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Original Research Article

Cranial nerve involvement: its role in intracranial tuberculosis

Baiakmenlang Synmon[1]*, Ashok Kayal[2]

[1]Department of Neurology, NEIGRIHMS, Shillong, Meghalaya, India
[2]Department of Neurology, Apollo Hospital, Guwahati, Assam, India

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***Correspondence:**
Dr. Baiakmenlang Synmon,
E-mail: baiakmenlangsynmon@gmail.com

ABSTRACT

Background: Tubercular meningitis is the most severe form of extra pulmonary involvement. Lack of specific and sensitive test calls for a multi-displinary and combined approach to make the diagnosis at the earliest. Various factors guide us to the etiology of meningoencephalitis but cranial nerve involvement has the highest predictive value.
Methods: A prospective study from August 2013 to September 2015 carried in GMCH, Guwahati where 93 patients of intracranial tuberculosis was included.
Results: This present study comprised of 36 females (38.7%) and 57 males (61.3%) with a mean age of 32.3±17.05 and a range of 2-72 years. The typical clinicalfeatures of meningitis was found in 78.6%. Focal neurological deficit and cranial nerve involvement was seen in 40 (43%) and 58 (62.4%) respectively. Among the cranial nerves (CN), the most commonly involved is the 2nd CN seen in 33 (35.5%), followed by 6th (16.1%), 7th (11.8%), 3rd (7.5%), 8th (3.2%), 9th and 10th, (2.2%) 4th (1.1%) and 5th (1.1%). Six patients developed visual loss and two patients hearing loss as sequelae. The presence of cranial nerve involvement and focal neurological deficit was shown to be associated with a poor prognosis (p value=0.04**, significant; Fisher's exact test).
Conclusions: Bedside clinical examination of patients of meningoencephalitis to detect cranial nerve involvement will definitely help us with the diagnosis and prognosis of tubercular meningitis.

Keywords: Cranial nerve involvement, Tubercular meningitis

INTRODUCTION

India is one of the highest Tuberculosis (TB) burden bearing country according to World Health Organization (WHO) statistics for 2011. Tubercular meningitis being the most severe form of extra pulmonary involvement whose mortality and morbidity is close to half of the patient's affected.[1] The cornerstone in the diagnosis of intracranial tuberculosis is the detection of tubercle bacilli in cerebrospinal fluid or tissue biopsy which is highly specific (98%) but less sensitive (20-55%). So a combined and multi-displinary approach is required for making its diagnosis at the earliest. Various clinical findings help us in differentiating tubercular meningitis from other meningitis. Duration of symptom, altered sensorium at presentation, seizure, focal neurological deficit and cranial nerve involvement helps us to differentiate the various causes of meningo-encephalitis. Among those mentioned above only cranial nerve involvement has shown to have a positive predictive factor with odd ratio of 1.980(1.161-3.376) with a P value of 0.006. [2]

Cranial nerve involvement shows a positive predictive value in making the diagnosis of TBM and differentiating it from acute bacterial meningitis and is also an important

predictor of poor outcome.[3,4] With this in mind we aim to study the various cranial nerve involvement in intracranial tuberculosis.

METHODS

A prospective study carried in GMCH hospital Guwahati from August 2013 to September 2015. Ninety three (93) patients of intracranial tuberculosis were included in the study. The diagnosis was made based on a combination of clinical criteria, laboratory findings and Neuroimaging findings.

Detail history, clinical examination, blood investigation, radiograph and ultrasonograpghy (USG) whole abdomen was done in all the patients. HIV and other viral markers were tested. Cerebrospinal fluid (CSF) analysis like cell count, protein, sugar, adenosine level (ADA), acid fast bacilli (AFB), gram and fungal stains, cryptococcal antigen, culture and PCR study to confirm tuberculosis and to exclude other infection was done. CSF culture was done by automated BACTEC MGIT 960 system, designed for the rapid and optimal detection of mycobacterium. Associated test of AFB-Xpert panel were used for detection of rifampicin resistance. PCR study which is a nucleic amplification technique was done using MYCOREAL Real time PCR method. Neuroimaging (CT head or MRI or both) was obtained in all patients. The patients were graded by Glasgow coma scale (GCS) and clinical stages according to British Medical Research Council (MRC):[5]

The patients were treated with conventional ATT regimen, steroid & anti epileptics; they were followed up and outcome was noted. Outcome was divided into three groups, death, neurological sequelae and complete recovery. An attempt was made to analyze the various cranial nerve involved and their effect on the prognosis of these patients.

