Pakistan Journal of Neurological Sciences (PJNS)

Volume 12 | Issue 1 Article 7

3-2017

Central nervous system tuberculosis in children

Tipu Sultan

The Children's Hospital & Institute of Child Health, Lahore, Pakistan, tipusultanmalik@hotmail.com

CENTRAL NERVOUS SYSTEM TUBERCULOSIS IN CHILDREN

Tipu Sultan
Associate Professor in Pediatric Neurology Department of Pediatric Neurology
The Children's Hospital & Institute of Child Health, Lahore, Pakistan.

Correspondence to: *Email: tipusultanmalik@hotmail.com*

Date of submission: *May 26, 2016* ***Date of revision:*** *August 22, 2016* ***Date of acceptance:*** *September 25, 2016*

ABSTRACT

Brain and spinal cord tuberculosis are one of the commonest neurological infection in developing countries. Its associated with high morbidity and mortality. Diagnosis is based on clinical features, cerebrospinal fluid and brain imaging. Combination of antituberculous drugs should be started as early as possible to prevent the complications. The patient's clinical stage at presentation is the most important prognostic factor. Surgical procedures are directed at management of the hydrocephalus. Focal lesions, intracranial tuberculomas, and tuberculous abscesses, are usually located in cerebral or cerebellar hemispheres, uncommonly in brainstem and very rarely in spinal cord. They do not usually require surgical intervention and respond well to antituberculous treatment, along with corticosteroids. All these fsctors pertaining to tuberculosis of brain and spine will be adressed in this review article.

INTORODUCTION:

Tuberculosis remains a major public health problem and a concern globaly after its resurgence in developed countries.[1] Several risk factors have been identified for this phenomenon.[2] These include the over-crowding, malnutrition, multi drug-resistant strains of tuberculosis, ineffective tuberculosis control programmes and increasing prevalence of HIV infection. The incidence of tuberculosis varies from 9 cases per 100 000 population per year to as high as 110-165 cases per 100 000 population in the developing countries of Asia and Africa.[3] Tuberculous involvement of the central nervous system (CNS) is an important and fatal extra-pulmonary type. Approximately 10% of all patients with tuberculosis have CNS involvement.[4] Its incidence is directly proportional to the prevalence of tuberculosis infection in general population. In developing countries CNS tuberculosis is a disease of younger age group.[5]

We have searched Pubmed central with a keyword of central nervous system tuberculosis. A total of 2557 articles were present, however when we restrict it to the last five years, than 185 articles left.

Tuberculous meningitis (TBM) is associated with very high morbidity. Early treatment is important because the outcome correlates closely with the stage of TBM at the time the treatment is initiated.[6] TBM accounts for 2-45 of all types of tuberculosis (TB) among children when compared with only 2.9-5.8% of adult TB.[7] Most studies have suggested that combination of various factors like delayed diagnosis and treatment and advanced stages disease at presentation many contribute to the high morbidity and mortality rate.[8] Tuberculosis (TB) kills 2 million people each year in the world with significant proportion of TBM, of which 250,000 are children.[9] Accurate and early recognition of the disease and effective treatment of TBM is important.[10] Although children and adults are at equal risk to develop TB when exposed to a person with an infectious TB, but children are substantially at greater risk of developing TB especially miliary TB and TBM.[11]

Factors that determine the risk of TB are difficult to interpret. Prolonged and close exposure to infectious cases, malnutrition, lack of vaccination, poverty, and lack of early recognition at either pulmonary tuberculosis or TBM stage I and II are the major risk factors.[12] TBM is well recognized entity but there are few more types of central nervous system tuberculosis like tuberculoma, tuberculous brain abscess and tuberculous encephalopathy. Being part of an area where TB is endemic, we have huge number of these clinical entities as well but they are poorly recognized

and may need to be considered when other causes are excluded. Mortality in TBM was significantly related to pre-admission illness, duration and CSF findings and brain imaging findings. Mortality can be reduced by early and appropriate recognition. Antituberculous drugs and supportive therapy should be initiated promptly followed by supportive measures to prevent the long term complications.[13] Children who develop pulmonary tuberculosis are least likely to have cavity lesions, thus very unlikely to be sputum smear positive an it hinders the diagnosis. The detection of mycobacterium tuberculosis genome in the cerebrospinal fluid via the polymeraze chain reaction (PCR) test serves a useful test for early diagnosis but it is costly. Although the availability is limited and it is expensive, but when the diagnosis is doubtful they may help in diagnosis.[10]

