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Extra-Pulmonary Tuberculosis in HIV Sero-Positive and HIV Sero-Negative Individuals

Medical Science

KEYWORDS : HIV – Human Immunodeficiency Virus, V. M. – Vaishampayan Medical College, EPTB – Extra-pulmonary Tuberculosis

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ABSTRACT

Background

A study of various presentations of extra- pulmonary tuberculosis and comparison of the spectrum of extra-pulmonary tuberculosis among HIV sero- positive and HIV sero- negative patients was carried out in the Department of Medicine, Dr. V. M. Medical College, Solapur.

Methods

A total of 200 patients diagnosed to have extra-pulmonary tuberculosis on the basis of clinical features and laboratory investigations were screened for HIV infection.

Results

Extra-pulmonary tuberculosis was more common in young individuals in the HIV-seropositive group. Male preponderance was seen in both the groups. But male: female ratio was higher in HIV-seropositive group. In HIV-seropositive group, lymph node was the most common site to be involved (45%). Pleura were the most common site of involvement in HIV-seronegative patients (66%). Central nervous system involvement was more frequent in HIV-seropositive patients (20% vs.8%).

Conclusion

Extra-pulmonary tuberculosis has a highly varied presentation in HIV-sero-positive patients with disseminated and severe forms more common in HIV-seropositive patients.

INTRODUCTION

The proportion of extra-pulmonary tuberculosis (EPTB) cases has risen due to co-infection with HIV. About 30-60% of cases with AIDS associated tuberculosis have extra-pulmonary foci . The extra-pulmonary sites commonly involved are lymphnode, pleura, genito-urinary-tract, bones & joints, meninges and peritoneum . Lymphadenitis, characteristically involving cervical chain, is the most common form of EPTB.

Diagnosis of extra-pulmonary tuberculosis is essentially clinical. Clinical impression may be complemented by imaging – X-ray, ultrasound , computed tomography(CT), magnetic resonance imaging(MRI), etc; endoscopic appearances of organ systems; microscopic exam and staining of various tissue fluids and their culture; biochemistry and cytological assessment; fine needle aspiration cytology and biopsy.

The aim of the study was to study extra- pulmonary tuberculosis and compare the spectrum of extra- pulmonary tuberculosis among HIV sero- positive and HIV sero- negative patients.

MATERIALS AND METHODS

100 cases of extra- pulmonary tuberculosis with HIV-seropositive status and 100 cases of extra-pulmonary tuberculosis with HIV-seronegative status who were either admitted or attended the outpatient clinic were studied. Detailed clinical history was taken and physical examination was done in all patients. History included presence of constitutional symptoms like fever more than 3 weeks, loss of weight more than 3 weeks, loss of appetite more than 3 weeks and other symptoms like cough, breathlessness, abdominal pain, vomiting, altered sensorium and convulsions. Patients name, age, sex, occupation, history and clinical findings were recorded according to the proforma.

Routine haematological investigations like haemoglobin estimation and erythrocyte sedimentation rate (ESR) were done in all the patients. For localised diseases, specific samples as per site of involvement were collected and all the necessary radiological investigations done. 10 ml of aspirated fluid sample was collected in a sterile test tube under all aseptic precautions. Samples were divided and sent for cytology, biochemistry, Ziehl Neelsen (ZN) stain for acid fast bacilli and culture of M.tuberculosis. Fine needle aspiration from peripheral lymph node sites (cervical and axillary) done by using 25 gauge needle under all aseptic precautions. Pus from cold abscess was aspirated with a disposable needle and syringe, mounted and staining done.

Ultrasound was useful in diagnosing ascites, hypo/hyperechoic lesions in spleen and abdominal lymphadenopathy. Barium meal and barium enema studies were done to aid in the diagnosis of small and large intestinal tuberculosis. CT head was done in patients with clinical suspicion of tuberculous meningitis and tuberculomas. Hydrocephalus, cerebral infarcts, meningeal enhancement, cerebral edema and tuberculoma were looked for.

HIV testing was done in all patients diagnosed to have extra-pulmonary tuberculosis after proper counselling with one ELISA/ Rapid/simple. Reactive samples were tested again on different system and repeated twice at six month interval.

RESULTS

100 cases of extra-pulmonary tuberculosis with HIV-seropositive status and 100 cases of HIV-seronegative status were included in the present study to evaluate extra-pulmonary tuberculosis and to compare the differences between the two groups.

Mean age (± S.D) in HIV-seropositive group was 35.2 ± 9.04 years (n=100) and 39.3 ± 18.15 years (n=100). But male: female ratio was higher in HIV-seropositive group (3:1) than in HIV-seronegative group (1.3:1). Majority of HIV-seropositive patients were labourers and drivers by occupation. Most of the HIV-seronegative patients were labourers and farmers.

