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CLINICORADIOLOGICAL PRESENTATION OF TUBERCULOUS MENINGITIS IN PAEDIATRIC PATIENTS

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ABSTRACT

Objectives: To know the clinicoradiological presentation of paediatric patients suffering from Tuberculous Meningitis (TBM).

Material and Methods: This was a descriptive study done on 40 patients, which was carried out in the Department of Paediatrics Khyber Teaching Hospital, Peshawar from January 2007 to December 2008. In this study suspected cases of TBM were evaluated on clinical, laboratory and radiological basis.

Results: Forty patients with TBM with age range from 8 months to 12 years were included in this study. There were 24 (60%) male and 16(40%) female patients. The mean duration of illness was 30 days (range 1 to 90 days). Fever was present in 36 (90%) patients, weight loss in 28 (70%) patients, Signs of raised intrcranial pressure in 26 (65%) patients, vomiting in 20 (50%) patients, altered consciousness in 20 (50%) patients, and headache in 16 (40%) patients. Cerebrospinal fluid findings like raised protein, low glucose and lymphocyte pleocytosis were observed in 30 (75%) patients. CSF culture was positive only in 4 (10%) patients and CSF for AFB by Ziehl-Neelsen method was present in 5 (12.5%) patients. Eighty percent of patients with TBM presented with stage 2 and 3 disease. Twenty (50%) patients died during hospital stay. Fifteen patients recovered with neurological deficit. Only 5 patients had complete recovery. The most frequent neurological sequlae observed was 6th nerve palsy (30%).

Conclusion: Presentation of TBM patients is variable. Therefore a high index of suspicion is needed. Patients must be subjected to lumbar puncture for early initiation of anti-tuberculous therapy. Immunization status of the children should be improved and education about proper follow up should be given.

Keywords: Tuberculous, Meningitis, Paediatric, Clinical, Laboratory, Cerebrospinal fluid.

INTRODUCTION

Tuberculosis is one of the most important infectious disease all over the world. The World Health Organization estimates that 1/3rd of the world population (2 billion people) are infected with mycobacterium tuberculosis, 75% of them belonging to the developing countries.[1] During 1990 among 8 million new cases, 95% occurred in the developing countries. Every year 9-10 million new cases are being added and 3 million deaths are occurring due to this disease.[2] In 1997, World Health Organization projected that prevalence of tuberculosis and consequent deaths would rise to 11 millions by the year 2000.[3] Almost 1.3 million cases and 450,000 deaths occur among children each year.[4] Moreover, the disease has assumed alarming dimensions due to emergence of multiple drug resistant tuberculosis. The problem is further being compounded by the present ongoing pandemic of acquired immunodeficiency syndrome.[5]

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Tuberculosis is highly prevalent in Asian countries. Majority of the tuberculous patients belong to the developing countries of the East and South Asian countries.[6] TBM can be diagnosed in early stages.[7] There are estimated 2.5 million cases of active tuberculosis in Pakistan.[8] Thus Pakistan is an endemic area where exposure to Mycobacterium tuberculosis is highly prevalent and tuberculosis is a continuing public health problem.

Whereas the overall pattern of tuberculous infection is similar in developed and developing countries, there is a significant difference in the age distribution. In developed countries most infected individuals belong to the older age group while in developing countries it infects young age group more.[6] Furthermore, out of 09-10 million new cases that occur each year globally, almost 4 million are non-pulmonary tuberculous infection. Tuberculous meningitis is the most serious complication of tuberculous infection.[9]

Almost all patients with tuberculous meningitis have abnormal cerebrospinal fluid result. Typically there are several hundred white blood cells in cerebrospinal fluid, the majority of which are lymphocytes. An increased protein and decreased

glucose concentration are often found. Cerebrospinal fluid/ serum glucose ratio is 20-25%.[10] 10-15ml of cerebrospinal fluid after centrifugation will yield positive acid fast staining in up to 90% of cases.[11] The definite diagnosis of tuberculous meningitis depends on the growth of the organism from cerebrospinal fluid sample, a process that requires 04-06 weeks. A variety of new and rapid diagnostic methods have been developed including cerebrospinal fluid/serum bromide ratios, adenosine deaminase levels and mycobacterial antigens and antibodies. These methods have not consistently shown the high sensitivity necessary for a useful, rapidly diagnostic tool.[11] Polymerase chain reaction based methods can he used in the rapid diagnosis of tuberculous meningitis.[12]

TBM is a serious illness often with atypical clinical, biochemical and radiological features.[13] In our study the clinical profile, laboratory and radiological features in children with suspected tuberculous meningitis and the frequency of hydrocephalus in tuberculous meningitis were studied.