Diagnosis of TBM is based on clinical evaluation since the bacteriological diagnosis takes time and has a low yield.[11] However cerebrospinal fluid (CSF) and brain imaging are extremely powerful investigative tools for diagnosis, management and follow up assessment of these patients. CNS tuberculosis is endemic in many parts of world and recently its prevalence has been on the rise worldwide as a result of increased number of AIDS cases.[1] Since early diagnosis will result in earlier recognition and treatment, radiologic images may play a critical role in patient management. CT and MR imaging are the main imaging techniques used in its localization and characterization.13 The imaging features overlap with other intracranial diseases, such as cysticercosis, metastases, and primary brain neoplasm. Recently, in vivo proton MR spectroscopy has been found to be helpful in better characterizing such lesions; however, it may not always be possible to evaluate lesions smaller than 10 mm with in vivo spectroscopy owing to its sensitivity constraints.

Classification of CNS tuberculosis

Intracranial

- TBM
- TBM with miliary tuberculosis
- Tuberculous encephalopathy
- Tuberculous vasculopathy
- Ttuberculoma / Tuberculous abscess

Spinal

- Pott's spine and Pott's paraplegia
- Tuberculousarachnoiditis (myeloradiculopathy)
- Non-osseous spinal tuberculoma
- Spinal meningitis

Pathophysiology:

Most tuberculous infections of the CNS are caused by Mycobacterium tuberculosis. Less frequently, other mycobacteria may be involved. bacilli reach the CNS by the haematogenous route secondary to disease elsewhere in the body 6. CNS tuberculosis develops in two stages. Initially small tuberculous lesions (Rich's foci) develop in the CNS, either during the stage of bacteraemia of the primary tuberculous infection or shortly afterwards. These initial tuberculous lesions may be in the meninges, the subpial or subependymal surface of the brain or the spinal cord, and may remain dormant for years after initial infection.[14]

Later, rupture or growth of one or more of these small tuberculous lesions produces development of various types of CNS tuberculosis.[7] Specific stimulus for rupture or growth of Rich's foci is not known, although immunological mechanisms may play a role. Rupture into the subarachnoid space or into the ventricular system results in meningitis. The type and extent of lesions that result from the discharge of tuberculous bacilli into the cerebrospinal fluid (CSF), depend upon the number and virulence of the bacilli, and the immune response of the host. Infrequently, infection spreads to the CNS from a site of tuberculous otitis or calvarial osteitis.[8]

The pathogenesis of localised brain lesions is also thought to involve haematogenous spread from a primary focus in the lung (which is visible on the chest radiograph in only 30% of cases). It has been suggested that with a sizeable inoculation or in the absence of an adequate cell-mediated immunity, the parenchymal cerebral tuberculous foci may develop into tuberculoma or tuberculous brain abscess.[9]

In TBM a thick, gelatinous exudate around the brainstem leading to hydrocephalus as a consequence of obstruction of the basal cisterns, outflow of the fourth ventricle, or occlusion of the cerebral aqueduct. Hydrocephalus frequently develops in children and is associated with a poor prognosis. Basal exudates of tuberculosis are usually more severe in the vicinity of the circle of Willis, and produce a vasculitis-like syndrome and inflammatory changes.[12]

CLINICAL FEATURES:

In most patients with TBM there is a history of vague ill health lasting 2-8 weeks prior to the development of meningeal irritation. These non-specific symptoms include malaise, anorexia, fatigue, fever, myalgias, and

headache. The prodromal symptoms in infants include irritability, drowsiness, poor feeding, and abdominal pain. Eventually, the headache worsens and becomes continuous. Bulging fontanelles develop in infants, who become increasingly irritable. Nausea, vomiting and altered sensorium may develop. Continuous low-grade pyrexia is typically present in about 80% of patients. A prior history of tuberculosis is present in approximately 50% of children with TBM and 10% of adult patients.[1,3]

