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Original Research Article

Study of neurological deficits in patients with tuberculous meningitis and its association with urodynamic study

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ABSTRACT

Background: Tuberculous meningitis (TBM) is the main form of tuberculosis that affects the central nervous system and is associated with high rates of death and disability. The objective of this study was to study neurological symptoms in TBM patients using clinical diagnosis and MRI of spine and comparing with urodynamic study.
Methods: Fifty one patients diagnosed with TBM were studied in Neurology Department of KGM Medical University, Lucknow. Uroflowmetry and urodynamic study were done to divide the patients into normal and abnormal. A detailed history taking, general physical and neurological examination using MRI spinal cord was done and recorded on a predesigned proforma.
Results: Visual impairment, hemiparesis, paraparesis, abnormal tone and reflexes in lower limbs showed significant association with abnormality in urodynamic study. MRI spine showed significant relationship of spinal meningeal enhancement, lumbosacral arachnoiditis, with abnormal urodynamic study.
Conclusions: We found a significant association between neurological symptoms and abnormal urodynamic study.

Keywords: Hemiparesis, Meningeal enhancement, Tuberculosis meningitis, Uroflowmetry

INTRODUCTION

In 2015 a total 10.4 million peoples were diagnosed with Tuberculosis (TB). World Health Organization has run a program under the banner of "End TB Strategy" which aims at reducing TB-related deaths by 90% and TB incidence rate by 80% by 2030.

However, the incidence rates are still high which offers the ongoing evolving challenges faced in the prevention and treatment of tuberculosis.[1]

Tuberculosis meningitis (TBM) is the severe form of TB with highest mortality recorded among the children and individual with HIV-1 co-infection.[2,3] Hydrocephalus and cerebral vasculitis are the major complications of TBM which make the treatment complex.

The meningitic process may affect the cranial cerebrospinal fluid (CSF) pathway, the spinal subarachnoid pathway or both. Spinal tuberculous meningitis (STBM) usually occurs due to caudal extension of intracranial tuberculous basal meningitis, although spinal cord may be involved with parenchymal TB myelitis and tuberculoma formation rarely.[4] TBM usually presents as a chronic cranial meningitic syndrome with headache and fever being cardinal features. The spinal meningitis form is less frequent and may lead to

spinal arachnoiditis. Diagnosis of spinal arachnoiditis by MRI is possible even before symptom and signs develop.[5] The symptoms of arachnoiditis are constant low back pain usually radiating into both legs, and motor and sensory symptoms in the legs. Symptomatic bladder dysfunction is infrequent except in advanced cases.

Early diagnosis of these cases is extremely important because timely institution of proper medical treatment may ensure good recovery.[6] It is usually based on clinical features, CSF analysis, evidence of tuberculosis elsewhere in the body, especially meningitis, and characteristic imaging findings. But data of subclinical bladder dysfunction and arachnoiditis in patients of tuberculous meningitis is still lacking in existing literature and have not been evaluated so far in TBM by sensitive MRI and urodynamic studies. Hence in present study we tried to study the neurological symptoms in TBM patients using clinical diagnosis and MRI of spine.

METHODS

Fifty one TBM patients were studied who were attending Neurology OPD and indoor patients of GM and associated hospital of KGM Medical University, Lucknow.

All newly diagnosed cases of TBM fulfilling consensus diagnostic criteria of TBM as described by Marais et al, 2010 were included.[3]

For defining TBM two criterion were used (A; Clinical entry criteria plus one or more of the following: acid-fast bacilli seen in the CSF; *Mycobacterium tuberculosis* cultured from the CSF; or a CSF positive commercial nucleic acid amplification test, B; Acid-fast bacilli seen in the context of histological changes consistent with tuberculosis in the brain or spinal cord with suggestive symptoms or signs and CSF). Patients having local causes of bladder dysfunction (e.g. Cystitis, BPH, stress incontinence) and patients having compressive myelopathy due to vertebral tuberculosis (Pott's spine) or PIVD , stuporous and comatose patients (who were not able to follow commands in urodynamic study) and patients with more than 30 days of antituberculous chemotherapy were excluded from study. Written informed consent in Hindi/English to participate in the study was taken from the patient or the guardian/ relatives, prior to enrollment. The study was approved by the Institutional Ethics Committee, KGM Medical University. A detailed history taking, general physical and neurological examination was done and recorded on a predesigned proforma.

