Case report

An Unusual Case of Tuberculoma in a 19-Year-Old Man.

Abstract

Background : tuberculosis (TB) is ranked as one of the top 10 causes of death. *Mycobacterium tuberculosis* (M. TB) infection, the causative organism for TB affects approximately a quarter of the global populationplacing a burden on the healthcare system. Central nervous system tuberculosis (CNS TB) is seen in 5 to 10% of extrapulmonary TB cases and has the highest mortality. CNS tuberculoma is one of its manifestation. Clinical presentation of CNS tuberculoma depends on its location within the CNS and commonly include headache, seizures, and focal neurological deficits, due to the presence of a space occupying lesion, although patients can be asymptomatic.We report the case of a 19yr old man who had an unusual presentation of CNS tuberculoma, highlighting its clinical presentation, diagnosis and treatment.

Case Presentation: Index patient is a 19-year-old male college student who resides in a city. He presented with 15 days history of fever, headache, vomiting, vertigo, ataxia, and inability to concentrate.He received antimalarial, anti typhoid and body booster medications but had no improvement and had a history of weight loss despite no dietary change. He had never been diagnosed with TB and had all his childhood vaccinations given. Plain Magnetic Resonance Imaging (MRI)brain scan done revealed a posterior fossa mass lesion with perilesional edema. Futher, a contrast MRI brain scan showed multiple ring-enhancing conglomerates of lesion around the tentorium on the posterior fossa with intense contrast enhancement. The largest of this mass measured 4.5cmx2.5cmx2.5cm in the right superior cerebellum compressing the 4th ventricle and with effacement of the cerebellopontine angle. Lastly, an MRI spectrometry revealed elevated lipid lactate peak. His chest x-ray was unremarkable. Other blood parameters were essentially within range with the exception of Erythrocyte ESR and mantoux test. He received antitubercular drug (Isoniazid, Rifampin, Pyrazinamide, Ethambutol, Levoflox and Streptomycin) for 18th months with complete remission.

Conclusion: CNS tuberculomas are tuberculous masses that can be located anywhere from the brain to spinal cord. Advanced diagnostic modalities may guide clinicians towards making it's diagnosis. Treatment maybe medical(use of antitubercular drugs) or surgical excision with medical therapy being first choice. While the index patient had no obvious risk factors for his disease, his BCG vaccination pose a possible source of his exposure to TB infection. More research is needed on this however.

Keywords: Tuberculoma, unusual presentation, Antitubercular drugs, Tuberculosis, BCG vaccination

Introduction

"Worldwide, it is estimated that about 10 million people are affected with tuberculosis (TB) yearly" (1). "TB is ranked as one of the top 10 causes of death accounting for 1.5 million deaths" in 2021(1,2). "According to the most recent WHO study from 2022, *Mycobacterium tuberculosis* (M. TB) infection, causative organism for TB affects approximately a quarter of the global population". (3) "The high prevalence of TB worldwide places a burden on the healthcare system, with $13 billion needed annually for its prevention, diagnosis, and treatment(2). *Mycobacterium tuberculosis*, is a slow-growing aerobic, non-spore forming acid-fast bacillus with a slow doubling time" (4). TB is primarily a disease of the lungs however, may affect other organs through hematogeneous spread.

"Central nervous system tuberculosis (CNS TB) is seen in 5 to 10% of extrapulmonary TB cases, accounting for approximately 1% of all TB cases with the highest mortality making it one of the most deadly forms of tuberculosis" (1,5). "CNS TB mainly manifests as TB meningitis followed by tuberculoma, tubercular abscess and other forms" (1). "It most commonly affects children and immunocompromised patients. Immunocompromised state could be due to aging, alcoholism, malnutrition, malignancy, Human Immunodeficiency Virus (HIV) infection, or drugs, such as tumour necrosis factor-alpha inhibitors" (2,6). "Clinical manifestations of CNS tuberculoma depends on its location within the CNS and commonly include headache, seizures, and focal neurological deficits, due to the presence of a space occupying lesion, although patients can be free of major neurologic symptoms" (1,2).