Cranial nerve palsies occur in 20-30% of patients and may be the presenting manifestation of TBM. The sixth cranial nerve is most commonly affected. Vision loss due to optic nerve involvement may occasionally be a dominant and presenting illness. Ophthalmoscopic examination may reveal papilloedema. Funduscopy may reveal choroid tubercles, yellow lesions with indistinct borders present either singly or in clusters. These choroid tubercles are more frequent with TBM associated with miliary tuberculosis and are virtually pathognomonic of tuberculous aetiology, although they are present in only 10% of patients in whom the meningitis is not associated with miliary involvement.[7,12]

Hemiplegia may occur at the onset of the disease or at a later stage. Quadriplegia secondary to bilateral infarction or severe cerebral oedema is less common and occurs only at an advanced stage in a few patients. At times, abnormal movements may dominate the clinical picture. Choreiform or hemiballistic movements, athetosis, generalised tremors, myoclonic jerks and ataxia have been observed, more commonly in children than in adults. Seizures, either focal or generalised, may occur during acute illness or months after treatment.7 Apathy and irritability tend to progress to increasing lethargy, confusion, stupor and coma. The terminal illness is characterised by deep coma, decerebrate or decorticate rigidity, and spasm.

DIAGNOSIS

Preadmission illness of more than 2 weeks, lack of BCG vaccination, history of measles, 3rd degree malnutrition, contact to a TB patient among parents were seems to be important factors. Neurological findings including depressed sensorium, cranial nerve palsies, hemiplegia, hydrocephalus, CSF findings, brain imaging findings, and tuberculomas are important findings.

Diagnosis of TBM based on clinical history and examination findings, cerebrospinal fluid (CSF) findings and tomography of brain. CT scan has been proved helpful in diagnosis and evaluation of the complications of TBM. Modified Kenneth Jones Criteria have significant capacity for the early diagnosis of TBM if combined with history (prolonged illness) and clinical examination (CNS Symptoms like coma, hemiplegia, cranial nerve palsy, fits) along with CSF findings and brain imaging.

The abnormalities found in CSF of untreated patients with TBM are well described. Usually, there is a predominant lymphocytic reaction (60-400 white cells per ml) with raised protein levels (0.8-4 g/l). In the early stages of infection, a significant number of polymorphonuclear cells may be observed, but over the course of several days to weeks they are typically replaced by lymphocytes. There is a gradual decrease in the sugar concentration of the CSF, which is usually less than 50% of serum glucose concentration, the values may range between 18-45 mg/dl.[10,12] Definitive diagnosis of TBM depends upon the detection of the tubercle bacilli in the CSF, either by smear examination or by bacterial culture and highest detection rates being achieved in ventricular fluid. Rates of positivity for clinically diagnosed cases range from 25% to 70%.[11]

Diagnostic features of TBM

Clinical

- fever and headache (for more than 14 days)
- vomiting
- altered sensorium or focal neurological deficit

CSF

- pleocytosis (more than 20 cells, more than 60% lymphocytes)
- increased proteins (more than 100 mg/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 sylvian fissure hydrocephalus
- infarcts (basal ganglionic)
- gyral enhancement
- tuberculoma formation

Evidence of tuberculosis elsewhere

Methods to increase mycobacterial yield of CSF smear examination

- examine the deposit on centrifugation of a 10 ml CSF sample
- examine the deposit for at least 30 min
- examine several CSF samples over a few days

Antibodies against tubercle bacilli can be detected with enzyme-linked immunosorbent assay (ELISA) with variable success,. latex particle agglutination test, which allows the rapid detection of tubercle bacillus antigen in CSF.16 The intradermal tuberculin skin test is helpful when positive. The test may, however, be

falsely negative even in the absence of immunosuppression and in association with a positive reaction to common antigens used to determine anergy. The tuberculin skin test has been reported to be negative initially in 50-70% of cases and often becomes positive during therapy. The best method for diagnosing mycobacterial infection, however, is the polymerase chain reaction, in which cDNA probes are used to identify mycobacterial RNA or DNA sequences in CSF. This test is highly sensitive and specific in the diagnosis of TBM.[10,11]

IMAGING

Computed tomography (CT) or magnetic resonance imaging (MRI) of the brain may reveal thickening and intense enhancement of meninges, especially in basilar regions. Ventricular enlargement is present in a majority of patients. The degree of hydrocephalus correlates with the duration of the disease. Infarcts are another characteristic imaging feature (figures 1 and 2) of TBM.[13] The reported frequency of infarcts demonstrated by CT varies from 20.5% to 38%, however, in general, the incidence of infarction is significantly higher on MRI than on CT. Tuberculomas are infrequently seen on brain immaging of patients with TBMr. Multiple small intracranial tuberculoma are frequent when TBM is part of miliary tuberculosis.[15,16]