MATERIAL AND METHODS

This study was conducted at the Department of Pediatrics at Khyber Teaching Hospital, Peshawar from January 2007 to December 2008. Forty cases of suspected tuberculous meningitis in children aged less than 16 years were selected from indoor patients. The diagnosis was based on history and physical examination suggestive of tuberculosis meningitis, e.g. fever, vomiting, irritability, signs of meningeal irritation, seizures, cranial nerve involvement, progressive stupor/coma. A positive contact with tuberculosis patient was included in the history. The diagnosis was supported by the following investigations: CSF findings like raised protein, low glucose and increased WBC count with predominantly lymphocytic pleocytosis. Moreover, supportive evidence for tuberculosis was based on raised ESR, reactive MT/BCG, chest x-ray suggestive of tuberculosis, positive CSF culture for AFB, and gastric lavage for Ziehl-Neelsen staining.

All patients with suspicion of tuberculous meningitis were subjected to CT brain and findings recorded. The inclusion criteria was age less than 16 years with history and clinical findings suggestive of tuberculous meningitis, positive CSF culture for AFB or positive Ziehl-Neelsen staining, basal enhancement, hydrocephalus, or tuberculoma on CT scan.

Final outcome was divided into three,

(i) Complete recovery with no residual sequelae.

(ii) Recovery with sequelae like focal motor deficit, sensory disturbances (blindness, deafness), mental retardation, seizures, hemi paresis, paraplegia.

(iii) Death.

Data collected was analyzed on SPSS 10.0. Simple frequencies were calculated for each variable.

RESULTS

Age and sex distribution of forty patients with tuberculous meningitis is shown in Table 1. The mean duration of illness was 30 days (range 1-90 days). The most frequent symptoms and signs are shown in Table 2. BCG immunisation status, history of contact with tuberculous patients, CSF findings and diagnostic BCG status is shown in Table 3.

CSF culture was positive only in 4 (10%) patients and CSF for AFB by Ziehl-Neelsen was positive in 5 (12.5%) patients. Chest X-ray and CT brain findings are shown in Table 4.

Apart from the above mentioned findings, 32 (80%) of the patients with tubreculous meningitis were presented with stage 2 and 3. Twenty patients died during hospital stay. 15 (37.5%) patients recovered with neurological deficit, while only 5 patients had complete recovery. The most frequent neurological sequela observed was 6th nerve palsy (30%).

Table 1: Age and sex Distribution

Age group	No. and Frequency Count of patients
8-12 months	2 (5%)
13-24 months	14 (35%)
25-36 months	4 (10%)
3- 6 Years	6 (15%)
6-10 Years	4 (10%)
10-12 Years	10 (25%)
Sex	
Male	24 (60%)
Female	16 (40%)

Table 2: Signs & Symptoms at Presentation

Signs and Symptoms	No. of patients and %age
Fever	36 (92%)
Weight Loss	28 (70%)
Raised intracranial pressure sign	26 (65%)
Focal neurological signs	25 (62.5%)
Fits	24 (60%)
Vomiting	20 (50%)
Drowsiness	20 (50%)
Neck stiffness	20 (50%)
Headache	16 (40%)
Cough	12 (30%)

Table 3: Status of BCG, CSF positivity and History of contact with TB

Type	Findings	No. of patients with %age
BCG vaccination	Positive	7 (17.5%)
	Negative	33 (82.5%)
History of contact	Positive	22 (55%)
	Negative	18 (45%)
Diagnostic BCG	Reactive	8 (20%)
	Non-Reactive	32 (80%)
CSF findings	Positive	30 (75%)
	Negative	10 (25%)