MRI spinal cord (focus on LS region)

MRI spinal cord (focus on LS region) with Gadolinium contrast was performed in all patients using 1.5 tesla GE MRI machine at baseline. MRI spine with Gad was done with screening of whole spine and detailed study on LS spine with fat suppressed images were studied for presence of lumbosacral arachnoiditis, meningeal enhancement, obliteration of the spinal subarachnoid space, CSF loculation, myelitis, tuberculoma and syrinx. Lumbosacral arachnoiditis was classified according to Delamarter's MRI classification.

Uroflowmetry and urodynamic study

Uroflowmetry was done in all patients at department of urology. It was done in standing position when possible, otherwise in sitting position. Maximum and average flow rates were measured. Machine used in uroflowmetry was Medtronic Duet Logic G. Residual volume was measured by catheterisation. Medium fill water cystometry was performed on all the patients with all aseptic precautions. Triple lumen catheter was used. One lumen was used to fill bladder and one for measuring vesicle pressure. During filling phase first desire, normal desire, strong desire, urgency and bladder capacity were noted. EMG activity was noted.

On cystometrogram urinary flow rate, abdominal pressure, vesicle pressure graph recorded. And also, the derived pressure i.e. detrusor pressure graph was recorded. All volumes and pressures were measured in millilitre and centimetre of water. The normal range of urodynamic studies were residual urinary volume <30 ml; first desire to void (FDV) >100 ml but <300 ml, and maximum desire to void (MDV) >200 ml but <600 ml. Increased FDV, or MDV, or both indicates disturbed bladder sensation. The methods and definitions used for the urodynamic studies conformed to the standards proposed by the International Continence Society. An abnormal bladder-filling phase was indicated by detrusor (bladder) overactivity (i.e., involuntary phasic bladder contractions) and low compliance detrusor (or involuntary tonic bladder contractions with detrusor contraction/detrusor pressure rise <20 ml/cmH2O). An abnormal bladder-voiding phase was indicated by detrusor acontractility (i.e. the inability to contract the detrusor and produce urinary flow/ low flow) or underactive detrusor. Detrusor underactivity is defined as a detrusor contraction of inadequate magnitude and/or duration to effect complete bladder emptying in the absence of urethral obstruction. Detrusor sphincter dyssynergia was defined as a detrusor contraction concurrent with an involuntary contraction of the urethral and/or periurethral striated muscle. First sensation of filling/desire to void occurred at approximately 50% of cytometric capacity. Normal desire to void was defined as the feeling that leads the patient to pass urine at the next convenient moment, but voiding can be delayed if necessary. It is felt at about 75% of cystometric capacity. Strong desire to void- This was defined as a persistent desire to void without the fear of leakage. It is felt at approximately 90% capacity.

The statistical analysis was performed with the use of Statistical Package for Social Sciences, Version 20.0 for

Windows (SPSS, Chicago, IL, USA) and Microsoft Excel. Predictors were identified using univariate and multivariate analysis.

Univariate analysis was performed by Chi-square test for non-parametric data and student's "t" test for independent variables for parametric data and relative risks with 95% confidence interval were ascertained. For multivariate analysis, binary logistic regression was performed to see the significance of results. Kaplan-Meier analysis was performed to estimate the event free survival for the outcome with or without urodynamic abnormality using to Log Rank test. Statistical significance was defined at a p value of < 0.05 and wherever analysis was done it was two-tailed.

RESULTS

Mean age of study cohort was 28.5±13.34 years with Male: Female of 29:22. Mean duration of illness (days) was 71.7+52.9. History of tuberculosis was present in 11 (21.5%) patients out of 51.