Tuberculous encephalopathy:

Tuberculous encephalopathy, a syndrome exclusively present in infants and children, has been described with pulmonary tuberculosis.[17] The characteristic features of this entity are the development of a diffuse cerebral disorder in the form of convulsions, stupor and coma without signs of meningeal irritation or focal neurological deficit. CSF is largely normal or may show a slight increase in proteins and cells. Pathologically, there is diffuse oedema of cerebral white matter with loss of neurons in grey matter. A picture resembling haemorrhagic leukoencephalopathy or a post-infectious demyelinating encephalomyelitis may be observed.[16]

Tuberculomas:

Tuberculomas are firm, avascular, spherical granulomatous masses, measuring about 2-8 cm in diameter.18 They are well limited from surrounding brain tissue which is compressed around the lesion and shows oedema and gliosis. The inside of these masses may contain necrotic areas composed of caseous material, occasionally thick and purulent, in which tubercle bacilli can be demonstrated. In developing countries young adults and children are predominantly affected while in developed countries they are more common in older patients.[19] The symptoms produced by tuberculoma are related to their location. Low-grade fever, headache vomiting, seizures, focal neurological deficit, and papilloedema are characteristic clinical features of supratentorial tuberculomas. Intratentorial tuberculomas are more common in children and may present with brainstem syndromes, cerebellar manifestations, and multiple cranial nerve palsies.[20]

On CT, tuberculomas are characterised as low- or high-density and rounded or lobulated masses and show intense homogenous or ring enhancement after contrast administration. They have an irregular wall of varying thickness. Moderate to marked perilesional oedema is frequently present. Tuberculomas may be single or multiple and are more common in frontal and parietal lobes, usually in parasagittal areas. On CT, the `target sign', a central calcification or nidus surrounded by a ring that enhances after contrast administration, is considered pathognomonic of tuberculoma. On CT scanning, tuberculoma measure more than 20 mm in diameter, are frequently irregular in outline, and are always associated with marked cerebral oedema (leading to midline shift) and progressive focal neurological deficit. Images after contrast administration show ring enhancement. Stereotactic diagnostic biopsy can help in establishing an accurate diagnosis.

Tuberculous brain abscess

Tuberculous brain abscess is a condition distinct from CNS tuberculoma. In developing countries, tuberculous abscesses have been reported in 4% to 7.5% of patients with CNS tuberculosis. The histopathological diagnosis of tuberculous brain abscess depends on the following criteria: microscopic evidence of pus in the abscess cavity, microscopic changes in the abscess wall, and isolation of M tuberculosis.[11,21] Abscesses are usually solitary and larger and progress much more rapidly than tuberculomas. CT and MRI pictures of a tuberculous abscess show a granuloma with a liquid centre, however, they are much larger and frequently multiloculated and with marked surrounding oedema.

Clinical features include partial seizures, focal neurological deficit, and raised intracranial tension. Surgical exploration and drainage of pus along with ATT produce excellent long-term results.[21]

Tuberculosis of Spinal cord (Pott's spine)

It is estimated that involvement of the spine occurs in less than 1% of patients with tuberculosis.[22] It is a leading cause of paraplegia in developing world. Infection in the vertebral bodies led to vertebral destruction leads to collapse of the body of the vertebra along with anterior wedging.[23] Spinal cord compression in Pott's spine is mainly caused by pressure from a paraspinal abscess which is retropharyngeal in the cervical region, and spindle shaped in thoracic and thoracolumbar regions. Neurological deficits may also result from dural invasion by granulation tissue and compression from the debris of sequestrated bone, a destroyed intervertebral disc, or a dislocated vertebra. Neurological involvement can occur at any stage of Pott's spine and even years later, when there has been apparent healing, because of stretching of the cord in the deformed spinal canal. The thoracic spine is involved in about majority of cases.[24]

Causes of parapalegia in CNS tuberculosis

- Pott's paraplegia
- non-osseous compressive myelopathies (tuberculoma): extradural, intradural, extramedullary, intramedullary
- transverse myelitis
- spinal meningitis
- spinal tuberculous abscess
- tuberculous arachnoiditis (myeloradiculopathy)
- syrinx formation