Table 4: Chest X-ray and CT Scan findings

Type	Findings	No. of patients with %age
Chest X-ray Findings	Clear	18 (45%)
	Increasedhilar shadowing	10 (25%)
	Bilateral soft shadow	6 (15%)
	Rt. upper lobe patch	6 (15%)
CT Scan findings	Hydrocephalus	27 (67.5%)
	Basal Enhance-ment	5 (12.5%)
	Tuberculoma	4 (10%)
	Brain Atrophy	2 (5%)
	Brain Edema	2 (5%)

DISCUSSION

Tuberculous meningitis is a serious illness that can be difficult to diagnose in a timely fashion and can cause significant morbidity and mortality. Tuberculous meningitis has never been a primary localization of tuberculous infection, rather it is disseminated from some primary extra meningeal focus, which is frequently clinically not apparent. The total number of tuberculosis cases in the world is increasing. It has been estimated that without intervention 200 million people alive today will develop tuberculosis.[14]

Before the discovery of HIV the most important determinant for the development of tuberculous meningitis was age. In population with high TB prevalence TBM differs from pulmonary and other extra pulmonary tuberculosis, in that the peak age is from 0-4 years.[15] In our study 50% of cases were between 0 and 4 years.

The variable natural history and accompanying clinical features hinders the diagnosis. No symptoms or signs are specific or characteristic for clinical diagnosis of TBM. In one study of 205 children, 38% had fever at presentation and 14% remained free from meningism throughout the illness.[16] The duration of presenting symptoms varied from 1 day to 9 months, although 55% presented with less than two weeks of symptoms. In another study of 48 cases admitted to a French intensive care unit 65% had fever, 52% had focal neurological signs and 58% had meningism.[16,17] In our study 92% had fever, 65% had signs of raised intracranial pressure, and 50% had meningism.

Recent contact with tuberculosis should be determined; several studies have shown that between 70% and 90% of children have had recent contact with tuberculosis.[18] In our study the history of contact was positive in 55% of children.

The extent to which BCG vaccination provides protection against TBM is still debated. A meta-analysis of the published trials on the efficacy of BCG vaccination suggested a protective effect of 64% against TBM.[19] Overall, these and other studies support the view that BCG vaccination is protective against TBM. In our study only 17.5% of patients had BCG scar. Normal chest radiographs are not uncommon in TBM.

Normal chest x-rays have been reported in 10-50% of cases with tuberculous meningitis.[20] In our study too, 45% cases had normal chest radiographs. The presence of extra meningeal tuberculosis can be helpful in the diagnosis of tuberculous meningitis.[21]

Tuberculin testing is of limited value. Some studies suggest that tuberculin testing may be more useful in children, with 86% having greater than 15mm of indurations with 5 units of purified protein derivative (PPD).[18] In our study it was reactive in only 20% of cases, one reason of which can be faulty technique.

Diagnosis is dependent on lumbar puncture and CSF examination. Those with depressed cell mediated immunity may have atypical findings on CSF examination.[22] Raised CSF protein occurs in most and CSF glucose will be reduced in 70%.[23] These findings were present in 75% of our cases. The search for acid-fast bacilli is the most crucial part of the investigation. Acid-fast bacilli are seen in CSF smears in about 10% to 20% of those with TBM,[24] although this figure varies considerably. Our results (10%) are consistent with these reports.

The advent of CT and MRI has provided insight into disease progression, and gives prognostic and

diagnostic information.[25,26] In a CT study of 60 cases of TBM, hydrocephalus was reported in 87% of children.[25] The incidence of hydrocephalus is greater in the young, and increases with duration of illness. In children hydrocephalus is almost always present after 6 weeks of illness.[26] In our study 27 cases (67.5%) had hydrocephalus on CT scan.

CONCLUSION

High index of suspicion is needed to diagnose tuberculous meningitis. Immunization status of children should be improved. BCG vaccination should be expanded on mass scale to reduce the morbidity and mortality of tuberculous meningitis in paediatric population.

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