"The first line treatment of CNS TB involves the concurrent use of four drugs: rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE). RIPE has been shown to be the most effective treatment for TB and alternative therapies are saved for use in the setting of multi-drug resistant TB and hypersensitivity to therapy. More so,approximately 1–8 % of people who receive anti-TB therapy develop hypersensitivity reactions and alternative regimens must be evaluated" (2). Surgical resection is also a treatment modality though not routinely performed.

We report a case of a 19yr old man who had an unusual presentation of CNS tuberculoma, highlighting clinical presentation, diagnosis and treatment.

Case presentation

Index patient is a 19-year-old male college student who resides in a city. He presented with 15 days history of fever, headache, vomiting, vertigo, ataxia, and inability to concentrate. His symptoms exacerbated 5 days prior to presentation. He received antimalarial, anti typhoid and body booster medications but had no improvement. While he had no history of contact with individuals or family members with chronic cough or TB, he had a history of weight loss despite no dietary change. He had never been diagnosed with TB and had all his childhood vaccinations given. He reported no history of smoking, alcohol use or use of psychoactive substances. family history and his past medical history were unremarkable. On examination, nystagmus along with ataxia were prominent. He had a plain Magnetic Resonance Imaging (MRI)brain scan that revealed a posterior fossa mass lesion with perilesional edema. Futher, a contrast MRI brain scan showed multiple ring-enhancing conglomerates of lesion around the tentorium on the posterior fossa with intense contrast enhancement. The largest of this mass measured 4.5cmx2.5cmx2.5cm in the right superior cerebellum compressing the 4th ventricle and with effacement of the cerebellopontine angle. Lastly, an MRI spectrometry revealed elevated lipid lactate peak. His chest x-ray was unremarkable. Other blood parameters were essentially within range with the exception of Erythrocyte ESR and mantoux test. The index patient was treated with antitubercular drug (Isoniazid, Rifampin, Pyrazinamide, Ethambutol, Levoflox and Streptomycin) for 18th months, steroids and anti-epileptic(Keppra).

Follow-up:- He was followed up for 1.5 years every four months and then every 3 months. First follow-up consisted of an MRI Brain with contrast to see the treatment's effectiveness. His MRI showed the size of the tuberculoma had decreased gradually.He had complete remission in 18th months.

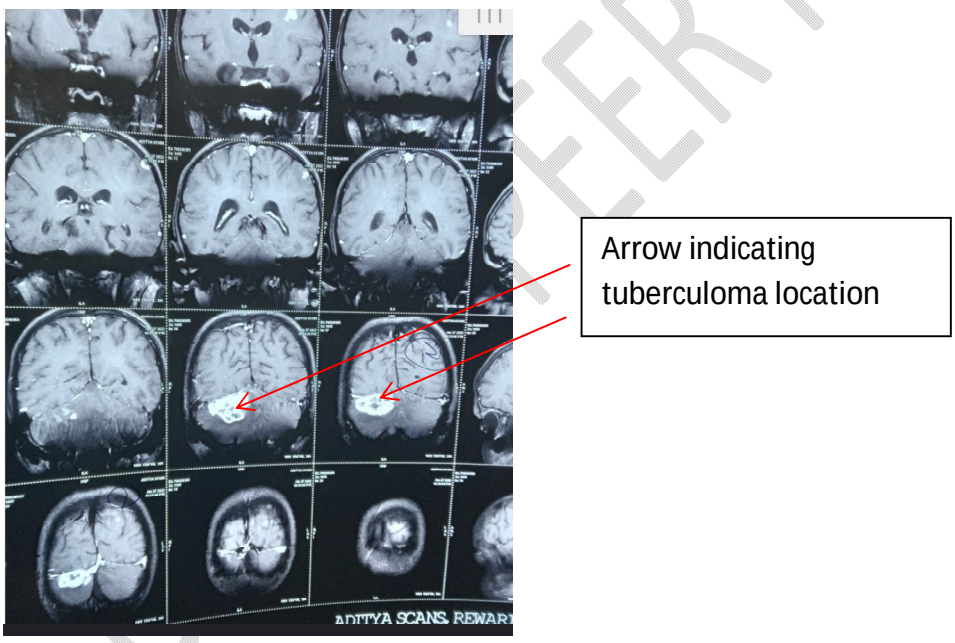
Table 1 showing results and reference ranges of laboratory investigations

