Case report

Tuberculoma: An unusual presentation in a 19yr old Man

Abstract

This case report presents a detailed examination of 19 years old male with Tuberculoma . The patient's presents with 15 days history of morning headache vertigo, fever , headache , vomiting ,ataxia and inability to concentrate . The association between symptoms and brain MRI finding is focal in this study, particularly considering the patient's MRI which shows posterior fossa mass leison with edema , multiple ring enhancing conglomerates with intense contrast enhancement, with largest lesion measuring 4.5cmx2.5cmx2.5cm. This case highlights the critical need for heightened awareness among clinicians regarding the implications of anti tubercular medications particularly in individuals with predisposing risk factors. Furthermore, it illustrates the complexity of diagnosing and managing Tuberculoma , a condition that may vary widely in its presentation and severity, necessitating a tailored approach to treatment that considers both the acute manifestations and underlying contributory factors and treatment with complete remission in 18 months.

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 affects approximately a fourth of the global population. (3) The high prevalence of TB worldwide places a burden on the healthcare system, with $13 billion needed annually for TB prevention, diagnosis, and treatment. (2)

Tuberculosis is caused by Mycobacterium tuberculosis, 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, and accounts for approximately 1% of all TB cases and has 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 caused by aging, alcoholism, malnutrition, malignancy, HIV infection, or drugs, such as tumour necrosis factor-alpha inhibitors (2,6). Clinical manifestations of CNS tuberculoma depends on its location 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. 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 tuberculoma highlighting clinical presentation, diagnosis and treatment.

Case presentation

Index patient is a 19-year-old male college student who reside in a city. He presented with 15 days history of fever, headache, vomiting, vertigo, ataxia, and inability to concentrate. His symptoms such as morning headache, ataxia and vertigo have exacerbated 5 days prior to presentation. History of weight loss despite no change in diet. He received antimalarial, anti typhoid and body booster medications but had no improvement. No history of contact with individuals with chronic cough or TB. He has never been diagnosed with TB. Had all childhood vaccinations given. No history of smoking, alcohol use or use of psychoactive substances. family history was unremarkable. On examination, nystagmus along with ataxiae were prominent.

Investigation; A plain MRI Brain scan showed a posterior fossa mass lesion with edema. A contrast MRI Brain scan revealed 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. An MR Angiography Brain- No evidence of AVM/ aneurysm. An MR Venography Brain- No evidence of venous sinus compression. MRI spectrometry revealed elevated lipid lactate peak.

Chest X-ray was unremarkable. Other blood parameters were essentially within range with the exception of ESR and mantoux test.

Treatment Plan:- Antitubercular drug (Isoniazid, Rifampin, Pyrazinamide, Ethambutol, Levoflox and Streptomycin) for 18th months, steroids, antiepileptic(Keppra) and other meds(Benadon, Heptagon, Syrup A to Z and Pantocid).

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. Streptomycin and levofloxacin were stopped in 2 months. Ethambutol stopped in 6 months pyrazinamide stopped in 9 months, the steroid stopped in 35 days.

Conclusion:- Antitubercular drug is effective in tuberculoma with 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 glucose	**103**	**80-120 mg/dl**
Hemoglobin	**12.8**	**13-17 g/dl**
Total White Blood Cell	**6500**	**4000-10000 /cumm**
HIV	**Negative**	
Hepatitis BSAg	**Negative**	
Hepatitis 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**