Typically, there is a history of local pain, tenderness over the affected spine or even overlying bony deformity in the form of gibbus. Conventional spinal X-rays are usually adequate to demonstrate the destruction of adjacent vertebral bodies and intervening disc spaces. However, MRI spine is the modality of choice. A combination of surgical decompression and treatment with antituberculous drugs is needed for the majority of patients with Pott's paraplegia. A period of 12 months of postoperative antituberculous therapy is adequate.[25]

Non-osseous spinal cord tuberculosis:

Non-osseous spinal cord tuberculosis can occur in the form of tuberculomas. In one of the case series of tuberculous paraplegia without evidence of Pott's disease and observed that extradural tuberculomas occured in 64% while arachnoid lesions without dural involvement, and subdural/extramedullary lesions occured in 8% of patients in each group. Intramedullary tuberculomas are extremely rarely reported, reports from developing countries have also been sporadic. The clinical features are indistinguishable from those of any extramedullary or intramedullary tumour, although acute worsening may occur. Intramedullary lesions are frequently located in the thoracic region. More than one site in the spinal cord may also be affected. One case with conus medullaris syndrome has been described. Non-osseous spinal cord tuberculomas may increase in size while the patient is on antituberculous therapy. MRI is the investigation of choice for these lesions.[26]

Spinal TB:

A predominantly spinal form of TBM may result from rupture of Rich's focus into the spinal arachnoid space rather than the basal meninges. The acute form presents with fever, headache, and radiating root pains, accompanied by myelopathy. The chronic form, usually localised to a few segments, presents with progressive spinal cord compression and may suggest a spinal cord tumour. The characterisic MRI features include CSF loculation and obliteration of the spinal subarachnoid space with loss of outline of spinal cord in the cervico-thoracic region and matting of nerve roots in the lumbar region. Spinal forms of TBM may be associated with syrinx formation.[22,27]

Tuberculous arachnoiditis:

Tuberculous arachnoiditis is a relatively common cause of myeloradiculopathy in countries endemic for tuberculosis. The inflammatory exudate surrounds, but does not infiltrate, the spinal cord and nerve roots. Neuronal structures are damaged by direct compression as well as by ischaemia. The changes of arachnoiditis may be focal, multifocal, or diffuse.[24] In tuberculous arachnoiditis features of spinal cord or nerve root involvement may predominate but most often there is a mixed picture. Frequently, there is clinical evidence of multifocal radiculomyelopathy, but even when meningeal involvement is widespread, symptoms may arise from a single level. The hallmark of diagnosis is the characteristic myelographic picture, showing poor flow of contrast material with multiple irregular filling defects, cyst formation, and sometimes spinal block. The CSF changes are those of a chronic meningitis. These patients need adequate antituberculous treatment for at least one year. If the patient does not respond to medical treatment, surgery may be required.[28]

Management

In majority of children, there is sifnificant improvemt with oral drugs over 4 to 6 weeks. Recommended treatment includes isoniazid (10-20 mg/kg/day up to 300 mg), rifampicin (10-20 mg/kg/day, up to 600 mg/day) and pyrazinamide (15-30 mg/kg/day, up to 2 grams a da).30. Patients should be monitored for

hepatotoxicity from rifampicin which is seen in up to 20% of patients. Ethambutol or streptomycin may be added if the response is not satisfactory. The duration of therapy should be at least 9 months and in some instances up to 12-15 months treatment is required. The World Health Organization (WHO) put CNS tuberculosis under TB treatment Category 1, and recommend initial phase therapy (for 2 months) with streptomycin, isoniazid, rifamipicin and pyrazinamide, followed by a 10 month continuation phase with isoniazid and rifampicin. A similar drug regimen has been recommended for all forms of CNS tuberculosis. In case of drug resistence and side effects, 2nd line derug can be considered which includes azithromycin (500-100 mg/day) and clarithromycin (500 to 1000 mg/day) and ciprofloxacin.[23]

ROLE OF CORTICOSTEROIDS:

One of the controversial aspects of treatment of TBM is the use of corticosteroids. The response to steroids may be dramatic with rapid clearing of sensorium, regression of abnomalities of CSF, defervescence and relief of headache. They observed that, in addition to survival, corticosteroids significantly improved intellectual outcome and enhanced resolution of the basal exudates and intracranial tuberculoma were shown by serial CT scanning. Prednisolone treatment (1-3 mg/kg/day) is suggested in patients with TBM. The dosage may reduced by 50% in the second and third week and then be tapered gradually over the next 4 weeks.[23]

