showed 55.6% sensitivity compared to the Lumin (72.8%), which is also in line with the superiority of fluorescent microscopy reported in literature.

Two vs. three sputum samples for microscopic detection of Tuberculosis in a high HIV prevalence population

J. Noeske, E. Dopico, G. Torrea, H. Wang and A. Van Deun. *Int J Tuberc Lung Dis* 2009; **13(7)**: 842-47

Objective was to compare the yield in bacteriologically proven tuberculosis (TB) cases examining two morning vs. three spot-morning-spot sputum specimens (MM vs. SMS) by direct microscopy for acid-fast bacilli (AFB) with the design of repeated temporal cross-over between MM and SMS sampling for successive TB suspects, using culture as gold standard. A total of 799 suspects were screened using the MM strategy, identifying 223 smear-positives, and 808 suspects with the SMS strategy, yielding 236 smear-positives. Of the MM, 256 were culture-positive, of whom 195 (76%) were smear-positive. For SMS, these figures were respectively 281 and 206 (73%), a non-significant difference. The MM and SMS strategies also detected respectively 28 and 30 smear-positive cases not confirmed by culture. No cases were lost to treatment with either strategy. In this population with a high prevalence of human immunodeficiency virus (HIV) with late case presentation, smear microscopy of two morning specimens detected at least as many positive cases as the classical strategy, and no cases were lost before treatment. Two specimens for initial TB suspect screening can thus be recommended, also without excessive workload. Comparative studies in populations presenting with paucibacillary sputum are needed to determine the equivalent quality and yield of an alternative strategy with two spot specimens at consultation.

High prevalence of *Mycobacterium tuberculosis* infection and disease in children and adolescents with type 1 Diabetes Mellitus

E.A. Webb, A.C. Hesseling, H.S. Schaaf *et al*. *Int J Tuberc Lung Dis* 2009; **13(7)**: 868-74

The objective was to describe the prevalence of tuberculosis (TB) infection and disease in children with type 1 diabetes and to investigate the association between glycaemic control and prevalence of TB infection and disease. It is a cross-sectional hospital-based study conducted at two public referral hospitals. All children and adolescents (aged <21 years) with type 1 diabetes underwent a Mantoux tuberculin skin test (≥10 mm classified as

Mycobacterium tuberculosis infection), measurement of glycosylated haemoglobin and a chest radiograph. Patients with symptoms suggestive of TB were investigated using mycobacterial culture. Radiologically and/or bacteriologically confirmed disease was classified as TB disease. Of 291 eligible patients, 258 (88.7%) were included (58% female). The prevalence of *M. tuberculosis* infection was 29.8% (95% CI 24.2-35.4); nine patients were diagnosed with prevalent TB disease (point prevalence disease 3488 per 100000 population). Poor glycaemic control (hazard ratio 1.39, 95% CI 1.18-1.63 per unit increase in glycated haemoglobin [HbA1c]) and contact with a TB source case (P = 0.0011) was associated with prevalent TB disease. There is a high prevalence of TB disease in diabetic children and adolescents in this setting. Routine TB screening of children with type 1 diabetes may be indicated in settings highly endemic for TB. Preventive treatment should be considered for diabetic children with proof of TB exposure and/or infection.

Immunophenotypic and Intracellular Cytokine Profile of Indian Patients with Tuberculosis with and without Human Immunodeficiency Virus Co-infection

A. Wanchu, A. Bhatnagar, J. Talreja, S. Sapra, B.S. Suryanarayana and P Suresh. *Indian J Chest Dis Allied Sci* 2009; **51**: 207-11