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

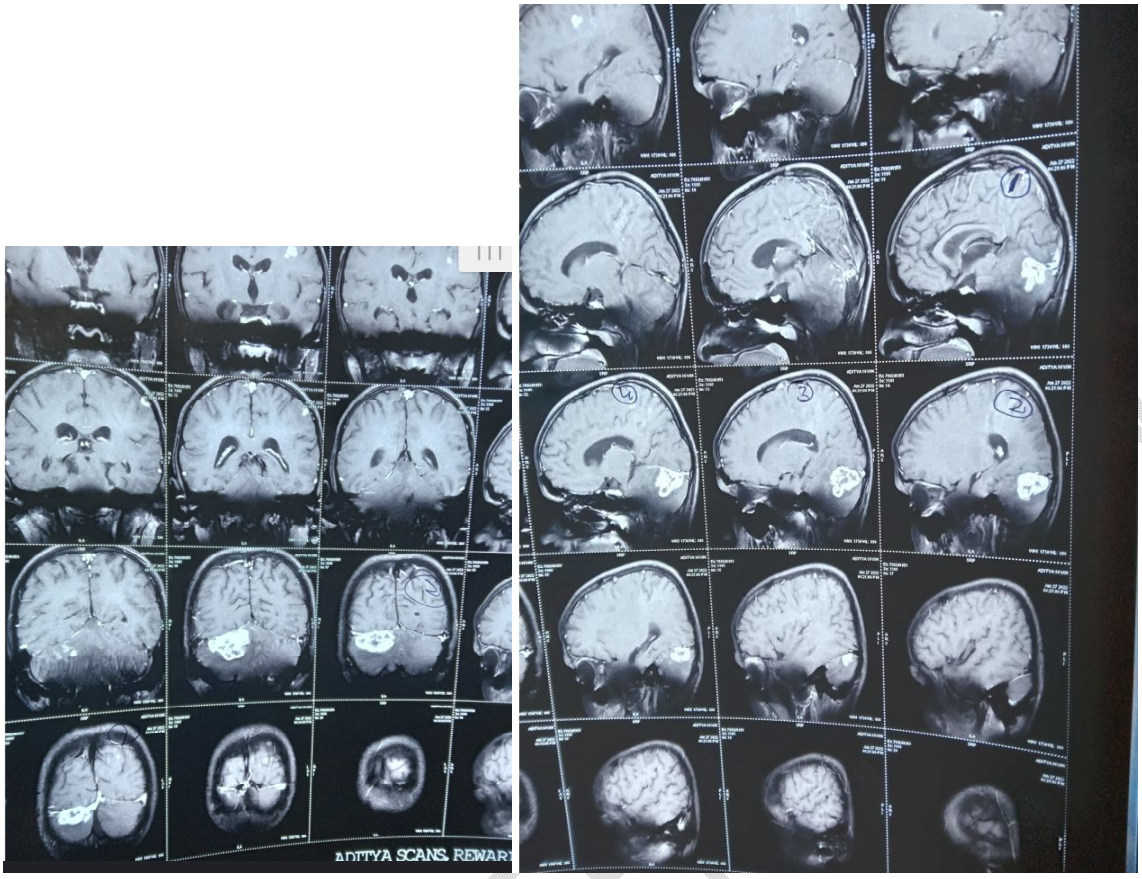

Figure 2: MRI contrast scan showing various tuberculomas in different parts of the brain. Largest mass can be seen in Cerebellum.