Table 1: Neurological deficits in patients of TBM.

Neurological Symptoms	Normal urodynamic study (n=15)	Abnormal urodynamic study (n=36)	Total (n=51)	χ^2, p value
Meningeal signs	9 (60)	34 (94.4)	43 (84.3)	5.525, 0.002
Visual impairment	0 (0)	9 (25)	9 (17.6)	4.554, 0.033
Papilloedema	6 (40)	13 (36.1)	19 (37.3)	0.027, 0.870
Cranial nerve involvement	8 (53.3)	12 (33.3)	20 (39.2)	0.069, 0.794
Hemiparesis	1 (6.6)	14 (38.8)	15 (29.4)	5.295, 0.021
Wasting LL	1 (6.6)	6 (16.6)	7 (13.7)	0.894, 0.344
Paraparesis	0 (0)	9 (25)	9 (17.6)	4.554, 0.033
Tone abnormal	0 (0)	18 (50)	18 (35.2)	11.591, 0.001
Increased	0 (0)	11 (30.5)	11 (21.5)	3.381, 0.066
Decreased	0 (0)	7 (19.4)	7 (13.7)	5.844, 0.016
Reflexes abn	3 (20)	25 (69.4)	28 (54.9)	12.24, 0.002
Hyporeflexic	0 (0)	15 (41.7)	15 (29.4)	8.854, 0.003
Hyperreflexic	3 (60)	10 (27.8)	13 (25.5)	0.337, 0.561

Out of 36 patients who had abnormal urodynamic study, 34 (94.4%) had meningeal signs, 9 (25%) had Visual impairment, 13 (36.1%) had papilloedema, 12 (33.3%) had cranial nerve involvement, 14 (38.8%) had hemiparesis, 6 (16.6%) had wasting LL and 9 (25%) had paraparesis. Authors found that visual impairment (p=0.033), hemiparesis (p=0.021), paraparesis (p=0.033), abnormal tone (p=0.001) and reflexes (p=0.002) in lower limbs showed significant association with abnormality in urodynamic study (Table 1).

Out of 36 patients who had abnormal urodynamic study spinal meningeal enhancement was present in 32 (88.8%), lumbosacral arachnoiditis in 22 (61.1%), myelitis in 10 (27.8%), CSF loculations in 6 (16.6%), Cord atrophy in 5 (13.9%), cord tuberculoma in 2 (5.6%) and syrinx in 1 (2.8%) patients. MRI spine showed significant relationship of spinal meningeal enhancement (p<0.001) and lumbosacral arachnoiditis (p=0.007) with abnormal urodynamic study (Table 2).

Table 2: MRI spine findings (neurological symptoms) in patients of TBM.

Neurological Symptoms	Normal urodynamic study(n=15)	Abnormal urodynamic study(n=36)	Total (n=51)	χ^2, p value
Spinal meningeal enhancement	5 (33.3)	32 (88.8)	37 (72.5)	16.409, <0.001
Lumbosacral arachnoiditis	3 (20)	22 (61.1)	25 (49)	7.161, 0.007
Myelitis	2 (13.3)	10 (27.8)	12 (23.5)	1.228, 0.268
CSF loculations	0 (0)	6 (16.6)	6 (11.8)	2.833, 0.092
Cord atrophy	0 (0)	5 (13.9)	5 (9.8)	2.310, 0.129
Cord tuberculoma	0 (0)	2 (5.6)	2 (3.9)	0.867, 0.352
Syrinx	0 (0)	1 (2.8)	1 (1.9)	0.425, 0.514

DISCUSSION

Tubercular infection of central nervous system causes a granulomatous inflammatory reaction that involves the CNS meninges and parenchyma. Here we have assessed subclinical bladder abnormality by urodynamic study and the patterns of urodynamic abnormality in TBM patients in Indian population and also correlated urodynamic abnormalities with MRI findings.