Statistical methods

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max), standard error of mean (SEM) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

RESULTS

This present study comprised of 36 females (38.7%) and 57 males (61.3%) having a male to female ratio of 1.6:1. The common clinical feature noted was headache (90.3%), fever (84.9%) and meningeal sign (81.7%). The typical picture of meningitis (fever, headache and signs of meningeal irritation) was found in 78.6%. Focal neurological deficit (hemi paresis, paraparesis and ataxia) and cranial nerve involvement was seen in 40 (43%) and 58 (62.4%) respectively.

Table 1: Number of patient with various cranial nerve involvements.

Cranial nerves	Gender		Total (n=93)
	Female (n=36)	Male (n=57)	
2nd	14 (38.9%)	19 (33.3%)	33 (35.5%)
3rd	4 (11%)	3 (5.3%)	7 (7.5%)
4th	1 (2.8%)	0 (0%)	1 (1.1%)
5th	1 (2.8%)	0 (0%)	1 (1.1%)
6th	9 (25%)	6 (10.5%)	15 (16.1%)
7th	9 (25%)	2 (3.5%)	11 (11.8%)
8th	2 (5.6%)	1 (1.8%)	3 (3.2%)
9th and 10th	1 (2.8%)	1 (1.8%)	2 (2.2%)

Table 2: Clinical features and examination according to outcome.

Clinical features and examination	Outcome			Total (n=93)	P value
	Death (n=25)	Sequelae (n=38)	Complete Recovery (n=30)		
Fever	21 (26.6%)	36 (45.6%)	22 (27.8%)	79 (84.9%)	0.058
Headache	22 (26.2%)	34 (40.5%)	28 (33.3%)	84 (90.3%)	0.713
Seizure	8 (21.6%)	15 (40.5%)	14 (37.8%)	37 (29.8%)	0.373
Altered Sensorium	19 (30.2%)	27 (42.9%)	17 (27%)	63 (67.7%)	0.154
Focal neurological deficit	7 (19.4%)	22 (61.1%)	7 (19.4%)	36 (38.7%)	0.042**
cranial nerves	18 (31%)	26 (44.8%)	14 (24.1%)	58 (62.4%)	0.040**
Meningeal sign	20 (26.3%)	34 (44.7%)	22 (28.9%)	76 (81.7%)	0.162

Fischer's Exact test applied

Among the cranial nerves (CN), (Table 1) the most commonly involved is the 2nd CN seen in 33 (35.5%), followed by 6th (16.1%), 7th (11.8%), 3rd (7.5%), 8th (3.2%), 9th&10th, (2.2%) 4th (1.1%) and 5th (1.1%).

Six patients developed visual loss as sequelae due to secondary optic atrophy, primary (vascular) optic atrophy, opticochiasmaitic arachnoiditis, occipital lobe infarct and uveitis two patients develop hearing loss as sequelae due to vasculitis.

The presence of cranial nerve involvement and focal neurological deficit was shown to be associated with a bad outcome (p value=0.04**, significant; Fisher's exact test).

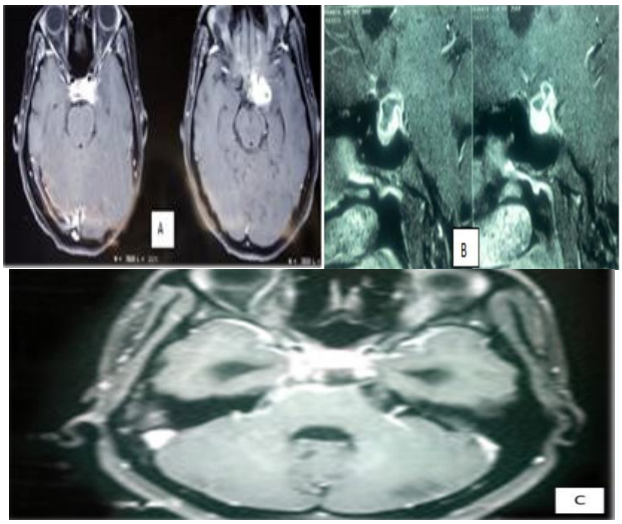

Figure 1: MRI brain of patients. A) Axial section MRI brain l T1 contrast study showing a conglomerated heterogenous rim, nodular enhancing lesion in the left parasellar region with dense enhancing basal exuduates encasing the ipsilateral internal carotid artery. B) Saggital section MRI brain T1 contrast study showing ring enhancing lesion involving optic chiasma with enhancement of supra cellar structure. C)Axial section of MRI brain T1 Contrast study showing exudates across base of brain ,optico chiasmatic arachodinitis along with dialation of temporal horn of lateral ventricles and fourth ventricle.

