ORIGINAL ARTICLE

LATERAL RECTUS PALSY: AN IMPORTANT SIGN IN DIAGNOSING TUBERCULOUS MENINGITIS

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ABSTRACT

Objective: *To find out the association of lateral rectus palsy in patients with tuberculous meningitis (TBM).*

Material and Methods: *This study was conducted at Department of Neurology, Lady Reading Hospital, Peshawar from January 2008 to December 2009 on 43 diagnosed patients of TBM. The diagnosis was made on the basis of history, clinical presentation, laboratory and radiological findings. Patients of tuberculous meningitis with or without intracranial tuberculomas or having any extra cranial tuberculosis were included while cases presenting with similar clinical picture but having non tuberculous CNS pathology were excluded from the study.*

Results: *Out of 43 patients, 27 (62.8%) patients were females and 16 (37.3) were males. The age range was from 7 years to 65 years with mean age of 36 years. Out of 43 patients, 11 (25.58%) patients were assigned stage I, 23 (53.48%) stage II and 9 (20.93%) stage III, according to Medical Research Council classification for tuberculous meningitis. Fourteen out of 43 (32.6%) were found to have unilateral or bilateral lateral rectus palsy.*

Conclusion: *The presence of recent onset lateral rectus palsy is an important sign towards the diagnosis of TBM. However more studies are needed to establish the diagnostic value of lateral rectus palsy in diagnosing TBM.*

Key words: *Lateral Rectus Palsy, Tuberculous Meningitis (TBM), Meningism, Cerebrospinal Fluid (CSF).*

This article may be cited as: Zafar A, Irfan M. Lateral rectus palsy: An important sign in diagnosing tuberculous meningitis. KUST Med J 2011; 3(1): 10-14.

INTRODUCTION

Tuberculosis (TB) is one of the major global causes of morbidity and mortality and majority of these deaths are in developing countries.[1] More than 2000 million people in the world are infected with tubercle bacilli (1/3 of world's population). The incidence of TB varies from 9 cases per 100,000 population per year in the United States to 110-165 cases per 100,000 population in the developing countries of Asia and Africa.[2-4] In 2009, the global incidence of TB was estimated as 9.4 million cases worldwide equivalent to 137 cases per 100,000 population.[1]

Tuberculous meningitis (TBM) occurs in approximately 7-12% of patients with tuberculous disease.[5] The incidence of TBM is directly related to the prevalence of TB infection in general population, which in turn is dependent on the socio-economic and hygienic conditions of the community. It accounts for 20-45% of all types of tuberculosis among children.[6] Although TBM is not uncommon in Pakistan, there is no community based study available and the published data regarding TBM in Pakistan is also very limited.[7]

TBM is a critical central nervous system (CNS) infection with serious consequences of missed or delayed diagnosis.[8] Prognosis of TBM depends on the stage of the illness (stage 1 to stage 3) at the time of diagnosis, according to British Medical Research Council criteria for severity of TBM.[9] Despite the availability of newer and rapid diagnostic and radiologic tools, TBM is always a diagnostic challenge for clinicians.[5,10,11] Due to the broad, variable and nonspecific clinical spectrum, the early diagnosis of TBM is very difficult.[10] The wide range of presentations of TBM include low grade fever, malaise, headache vomiting and signs of meningism to cranial nerve palsies, seizures and features of hydrocephalus.[10-13] Advanced cases may progresses to severe encephalopathy with mental state changes, coma and ultimately death. A high index of clinical suspicion of TBM is usually required especially in cases with absence of meningism like in elderly.[14] Although the diagnosis of TBM solely on the basis of clinical findings is not possible, still certain clinical features like cranial nerve palsies and nuchal rigidity increase the likelihood of TBM in high risk groups. Verma et al showed that cranial nerves were involved in

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Date Submitted: December 17, 2010
Date revised: June 06, 2011
Date Accepted: June 12, 2011

more than 1/3rd cases of TBM and 6th cranial nerve (32.3%) was the most commonly affected cranial nerve.[15] A unilateral or bilateral lateral rectus palsy (abducens/ 6th cranial nerve palsy) can be a false localizing sign of increased intracranial pressure caused by TBM and pontine glioma.[16,17] This study was planned to find out the association of lateral rectus palsy in patients with tuberculous meningitis.

MATERIAL AND METHODS

This prospective, observational study was conducted in Neurology Unit, Lady Reading Hospital, Peshawar from January 2008 to December 2009. All admitted patients who were diagnosed as tuberculous meningitis during the above mentioned period in Neurology Unit Lady Reading Hospital, Peshawar were included in the study. Patients who presented with clinical picture mimicking TBM but having non-tuberculous CNS pathology and those who had medial strabismus either due to birth defect or secondary to refractory error or some other pathology later in life but before the suspicion of tuberculous meningitis were excluded from the study. All patients were selected on probability convenient sampling method. All the patients underwent routine baseline investigations including blood complete picture, ESR, random blood sugar, serum electrolytes, serum urea, serum bilirubin, SGPT, Chest X-ray (PA view). Specific investigations included Sputum for acid fast bacilli (AFB), cerebrospinal fluid (CSF) routine examination and culture for mycobacterium tuberculosis, Ziehl-Nelson staining for AFB bacilli and PCR test for mycobacterium tuberculosis DNA in the cerebrospinal fluid, as well as CT and/or MRI images of brain both with and without contrast.