Tuberculosis (TB) occurs in more than 50% of human immunodeficiency virus (HIV) infected Indian patients. This study was carried out to determine the immunophenotypic and intracellular cytokine profile of patients with HIV-TB co-infection. Fifteen patients with HIV-TB co-infection and 15 each with TB alone and healthy individuals were studied. lmmunophenotypic analysis and intracellular cytokines were measured using appropriate antibodies on a flowcytometer. Percentage of CD3+ did not differ significantly in the three groups. The ratio of CD4+: CD8+ was reversed among patients with TB and HIV-TB.CDI9+ and CD25+ were present on fewer cells of healthy individuals but this was not statistically significant. Significantly higher percentage of cells of patients with TB and HIV-TB were CD69 positive. Interferon-gamma (INF-ã) and tumour necrosis factor-alpha (TNFá) levels are significantly reduced in the CD4+ cells of patients with HIV-TB when compared with those with TB and healthy individuals. In CD8+ cells of patients with HIV-TB, levels of TNF-á are higher when compared with the other two groups. Interleukin-2 (IL-2) producing cells were not significantly different in any of the above subsets. Monocytes in individuals with HIV-TB had significantly higher interleukin-6 (IL-6) and TNF-á. T-helper cells among patients with HIV-TB have significantly lower cytokine production. T-suppressor cells and monocytes produce more TNF-á. These findings may be significant in view of recent attempts to treat HIV-TB co-infected patients with anti-TNF therapy.

A Study of High-Sensitivity C-Reactive Protein in Bronchial Asthma

Ramesh Chandra Sahoo, Preetam Rajgopal Acharya, T.H. Noushad *et al*. *Indian J Chest Dis Allied Sci* 2009; **51**: 213-16

Relevance of C-reactive protein an acute phase reactant and a sensitive marker of low-grade systemic inflammation in bronchial asthma has not been fully studied. Objective was to evaluate the significance of high-sensitivity C-reactive protein (hs-CRP) in atopic and non-atopic asthma using an ultra sensitive assay. The levels of hs-CRP of 200 patients with bronchial asthma and 50 non-asthmatic control subjects were measured using a Latex enhanced immunoturbidimetric test. Spirometry with reversibility study, serum immunoglobulin-E (IgE) measurement and skin test for allergy was done in all the patients. There was a significant increase in hs-CRP levels with age in atopic asthmatics but no such association was observed in the non-atopic asthmatics and control subjects. The hs-CRP levels were not influenced by sex in any group. Smokers in all the three groups had a significantly higher hs-CRP levels as compared to non-smokers. Patients with asthma had higher hs-CRP values as compared to controls. Patients with non-allergic asthma had

higher mean hs-CRP as compared to atopic asthmatics and control subjects. The study suggests that there exists a certain degree of low-grade systemic inflammation in addition to the local bronchial inflammation in non-atopic asthmatics. Hence, hs-CRP may be used as a surrogate marker for the airway inflammation in non-atopic asthma patients.

Identification of environmental mycobacteria isolated from Agra, north India by conventional and molecular approaches

Deepti Parashar, Ram Das, D.S. Chauhan *et al*. *Indian J Med Res* 2009; **129**: 424-31

Several environmental mycobacteria have been shown to be important human pathogens linked to immunomodulation especially in relation to effect on vaccination. Hence identification of mycobacteria to the species level is not only relevant to patient management but also to understand epidemiology of mycobacterial diseases and effect on vaccination. We undertook this study to assess the usefulness of various conventional and molecular methods in identification of environmental mycobacterial species from Agra, north India. One hundred nineteen isolates of environmental mycobacteria were grown from 291 (116 soil and 175 water) samples. These isolates were identified by standard biochemical tests, and a simple, rapid and cost-effective in-house developed gene amplification restriction analysis targeting 16S-23S rRNA spacer and flanking region and 16S rRNA sequencing. Biochemical tests could clearly identify only 68.1 per cent (81/119) of isolates to species level. An in-house developed gene amplification-restriction analysis method could confirm the identity of 102 of 119 (85.7%) isolates and the remaining 17 isolates (14.3%) were confirmed by 16S rRNA sequencing also. These 119 environmental mycobacterial isolates, included several potentially pathogenic species such as *M. fortuitum, M. chelonae, M. avium, M marinum, M. manitobense, M. kansasii* and others belonged to nonpathogenic species, *M. terrae, M. smegmatis* and *M flavescens. M. chelonae* was isolated from water samples only whereas *M. fortuitum* was isolated from both water as well as soil samples. The in-house developed gene amplification restriction analysis method though failed to accurately identify 14.3 per cent of isolates, facilitated rapid differentiation of most of environmental mycobacteria including potential pathogens from this area and thus would have diagnostic potential in cases with NTM infections. This combination strategy using PCR-RFLP and 16S rRNA sequencing may be useful for characterization of mycobacteria from similar environmental settings from other parts of world.