The mean age of our study subjects was 28.5±13.34 years. The age distribution in our study population shows involvement of the young and economically productive member of the family. The mean age of our study population was comparable to 26.6 and 26. 7 years reported by other workers from India.[7,8] However, a recent study involving 160 patients showed a median age of 32.18 years which was higher compared to our subjects.[9]

Male to female ratio in our study was 1.31 (29 vs. 22) which was showing slight male predominance. This was comparable to the data of study conducted in Vietnam with ratio of 3:2 in favour of males.[10] However, female preponderance has been shown in data of Kumarvelu et al.[8]

Urodynamic study determines the pattern of urinary abnormality and possible mechanism behind it. Urodynamic study was carried out on admission in all 51 patients of TBM at admission with or without micturition symptoms. We found urodynamic abnormality was present in 70.6% patients. Various studies had shown a variety of bladder dysfunctions in caudaequina lesions including detrusor areflexia, delayed bladder sensations, and also detrusor hypereflexia.[11-13]

The presence of visual impairment, meningeal signs, paraparesis and hemiparesis, hypotonia, hyporeflexia in lower limbs was significantly associated urodynamic abnormality in patients of TBM than without it. The visual impairment seen in our study was comparable to what was observed in the adult population of Anuradha et al, and lower than Sinha et al.[14,15] The cranial nerve deficit and motor weakness comparable to Anuradha and Sinha et al, and Kalita J et al, but were seen in higher number of patients than the study by Thwaites et al.[15,16,10] The incidence of seizures seems to be similar to Sinha et al.[15] Paraplegia is an uncommon manifestation in patients with tuberculous spinal meningitis involving pia and arachnoid mater in a pattern of myeloradiculopathy. In our study paraplegia was found in 13.7% of cases and almost all resulted from spinal arachnoiditis, however one of our patients had intramedullary tuberculoma along with arachnoiditis.

Dastur et al, reviewed 74 cases of tuberculous paraplegia without evidence of Pott's disease and discovered that extra dual granuloma occurred in 64%, arachnoidal lesions without dural involvement in 20%, subdural lesion in 8% and intramedullary lesions in 8% of patients.[17]

MRI spine (focus at LS spine) with Gad was done in all patients where meningeal enhancement was seen in 72.5% patients. Lumbosacral arachnoiditis was seen in 49% patients. Myelitis was seen in 23.5% patients. CSF loculations were seen in 11.8% patients. Cord atrophy was seen in 9.8% patients .Tuberculoma in cord was seen in 3.9 % patients. Syrinx was seen in 1 (1.9%) patient. Patterns of lumbosacral arachnoiditis were central clumping (5.8%), empty thecal sac (17.6%), complete opacity (13.7%), mixed patterns (11.7%). Presence of spinal meningeal enhancement and lumbosacral arachnoiditis was significantly more in abnormal urodynamics group, suggesting strong relationship of bladder dysfunction with presence of arachnoiditis. It has been noted in post-mortem examination of TBM cases that widespread extension of the process into the spinal canal has remained asymptomatic, possibly because, although the spinal cord and/or nerve roots are surrounded by exudate, this has somehow not disturbed their function.[18] Authors findings indicate that arachnoiditis is largely asymptomatic and radiological diagnosis of spinal arachnoiditis is possible even before symptoms and signs develop which is supported by previous study of Srivastava and Kochar.[5] Arachnoiditis can cause syrinx formation by obliterating the spinal vasculature causing ischaemia. Present study is not devoid of limitations. Small sample size and cross sectional nature of the study restrict the utilization of findings to whole population, a large randomized clinical trial is needed to strengthen the present study findings.

CONCLUSION

Authors found that neurological symptoms like visual impairment, hemiparesis, paraparesis, abnormal tone and reflexes in lower limbs, showed significant association with abnormality in urodynamic study. MRI spine showed significant relationship of spinal meningeal enhancement, lumbosacral arachnoiditis, with abnormal urodynamic study.

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