Fever was the most common symptom in both the groups followed by loss of weight and appetite. Convulsions and altered sensorium were found predominantly in HIV-seropositive group. In HIV-seropositive group, lymph node was the most common site to be involved (45%). Pleura were the most common site of involvement in HIV-seronegative patients (66%). Central nervous system involvement was more frequent in HIV-seropositive patients (20% vs.8%).

Table 1 : Site of involvement in extrapulmonary tuberculosis

SITE	HIV REACTIVE (NO. OF PATIENTS)	HIV NONREACTIVE (NO. OF PATIENTS)
Pleura	36	66
Lymph node	45	15
Nervous system	20	08
Abdomen	18	22
Pericardium	8	5
Genitourinary	1	1
Skeletal	0	2
Disseminated	28	8
Miliary	1	1

Disseminated form was more common in HIV-seropositive patients (28%) than in HIV-seronegative patients (8%) ($p < 0.001$).

Hilar lymphadenopathy was a feature of HIV-seropositive patients.

In all the cases of pleural effusion, pleural fluid cytology revealed lymphocytic predominance and pleural fluid protein level was more than 3.5gram% in majority. Thus, there was no significant difference between the two groups. However pleural fluid AFB smear positivity was seen in 5 HIV-seronegative patients and none of the HIV-seropositive patients. Splenic involvement was a feature of abdominal tuberculosis affecting HIV-seropositive patients (13% vs.2%).

In CNS tuberculosis cases, CSF examination findings were similar in both the groups with lymphocytic predominance, reduced glucose and increased proteins. CT head scan findings revealed hydrocephalus as the most common sign followed by infarct secondary to vasculitis. However normal CT head scan was found in 3 HIV-seropositive patients.

Tuberculous pericardial effusion was diagnosed in 8 HIV-seropositive patients and 5 HIV-seronegative patients. All the patients had radiological evidence of cardiomegaly. On pericardial fluid examination, HIV-seropositive patients had a higher number of cells per high power field. Lymphocytic predominance and raised protein levels were common to both the groups.

Table 2: Results and distribution of samples according to site among HIV infected and non-HIV infected cases of tuberculosis.

	Pleural effusion HIV+	Pleural effusion HIV-	Ascitic fluid HIV+	Ascitic fluid HIV-	CSF HIV +	CSF HIV -	Pericardial fluid HIV+	Pericardial fluid HIV-
No. of cases	38	55	6	16	17	8	8	5
Cytology								
Lymphocyte predominant	20	32	5	9	13	6	4	2
Polymorph predominant	7	13	0	0	0	2	1	1
Equal	1	2	0	0	0	0	0	2
No cells	2	3	1	7	4	0	0	0
Biochemistry								
Cobweb	4	8	1	2	0	0	3	2
Protein(gr%)								
< 2.5	4	2	2	2	6	3	-	-
2.5 – 3.5	6	11	1	3	-	-	-	-
> 3.5	19	37	3	11	11	5	6	5
AFB seen	0	5	0	0	0	0	0	0
AFB culture positive	0	1	0	1	0	0	0	0

DISCUSSION

In our study, the mean age (± Standard Deviation) in HIV-seropositive group was 35.2 ± 9.04 years (n=100) and in HIV-seronegative group was 39.3 18 ± 15 years (n=100).Statistically, a significant difference ($p<0.05$) was found between the HIV-seropositive and HIV-seronegative groups. The male sex was more commonly affected than female sex in both HIV-seropositive and HIV-seronegative groups. But male: female ratio was 3:1 in HIV-seropositive group and 1.3 : 1 in HIV-seronegative group. Majority of patients in HIV-seropositive group were labourers and truck drivers, whereas, HIV-seronegative patients were labourers and farmers by occupation. (1-3)

Fever is the most common symptom in both HIV-seropositive (74%) and HIV-seronegative (72%) patients, loss of weight and appetite was the next common symptom. In our study, convulsions and altered sensorium were found in a higher proportion of patients in HIV-seropositive group than in HIV-seronegative group ($p<0.05$, significant). In HIV-seropositive group, lymph node was the most common site (45%) as compared to 15% in HIV-seronegative group ($p<0.001$, highly significant). Pleural involvement was seen in 36% of HIV-seropositive and 66% of HIV-seronegative patients ($p<0.001$, highly significant). (6)