Parameter	Value	Reference range/Units
Hematology		
ESR	**38**	**0-15 mm/hr**
CRP	**5.3**	**<6 mg/dl**
Liver Profile		
Total Bilirubin	**0.7**	**0.2-1.1 mg/dl**
Direct Bilirubin	**0.3**	**Up to 0.4 mg/dl**
Indirect Bilirubin	**0.4**	**0.2-0.6 mg/dl**
S.G.P.T	**20**	**0-49 U/l**
S.G.O.T	**28**	**0-45 U/l**
Serum Alkaline Phosphatase	**139**	**100-250 U/l**
Total Protein	**6.7**	**6.6-8.3 Gm/dl**
Albumin	**3.5**	**3.5-5.0 Gm/dl**
Globulin	**3.2**	**2.6-3.3 Gm/dl**
A/G ratio	**1.09**	**1.5-2.5/1**
Mantoux test	**Positive (25*30mm)**	**mm**
GGTP	**28**	**15-73 U/l**
Kidney function Test		
Urea	**19**	**19-43 mg/dl**
Creatinine	**0.6**	**0.6-1.2 mg/dl**
Uric acid	**9.2**	**3.5-7.5 mg/dl**
Sodium	**142**	**137-145 mg/dl**
Potassium	**4.7**	**3.5-5.0 mg/dl**

Total Calcium	**8.7**	**8.4-10.3 mg/dl**
Inorganic phosphate	**4.5**	**2.5-4.5 mg/dl**
Random blood glucose	**103**	**80-120 mg/dl**
Hemoglobin	**12.8**	**13-17 g/dl**
Total White Blood Cell	**6500**	**4000-10000 /cumm**
HIV	**Negative**	
Hep BSAg	**Negative**	
Hep C	**Negative**	
FT3	**2.04**	**1.71-3.71 pg/ml**
FT4	**1.05**	**0.7-1.48 ng/dl**
TSH	**2.70**	**0.35-4.94 milU/ml**

ESR: Erythrocyte sedimentation rate; CRP: C-reacyive protein; S.G.O.T: Serum glutamic oxaoloacetic transaminase; S.G.P.T: Serum glutamic pyruvate transaminase; GGTP: Gammaglutamyl transpeptidase; fT4: free tetraiodothyronine; fT3: free triiodothyronine; HIV: Human immune deficiency virus; Hep BSAg: Hepatitis B surface antigen; Hep C: Hepatitis C virus; TSH: Thyroid stimulating hormone.

Figure 1: Chest X-ray showing clinically clear chest.