Indications for corticosteroids in TBM

- altered sensorium
- focal neurological deficit
- spinal fluid pressure in excess of 300 mmH_2O
- spinal block (CSF protein > 400 mg/dl)
- presence of tuberculomas
- basilar exudates

PARADOXICAL WORSENING:

It has been observed frequently that intracranial tuberculomas appear or paradoxically increase in size while patients are being treated for TBM or tuberculoma. These lesions are usually discovered accidentally when follow-up CT scan is performed routinely or when new neurological signs develop during the course of antituberculous therapy. A recent study noted that about 8% of patients developed asymptomatic tuberculoma during the first month of treatment. Concomitant steroid therapy probably has a preventive role against these focal lesions.[18]

SURGERY

Surgical procedures in patients with TBM are primarily directed to the treatment of hydrocephalus. Serial lumbar punctures with diuretics and osmotic agents are useful measure to relieve elevated intracranial pressure. If these steps fail, ventriculo-peritoneal shunt may relieve the signs and symptoms of hydrocephalus. Early shunting with drug therapy may offer the best therapeutic outcome. Intracranial tuberculomas that act as single space-occupying lesions with midline shifts and increased intracranial pressure, and that fail to respond to chemotherapy should be surgically removed. If these tuberculomas removed early during the cource of illness, prognosis is is exellent.[29]

PROGNOSIS AND SEQUELAE:

The single most important determinant of outcome, for both survival and sequelae, is the stage of TBM at which treatment has been started. If treatment is started in stage I, mortality and morbidity is very low, while in stage III almost 50% of patients die, and those who recover may have some form of neurological deficit. About 20% to 30% of survivors manifest a variety of neurological sequelae, the most important of which are mental retardation, psychiatric disorders, seizures, blindness, deafness, ophthalmoplegia and hemiparesis. Endocrinopathies may become evident months or year after recovery. The endocrinopathies are most probably due to progressive damage of either the hypothalamus itself or adjacent basal cisterns. Obesity, hypogonadism, diabetes inspidus, and growth retardation have been reported. Intracranial calcification develops in 20% to 48% of patients with TBM, usually becoming detectable 2 to 3 years after the onset of the disease.[29]

MRC staging of TBM

Stage I: prodromal phase with no definite neurological symptoms

Stage II: signs of meningeal irritation with slight or no clouding of sensorium and minor (cranial nerve palsies), or no neurological deficit

Stage III: severe clouding of sensorium, convulsions, focal neurological deficit and involuntary movements

Worst prognostic factors for TBM

- Stage III (mortality 50-70%)
- extreme of ages
- malnutrition
- presence of miliary disease
- presence of underlying debilitating disease, eg, alcoholism
- hydrocephalus
- focal neurological deficit
- low CSF glucose levels
- markedly elevated CSF protein

Conclusion

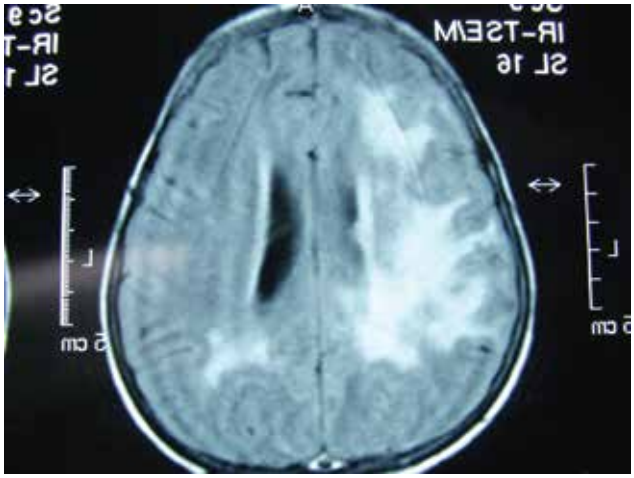
Spectrum of CNS tuberculosis is quite variable and now it become relevant for other parts of the world. The variable, natural history and accompanying clinical features of TBM hinders the early diagnosis. The World Health Organization (WHO) estimates that one third of the world's population is infected with mycobacterium tuberculosis, with the highest prevalence of tuberculosis in Asia, having TBM as one of the most common extra pulmonary tuberculosis. TBM continues to exact a devastating fall in developed and developing countries despite the availability of effective chemotherapy. One of the main reason for this failure is patients being diagnosed late, when they already have many complications of TBM or different types of CNS tuberculosis. The increasing problem of drug resistance has added a new challenge. The early recognition and timely treatment of the disease is critical if the considerable mortality and morbidity associated with the condition is to be prevented.