Cases were labeled as probable TBM either on the initial presentation of sub-acute meningitis with CSF pleocytosis, CSF protein exceeding 40mg/dl, CSF sugar less than 60% of blood sugar, negative bacterial and fungal culture and response to anti-tuberculous therapy. Evidence of tuberculosis elsewhere in the body was considered strongly supportive of the diagnosis of tuberculous meningitis (Table I).[18] Relevant data was collected on a predesigned proforma. The collected data was analyzed statistically, using SPSS windows version 14 software.

RESULTS

A total of 43 patients admitted in Neurology Department, Lady Reading Hospital, Peshawar were diagnosed AS tuberculous meningitis over a study period of 2 years. Out of 43 patients, 27 (62.8%) were female and 16 (37.2%) were male patients. The age ranged from 7 years to 65 years with mean age of 36 years. Patients were symptomatic for a period ranging from 10 days to 16 weeks. Out of 43 patients with TBM, 9 (20.9%) had been receiving anti-tuberculous therapy before admission, 7 (16.3%) patients were suffering from pulmonary tuberculosis with CNS involvement as extra pulmonary complication. Only 3 (7%) patients had a positive culture for Mycobacterium Tuberculosis, either in sputum or CSF. These were diagnosed as definite cases of tuberculous disease. Eleven patients (25.6%) were assigned stage I, 23 (53.5%) stage II and 9 (20.9%) stage III, according to medical Research Council classification for tuberculous meningitis (Table II).[9]

In our study, the common presenting complaints were malaise (n=40), anorexia (n=38) and headache

DIAGNOSTIC CRITERIA FOR TUBERCULOUS MENINGITIS[18]

Clinical	Fever & headache (for more than 14 days)
	Vomiting
	Altered sensorium or focal neurological deficits
Cerebro Spinal Fluid	Pleocytosis (more than 20 cells, more than 60% lymphocytes)
	Increased proteins (more than 100mg/dl)
	Low sugar (less than 60% of corresponding blood sugar)
	India ink studies and microscopy for malignant cells should be negative
Imaging	Exudates in basal cisterns or in Sylvain fissure hydrocephalus
	Infarcts (basal ganglionic)
	Gyral enhancement
	Tuberculoma formation
Evidence of tuberculosis elsewhere	

Table I

CLINICAL STAGES OF TUBERCULOUS MENINGITIS

Stage	Neurological syndrome	Frequency (n=43)
Stage I (early)	Nonspecific (e.g. generalized malaise, fever, anorexia)	11 (25.4%)
Stage II (Intermediate)	Lethargy	23 (53.5%)
	Meningism	
	Moderate focal neurological deficits (e.g. cranial nerve palsies)	
Stage III (Advanced)	Seizures	9 (20.9%)
	Severe neurological deficits (e.g. paresis)	
	Stupor or coma	

Table II

CHARACTERISTICS OF PATIENTS WITH TUBERCULOUS MENINGITIS

Characteristics	Frequency
• Total No. of patients with TBM	• 43
• Male	• 16 (37.2%)
• Female	• 27 (62.8%)
• Presenting complaints	• Malaise (n=40; 93%)
	• Anorexia (n=38; 88.4%)
	• Headache (n=35; 81.4%)
	• Fever (n=28; 65.1%)
	• Vomiting (n=22, 51.2%)
• Signs	• Meningism (n=35; 81.4%)
	• Hyper pyrexia (n=28; 65.1%)
	• Cranial Nerve Palsies (n=20; 46.5%)
	• Abducens (6^{th}) nerve palsy= (n=14; 32.6%)*Unilateral (n=10; 23.3%)Bilateral (n=4; 9.3%)Isolated 6^{th} nerve palsy (n=8; 18.6%)6^{th} nerve with other cranial nerves palsies (n=6; 13.9%)*
	• Alteration in Consciousness (n=9; 20.9%)
	• Papilledema (n=9; 20.9%)

Table III

(n=35) while most common signs were meningism (n=35), fever (n=28) and cranial nerve palsies (n=20) {table 3}. The most frequently involved cranial nerve was abducens (sixth) nerve which supplies the ipsilateral lateral rectus muscle of the eye ball and is responsible for abduction of the ipsilateral eye. Sixth nerve palsy was observed in 14 out of 43 (32.6%) patients with 10 patients having unilateral palsy and 4 patients with bilateral lateral rectus palsy. Eight patients with lateral rectus palsy were in stage II while six patients were in stage III. Six patients out of these 14 patients had multiple cranial nerve palsies besides having abducent nerve palsy while 8 patients had isolated abducens nerve palsy.