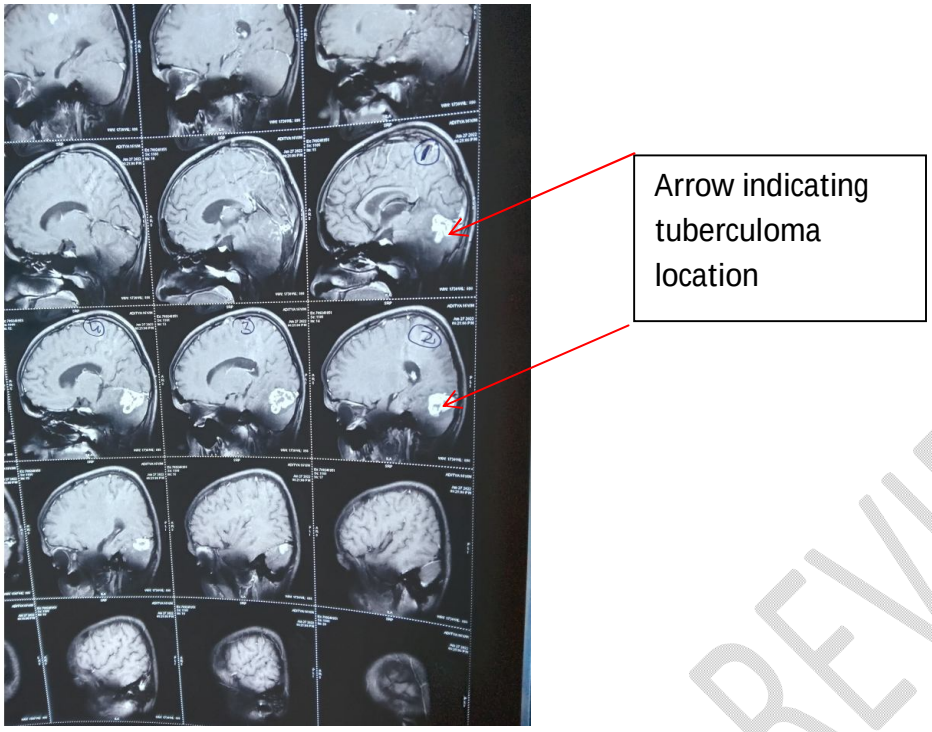


Figure 2: MRI contrast scan showing various tuberculomas in different parts of the brain. Largest mass can be seen in Cerebellum.