References:

1. Sultan T, Malik MA, Khan MMN. Clinical, radiological and laboratory variables indicators of early diagnosis of TBM in children. Pak Paed J 2007; 31(3):29-36.
1. Snider DE Jr, Roper WL. The new tuberculosis. N Engl J Med 1992;226:703-5.
2. Harries AD. Tuberculosis and human immunodeficiency virus infection in developing countries. Lancet 1990;335:387-90
3. Raviglione MC, Snider DE, Kochi A. Global epidemiology of tuberculosis. Morbidity and mortality of a world wide epidemic. JAMA 1995;273:220-26.
4. Wood M, Anderson M. Chronic meningitis. Neurological infections; major problems in Neurology, vol 16. Philadelphia: WB Saunders, 1998;169-48.
5. Rajajee S, Narayanan PR. Immunological spectrum of childhood tuberculosis. J Trop Pediatr 1992;21:490-96.
6. Newton RW. TBM. Arch Dis Child 1994;70:364-66.
7. Dastur DK, Manghani DK, Udani PM. Pathology and pathogenetic mechanisms in neuro tuberculosis. Radiol Clin North Am 1995;33:733-52.
8. Leonard JM, Des Prez RM. TBM. Infect Dis Clin North Am 1990;4:769-87.
9. Ahuja GK, Mohan KK, Prasad K, Behari M. Diagnostic criteria for TBM and their validation. Tubercle Lung Dis 1994;75:149-52.
10. Nguyen LN, Fox LFF, Pham LD, Kuijper S, Kolk AHJ. The potential contribution of polymerase chain reaction to the diagnosis of TBM. Arch Neurol 1996;53:771-76.
11. Davis LE, Rastogi KR, Lambert LC, Skipper BJ. TBM in the southwest United States: a community based study. Neurology 1993;43:1775-78.
12. Eide FF, Gean AD, So IT. Clinical and radiographic findings in disseminated tuberculosis of the brain. Neurology 1993;43:1427-29.
13. Gee GT, Bazan C III, Jinkins JR. Miliary tuberculosis involving the brain: MR findings. AJR 1992;159:1075-76.
14. Jinkins JR, Gupta R, Chang KH, Rodriguez-Carbajal J. MR imaging of central nervous system tuberculosis. Radiol Clin North Am 1995;33:771-86.
15. Jinkins JR, Gupta R, Chang KH, Rodriguez-Carbajal J. MR imaging of central nervous system tuberculosis. Radiol Clin North Am 1995;33:771-86.
16. Udani PM, Dastur DK. Tuberculous encephalopathy with and without meningitis: clinical features and pathological correlations. J Neurol Sci 1970;10:541-61.
17. Talamas O, Del Brutto OH, Garcia-Ramos G. Brainstem tuberculoma. Arch Neurol 1989;46:529-35.
18. Rajshekhar V, Chandy MJ. Tuberculomas presenting as isolated intrinsic brain stem masses. Br J Neurosurg 1997;11:127-33.
19. Van Dyk A. CT of intracranial tuberculomas with special reference to the "target sign". Neuroradiology 1988;30:329.
20. Farrar DJ, Flanigan TP, Gordon NM, Gold RL, Rich JD. Tuberculous brain abscess in patient with HIV infection: case report and review. Am J Med 1997;102:297-301.
21. Razai AR, Lee M, Cooper PR, Errico TJ, Koslow M. Modern management of spinal tuberculosis. Neurosurgery 1995;36:87-98.
22. Vidyasagar C, Murthy HKRS. Management of tuberculosis of the spine with neurological complications. Ann J Coll Surg Engl 1994;76:80-84.
23. Miller JD. Pott's paraplegia to day. Lancet 1995;340:264.
24. Mantzoros CS, Brown PD, Dembry L. Extraosseous epidural tuberculoma. Case report and review. Clin Infect Dis 1993;17:1032-36.
25. Garg RK, Karak B, Misra S. Acute paraparesis with TBM. Postgrad Med J 1998;74:269-71.
26. Gero B, Sze G, Sharif H. MR imaging of intradural