DISCUSSION

TBM is a life threatening and most severe form of extra-pulmonary tuberculosis which is associated with increased mortality and morbidity in developing nations.[19] The worst outcome of TBM is mainly due to delay in the diagnosis of TBM because of variable clinical presentation and the poor sensitivity and specificity of the available diagnostic tests.[20] Thwaites GE et al showed acid-fast bacillus (AFB) stain positivity in only 58% and culture for Mycobacterium tuberculosis in 71% of cases with TBM.[21] Sengoz G et al isolated Mycobacterium tuberculosis from CSF in 43% patients.[22] Malik ZI et al showed

positive smear AFB for CSF and sputum as low as 6.6% in cases of TBM.[23] Missing the diagnosis of TBM will deprive these patients of anti-tubercular therapy (ATT) which can be curative if timely given.

In our study, TBM was more common in females and mean age was 37 years. Other studies have shown increased frequency of TBM in males as compared to females.[20,23,24] Mean age was reported from 28.5 years,[20] to 46 years.[24] The common presenting complaints in our study were malaise (93%), anorexia (88.4%), headache (81.4%), fever (65.1%) and vomiting (51.2%). Malik ZI[23] had headache (86.7%), fever (80%), vomiting (76.7%) and anorexia (30%); while Sengoz G et al[22] showed that headache, alteration in consciousness and fever were the common presentation of TBM. Common signs observed in our study were meningism (81.4%), cranial nerve palsies (46.5%), papilledema *(*20.9%) altered conscious level (20.9%). The signs of meningism were not present in all patients (81.4%). This observation was also documented by Malik ZI[23] (90%), Verdon R[24] (88%), Thwaites GE et al[25] (91%), Yaramýþ H et al[26] (78%). Altered level of consciousness, observed in about 21% cases of our study is much lower than other studies.[23,25,26] Majority of our patients were in MRC stage II (53.5%) and stage 1(25.6%) only 20.9% were in stage III. These findings are consistent with other studies showing 53-64% patients in stage II and 13-23% in stage III.[22,23,27] However some studies showed majority of patients (60-62%) in stage III at presentation.[24,28] Our study favours the observation of Malik ZI[23] that the variations in the MRC stages at presentation are an important outcome measure.

Cranial nerve palsies occur in 20-30% of patients and may be the presenting manifestation of tuberculous meningitis.[29] According to Komolafe MA et al,[30] some gelatinous exudates are formed in TBM which settle at the base of the brain causing CNS pathologies through cerebral vasculitis, blockage of CSF pathways (hydrocephalus) and entrapment of cranial nerves. Third and sixth cranial nerves with their longest intracranial course are the most vulnerable ones. The sixth cranial nerve is usually involved first and is the most frequently affected.[31] The sixth cranial nerve also known as the abducens nerve, innervates the ipsilateral lateral rectus muscle which functions to abduct the ipsilateral eye. Patients with abducens nerve palsy usually present with binocular horizontal diplopia (double vision producing a side-by-side image with both eyes open) and esotropia (convergent squint) in primary gaze. Common causes of sixth nerve palsy are aneurysms, diabetic neuropathy, raised intracranial pressure, infections (meningitis or sinusitis), infarction, trauma, tumours.

In our case series of patients with tuberculous meningitis over a study period of 2 years, multiple cranial nerves including 3rd, 4th and 6th were found in 46.5% cases and 32.6% (n=14/43) patients had either unilateral or bilateral sixth nerve palsy. Other studies have also reported cranial nerve palsies in 31.3[24] and 22%[25] cases of TBM. In a case series by Tan CB, abducens nerve palsy was seen in 4 out of 7 cranial nerve palsies.[32] While in another study, amongst 96 patients with tuberculous meningitis, 6th nerve palsy was the most frequently observed in 25 patients (26%)[33]. In another case series of 45 patients with tuberculous meningitis cranial nerve palsies were noted in 5 (11.1 %) patients, with unilateral sixth nerve palsy in 3 patients, bilateral sixth nerve palsy in 1 patient and unilateral 3rd nerve palsy in 1 patient.[13] Reddy found abducens nerve palsy in 8 out of 30 cases of TBM.[34] Amitava AK however reported optic nerve to be the most commonly involved cranial nerve in tuberculous meningoencephalitis.[35] In a case series Bateman observed papilledema or ocular palsies in up to 20% of patients with this condition.[36] While Davis and Rastogi, et al reported cranial nerve palsies in up to 19% of patients with tuberculous meningitis.[37]

Outcome of TBM depends on the stage at which the ATT is initiated.[38] The vague clinical presentations and poor accuracy of available diagnostic tests are responsible for delayed diagnosis and hence delayed initiation of ATT. [20-23] The presence of recent onset lateral rectus palsy in patients with history of low grade fever, headache, alteration in mental status and meningism is an important although not a pathognomonic sign that can help in the diagnosis of tuberculous meningitis. Due to the high prevalence of tuberculosis in our community, treatment is often started empirically on the clinical suspicion of tuberculous meningitis because any delay in treatment results in significant morbidity, and failure to treat is associated with a high case-fatality rate. However, more research is needed in early clinical as well as laboratory diagnosis of TBM, to reduce the worst outcome of this serious neurological disease.

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CONFLICT OF INTEREST

Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE

NONE DECLARED