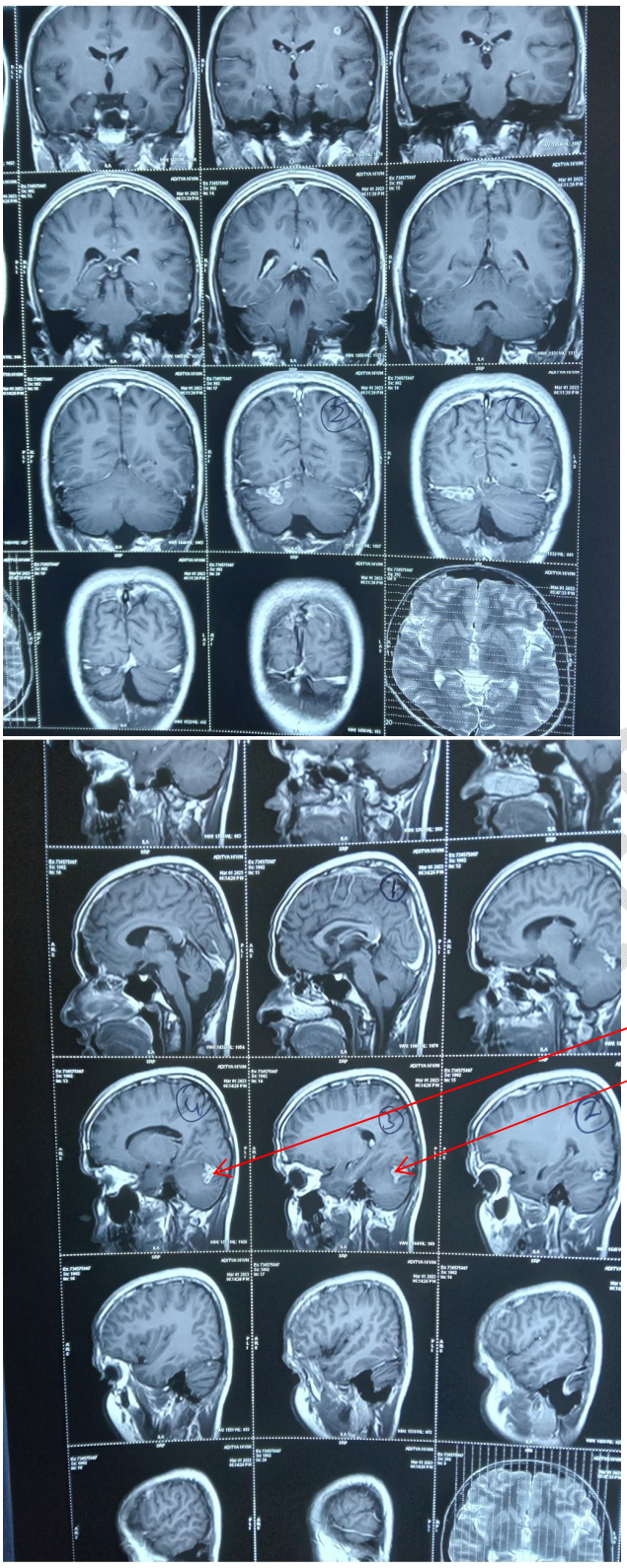


Fig 3: MRI contrast scan showing post treatment State of the brain with reduction in tuberculoma.

Discussion

"TB infection occurs through inhalation of droplets containing *mycobacterium tuberculosis* bacilli, which lead to its deposition in the lung alveoli and activation of T-helper cells. This T-helper cell immune-mediated response leads to the formation of granuloma and primary pulmonary TB. Prior to the containment of the infection, some bacilli are filtered into the lymphatic system, which leads to hematogenous dissemination to the distant parts of the body, which are highly oxygenated organs like the brain" (7).

"Although, CNS TB is rare, it can be life threatening (1). Individuals with an increased risk for miliary and extrapulmonary TB include patients in immunodeficiency state caused by aging(young and elderly), alcoholism, malnutrition, malignancy, HIV infection, or drugs, such as tumour necrosis factor-alpha inhibitors" (6,8). The index patient has no identifiable risk factors and have not been diagnosed previously with TB. His chest x-ray was unremarkable. Other laboratory investigations as presented in Table 1 were within normal reference range with the exception of ESR which was a pointer to an ongoing inflammatory process and a positive mantoux test. Why it is not clear the source of his TB exposure, a possibility is his BCG vaccination which may have been a link in this patient.

"CNS tuberculomas is estimated to account for approximately 33% of cerebral space-occupying lesions in developing countries reaching up to 50% in regions where TB is endemic" (3,9). "While supratentorial lesions are common in adults, infratentorial involvement is slightly more common in children" (10). "CNS tuberculomas are benign, non neoplastic, well circumscribed, granulomatous intraparenchymal masses with size varying between 2 cm and 10 cm in diameter. They are usually located in the cerebral or cerebellar hemispheres and uncommonly in the brainstem or spinal cord" (1,11). "The frontal lobe is the most commonly involved with 35.3% of the patients, followed by temporal and parietal lobes at 29.4% each, and at 5.9% for the occipital lobe" (1). "CNS tuberculomas may involve various structures in the CNS, including the meninges, ventricular system, pituitary gland and other brain structures" (12). Our patient had multiple tuberculomas identified in his cerebellum, occipital cortex, frontal cortex and post central cortex. The largest measured 4.5cmx2.5cmx2.5cm, irregularly shaped in his right superior cerebellum with compression of the 4th ventricle and effacement of the cerebellopontine angle and severe perilesional edema.

"Tuberculomas of the brain may present as a subacute or chronic illness, lasting from weeks to months. The clinical presentation depends on the size and anatomical location of the lesions" (1). "Also, it maybe asymptomatic or may present with headache, focal neurological deficits,

seizures, vomiting, hydrocephalus, meningeal irritation signs and intracranial hypertension with papilledema" (1,2). The anatomical location of the index patient's tuberculomas account for the symptoms (ataxia, headache, vomiting, vertigo, difficulty concentrating) he presented with and is in keeping with existing literature.