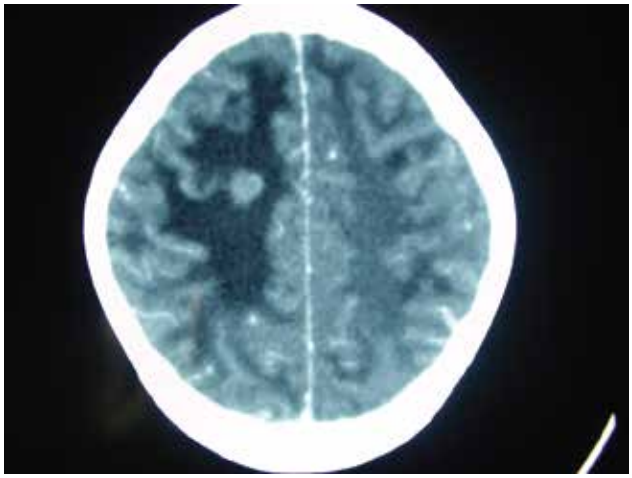
inflammatory disease of spine. Am J Neuroradiol 1991;12:1009-1019.
27. Donald PR, Gent WL, Seifart HI, Lamprecht JH, Parkin DP. Cerebrospinal fluid isoniazid concentrations in children with TBM: the influence of dosage and acetylation status. Pediatrics 1992;89:247-50.
28. Ellard GA, Humphries MJ, Allen BW. Cerebrospinal fluid drug concentrations and the treatment of TBM. Am Rev Resp Dis 1993;148:650-55.
29. Snider DE, Rieder HL, Combs D, Bloch AD, Hayden CH. Tuberculosis in children. Pediatr Infect Dis J 1988;7:271-78.

Figure-I



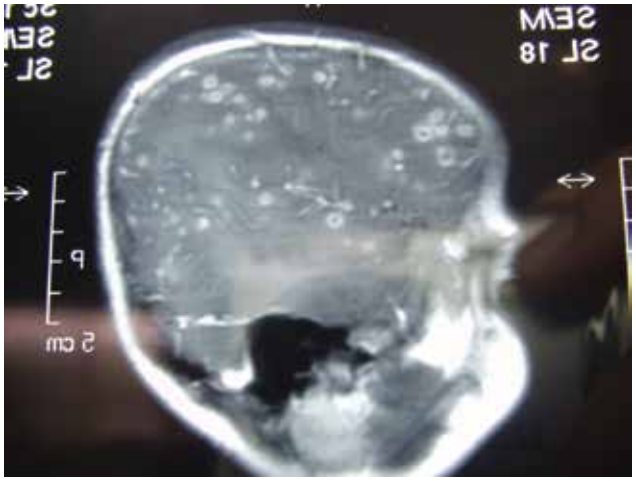
CNS Tuberculoma with massive edema

Figure-II



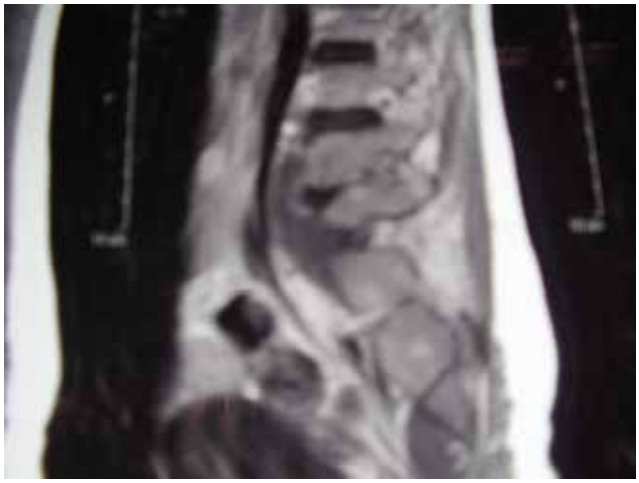
CNS Tuberculoma

Figure-III



Multiple CNS Tuberculoma

Figure-IV



TB Spine

Conflict of interest: Author declares no conflict of interest.
Funding disclosure: Nil

Author's contribution:
Tipu Sultan: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review