CT scan of head plain and contrast was done in all patients showing abnormality in 67 patients. Hydrocephalus was seen in 29(31.2%), infarct in 12(12.9%), ring enhancing lesion in 24(25.8%) and basal exudates and meningeal enhancement in 11(11.8%) patients. MRI brain (plain, contrast with MRS) was done in 47 patients. Basal exudates were seen in 24(25.8%), infarct in 8 (8.6%), hydrocephalus in 16(17.2%), abscess in 3(3.2%), tuberculoma in 35(37.6%) and brain oedema in 31(33.3%) patients. Optico-chiasmaticarachadonitis (Figure c) was seen in 2 patients.

Total 25 patients (26.9%) died and 38 patients (40.9%) developed neurological sequelae like hemiparesis, paraparesis, visual loss and hearing loss. The presence of hyponatremia, co-infection, development of complication like brain oedema, vasculitis, hydrocephalus, a low Glasgow scale of <10, MRC stage 2& 3, focal neurological deficit and cranial nerve involvement were associated with poor outcome but statically significant results are seen with the presence of cranial nerve deficit or focal neurological deficit (P=0.04) vasculitis (P<0.05), low GCS (P=0.004), and MRC grade 2&3 (P=0.001).

DISCUSSION

Cranial nerve palsy is seen in 20-30% of TBM cases, if optic neuropathy and visual impairments were included the percentage would go up higher. The most common is the sixth cranial palsy (after excluding optic nerve) which is similar in our findings.

Our study documented cranial nerve involvement in 58 cases (62.4%) as a presenting feature or as a complication during the course of the disease. The most common cranial nerve involved was 2nd (35.5%) followed by 6th (16.1%). The others seen were 7th, 3rd, 8th, 9th&10th, 4th and 5th. Hearing loss was seen in 2 patients and vision loss in 6 patients.

Sharma et al in 2011 evaluated 158 adults of tubercular meningitis, to see the incidence, predictors and prognostic value of cranial nerve involvement. He concluded that 60(38%) patients had cranial neuropathy; the most common was abducent nerve. Sixteen patients had involvement of two or more cranial nerves. Age >25 years, presence of vomiting, altered sensorium, diplopia, papilloedema, hemiparesis, meningeal irritation signs, severe functional disability, CSF protein >2.5gm/l, cell count >100/mm, optochiasmatic arachnoiditis and hydrocephalus are important predictors of cranial nerve involvement. The presence of cranial neuropathy was associated with a poor outcome.[4]

In our present study, the presence of cranial nerve involvement and focal neurological deficit was shown to be associated with a poor outcome (p value=0.04**, significant; Fisher's exact test- Table 2).

A retrospective study carried in Iran over 14 years (Ali et al, 2013) had noted cranial nerve palsy in 38 (35.5%) patients out of 109 TBM patients. Multi-variate logistic regression analysis had shown a positive predictive effect of cranial nerve palsy on diagnosis of TBM and a negative predictive effect of neck stiffness in comparison to acute bacterial meningitis. He concluded that Cranial nerve palsies has not only been a predictive factor for neurological sequelae but also the most important neurological factor to differentiate TBM from acute bacterial meningitis.[3]

Optic nerve involvement and abnormality is common with vision loss sequelae being a devastating clinical feature in tuberculosis.[6] In our study, 2nd cranial nerve involvement was seen in 33 (35.5%) patients in the form of decreased visual acuity. Six patients developed visual loss as sequelae; most common cause being secondary optic atrophy, other causes were primary (vascular) optic atrophy, optochiasmatic arachnoiditis, occipital lobe infarct and uveitis. The incidence of vision impairment in CNS TB varied from 27 to 72% in different studies. It may result from optochiasmatic arachnoiditis, compression of optic nerve or optic chiasma by tuberculoma, optic nerve granuloma, optic neuropathy caused by vascular cause, optic neuritis associated with anti tubercular therapy (ethambutol, sometimes isoniazid), secondary to hydrocephalus and raised intracranial tension, bilateral occipital infarcts due to vasculitis and chorioretinitis and local cause like uveitis.[7] Increase CSF protein was noted to be a predictive factor in vision impairment. Fundus examination may reveal secondary and primary optic atrophy (rare), papilloedema, neuroretinitis and choroid tubercles which are patho-gnomic of tuberculosis. Sinha et al in 2010 evaluated 101 patients of TBM for visual status over a period of 6 months. He found 27 patients with impaired vision at the end of his studies and concluded that papilloedema, markedly raised CSF protein (>1g/l), cranial nerve palsies and optochiasmatic arachnoiditis on MRI were predictors of visual deterioration in TBM.[8] Aaron et al reported a figure of 14% of optochiasmatic arachnoiditis and that young women having high CSF protein values are at risk of developing it.[9]

CONCLUSION

Cranial nerve involvement in intracranial tuberculosis can be a presenting feature or a complication of the disease process. Apart from being a predictor of poor outcome, cranial nerve involvement also shows a significant predictive value in differentiating TBM from another bacterial meningitis.

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