Neuroimaging studies including Computed Tomography (CT) scan and MRI scan with contrast enhancement and MR spectroscopy are the basis for diagnosis of CNS tuberculoma (1). MRI scan is usually the imaging of choice, given its superiority over CT scan in the diagnosis of CNS TB (6). Commonly,brain tuberculoma appear as a ring-enhancing lesion (target lesion) due to the absence of blood supply in the caseous necrosis centre within the tuberculoma (13). Our patient had a contrast MRI scan and an MRI spectrometry. While the MRI scan delineated the location of all tuberculomas and characterized them, the MRI spectrometry revealed elevated lipid lactate peak further supporting the diagnosis of tuberculoma.

Nonspecific symptoms and radiological characteristics mirror a range of different disease states leading to misdiagnosis hence tuberculomas must be differentiated from other space occupying lesions such as pyogenic abscess, toxoplasmosis, sarcoidosis, hydatidosis, intracranial hemorrhage, syphilitic gummas and primary/metastatic malignant lesions which can be associated with calcifications that produce the 'target sign' which could suggest reactivation or dormant tuberculosis. (1,3,13). Other differentials for the masses seen on the MRI where considered however the findings from the MRI scan and MRI spectrometry supported the diagnosis of multiple tuberculomas and hence a trial of anti-tuberculosis therapy in conjunction with other medications was conducted.

In cases of multiple brain tuberculomas, brain biopsy is the most reliable method for diagnosis (3). While evidence of extraneural TB will aid in the diagnosis (1), diagnostic proof of a TB infection is not required to initiate anti-TB treatment in patients with high clinical suspicion, and prognosis is heavily influenced by the stage of the disease course when treatment is started (12). Our patient did not have a biopsy and was diagnosed and treated based on the findings from his history, examination and MRI scans(contrast and spectrometry).

"Management of CNS Tuberculomas includes treatment with 4 ATT drugs; isoniazid, rifampicin, pyrazinamide and ethambutol with duration ranging from 6-36months. Corticosteroids and other adjunct medications maybe added" [1,2,9]. "Paradoxical enlargement or the development of new intracranial tuberculomas or abscesses in patients with CNS or extra-neural TB on appropriate treatment may occur, typically within the first six months after TB treatment initiation but may rarely be delayed for a year or more" (paradoxical reaction) (10). "Surgical resection of the lesion may be considered in some instances; 1) to relieve symptomatic or potentially life-threatening mass effect and/or hydrocephalus, and 2) to treat medically refractory seizures" (10,14). "Unlike CNS mass lesions, surgical resection of tuberculomas is associated with severe fatal meningitis. Hence medical management is recommended as first-line management" (7). Our patient received a mixture of antitubercular drugs (Isoniazid, Rifampin, Pyrazinamide,

Ethambutol for 18months), Levoflox, Streptomycin, steroids, antiepileptic(Keppra) and other meds. At followup, he showed marked clinical and radiological improvement (initial tuberculoma on MRI decreased from 4.5cmx2.5cmx2.5cm to 2.2cmx1.7cmx1.3cm with reduced perilesional edema). Surgery was not an option in this patient and he had no paradoxical reaction.

Conclusion

CNS tuberculomas are tuberculous masses that can be located anywhere from the brain to spinal cord. While there are a number of differentials, a high index of suspicion combined with advanced diagnostic modalities may guide clinicians towards making it's diagnosis. Treatment maybe medical(use of antitubercular drugs) or surgical excision with medical therapy being first choice. While the index patient had no obvious risk factors for his disease, his BCG vaccination may have been the source of his exposure to TB infection. More research is needed on this however.

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Ethical approval: Ethical approval was sought and obtained.

Consent

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

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Details of the AI usage are given below:

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