Nervous system involvement was more frequent in HIV-seropositive group (20%) than HIV-seronegative group (8%). Disseminated form i.e. involvement of two or more than two extra-pulmonary sites was more common in HIV-seropositive patients (28%) than in HIV-seronegative patients(8%) which is highly significant ($p<0.001$).Cervical lymph node was the most common peripheral lymph node group in HIV-seropositive as well as HIV-seronegative patients. Cervical lymph node involvement was more common in HIV-seropositive patients (16%) than HIV-seronegative patients (5%) ($p<0.01$, very significant). Abdominal lymphadenopathy was the next common site with a higher proportion occurring in HIV-seropositive patients ($p<0.01$, very significant). (6, 7)

Radiologically, extra-pulmonary involvement was seen in 34% of HIV-seropositive patients and 45% of HIV-seronegative patients. Pulmonary with extra-pulmonary involvement was seen in 18% of HIV-seropositive and 24% of HIV-seronegative patients. There was no statistically significant difference between the two groups. Hilar lymphadenopathy was present in 8% HIV-seropositive cases and 2% of HIV-seronegative cases, which is significant ($p<0.05$). (8)

A total of 38 cases of pleural effusion in HIV-seropositive group and 55 cases in HIV-seronegative group were studied. Eight HIV reactive and five HIV non-reactive patients were non tappable. In both the groups, lymphocyte predominance was seen in cytological examination of the pleural fluid. Protein values were more than 3.5 gram% in majority of individuals in both the groups. Acid fast bacilli (AFB) were seen in direct smear examination and Ziehl-Neelsen (ZN) staining in five HIV-seronegative cases. None of the samples from HIV-positive group revealed AFB. Culture for acid fast bacilli was positive in only one sample, which was from a HIV-negative patient. AFB growth was not found in any of the sample from HIV-seropositive group. (9, 10)

In the present study, hepatomegaly was observed in 9% of HIV-seropositive patients and 6% of HIV-seronegative patients ($p > 0.05$). Splenomegaly was strikingly more common in HIV-seropositive group (13%) than in HIV-seronegative group (2%) , ($p < 0.01$), which is very significant. Ascites was seen in 10% of HIV-seropositive patients ($p < 0.01$) which is significant. In both HIV-seropositive and HIV-seronegative groups, the fluid studies showed similar findings. Lymphocyte predominance was seen in 5 out of 6 patients with ascites in HIV-seropositive group and 9 out of 16 patients in HIV-seronegative group. Protein level was more than 3.5 gram% in majority of patients. Only one specimen from HIV-seronegative group was AFB culture positive. None of the samples from HIV-seropositive group was culture positive. (9, 11)

CNS tuberculosis was diagnosed on the basis of clinical findings,

CSF studies and radiological investigations. CSF findings in both groups were similar with lymphocyte predominance in cytological studies and high protein levels on biochemical examination in the majority ($p > 0.05$) CSF culture did not reveal any growth in both the groups. CT head (contrast enhanced) was done in 14 out of 17 HIV-seropositive patients and 8 out of 8 HIV-seronegative patients. Hydrocephalus was the most common feature followed by cerebral infarcts and meningeal enhancement. Multiple tuberculomas were seen in one patient (HIV-seropositive). In three HIV-seropositive patients, CT Head revealed no abnormal finding. (12, 13, 14, 15)

A diagnosis of tuberculous pericarditis is made on the basis of clinical findings, radiological investigations and examination of pericardial fluid. In our study, there were 8 patients in HIV-seropositive group and 5 in HIV-seronegative group. All the patients had positive clinical findings of muffled heart sounds and two patients had pericardial rub. On cytological examination, HIV-seropositive patients had higher number of cells per high power field (HPF) as compared to HIV-seronegative group. Lymphocyte predominance was observed in majority of HIV-seropositive patients (4 out of 5). In HIV-seronegative group, 2 out of 5 had equal number of lymphocytes and polymorphs. In all patients, protein level was more than 3.5 gram%. Pleural fluid smear for AFB and culture for AFB did not reveal positive finding in any of the group. Radiologically, all the patients had cardiomegaly on chest radiograph. (16, 17)

CONCLUSION

EPTB was more common in young individuals in the HIV-seropositive group.

Male preponderance was seen in both the groups. But male: female ratio was higher in HIV-seropositive group (3:1) than in HIV-seronegative group (1.3:1).

In HIV-seropositive group, lymph node was the most common site to be involved. Pleura was the most common site of involvement in HIV-seronegative patients. Central nervous system involvement and disseminated form was more frequent in HIV-seropositive patients.

Thus to conclude, extra-pulmonary tuberculosis has a highly varied presentation in HIV-seropositive patients. All cases of extra-pulmonary tuberculosis should thus be screened for HIV status.

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