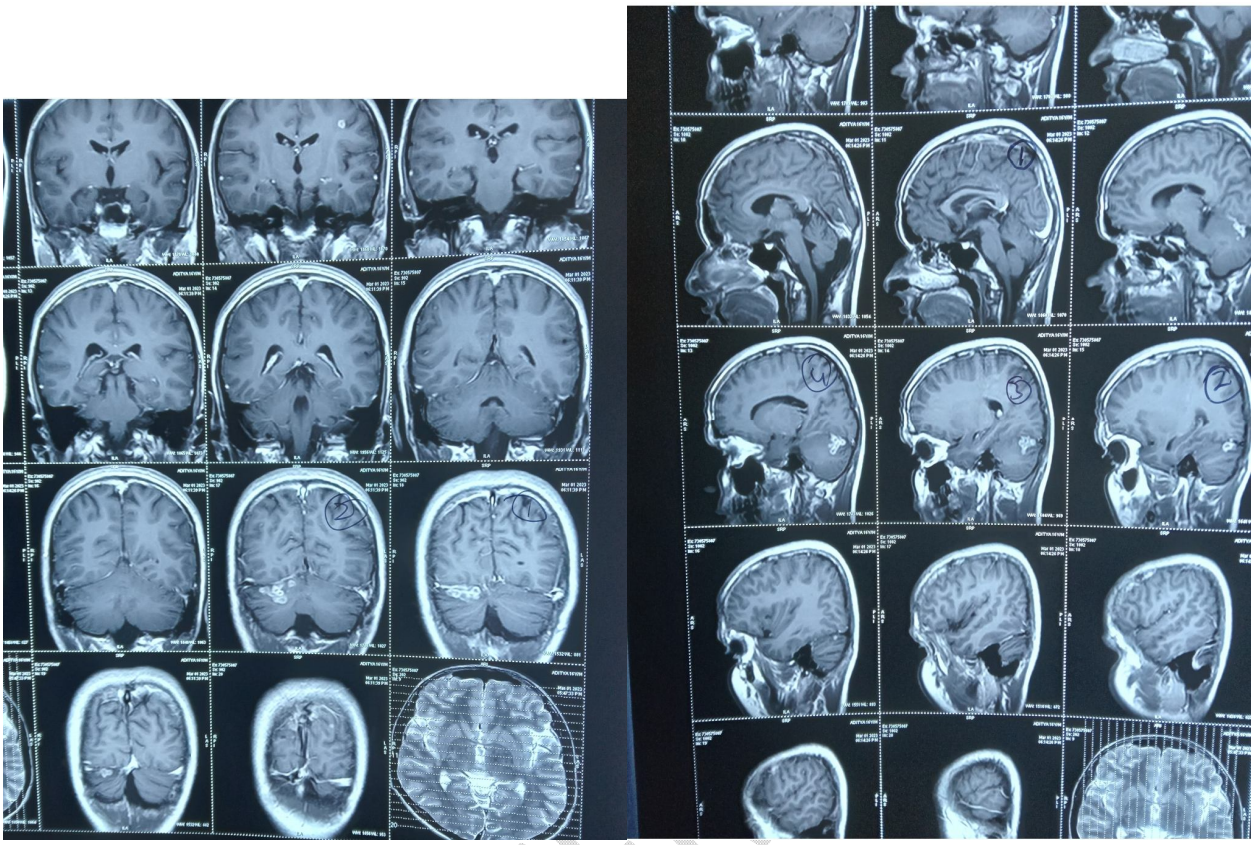

Fig 3: MRI contrast scan showing post treatment State of the brain with reduction in tuberculoma.

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 like the brain (7).

Although, CNS Tuberculosis is rare, it can be life threatening (1). Individuals with an increased risk for miliary and extrapulmonary TB include patients with immunodeficiency 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 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.

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, which are seen usually 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 perilseional edema.

Tuberculomas of the brain may present with 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 CT scan and MRI scan with contrast enhancement and MR spectroscopy are the basis for diagnosis of CNS tuberculoma (1). MRI is usually the imaging test of choice, given its superiority over CT in the diagnosis of CNS TB (6). The most common image of tuberculoma is 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' that suggests reactivation or dormant tuberculosis. (1,3,13). Other differentials for the masses seen on the MRI where considered however the findings from the MRI scans 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 i.e. 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 occur 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: 1) to relieve symptomatic or potentially life-threatening mass effect and/or hydrocephalus, and 2) to treat medically refractory seizures (10). 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 perilseional 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. Risk factors include immunodeficiency caused by aging(young and elderly), alcoholism, malnutrition, malignancy, HIV infection, or drugs, such as tumour necrosis factor-alpha inhibitors. Clinical features depends on the location of this lesions. While there are a number of differentials, 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.

Disclaimers: This article has not been submitted for publication elsewhere and/or presented at conferences or meetings.

Source(s) of fund support: None

Data Availability: The information used in this study was from publicly available published research papers.

Regulatory Approval or Research Subject Protection Requirements: This manuscript does not require regulatory approval.

Ethical approval: This paper does not require ethical approval

References

1) E.A. Ashok Kumar, Srirangam Ramya, Sai Mounika Neelamraju. A study of clinical profile and treatment outcomes in CNS tuberculoma. IAIM, 2022; 9(9): 21-29.

2) Huber B, Joshi S. CNS tuberculoma in an immunocompetent patient: A case report of multi-drug hypersensitivity to RIPE therapy. IDCases. 2023 Aug 23;33:e01886. doi: 10.1016/j.idcr.2023.e01886. PMID: 37674901; PMCID: PMC10477797.

3) Shankar GS, Nair S, Jacob T, Idikula MJ. Brain tuberculoma: a 52-year-old woman case report. Access Microbiol. 2023 Oct 16;5(10):000634.v4. doi: 10.1099/acmi.0.000634.v4. PMID: 37970079; PMCID: PMC10634481

4) Yee AC, Wong TTJ. An atypical presentation of CNS tuberculosis manifesting with meningoencephalitis and tuberculoma in a New York taxi driver. IDCases. 2023 May 23;32:e01810. doi: 10.1016/j.idcr.2023.e01810. PMID: 37273845; PMCID: PMC10238830.

5) Rezaee H, Tavallaii A, Keykhosravi E, Nazeminezhad R, Asghari R, Alenabi A. A rare case of disseminated tuberculosis; multiple intracranial and intramedullary tuberculomas with concurrent tuberculous spondylitis and meningitis. J Clin Tuberc Other Mycobact Dis. 2020 Jun 5;20:100169. doi: 10.1016/j.jctube.2020.100169. PMID: 32548312; PMCID: PMC7286962.

6) Vasconcelos G, Santos L, Couto C, Cruz M, Castro A. Miliary Brain Tuberculomas and Meningitis: Tuberculosis Beyond the Lungs. Eur J Case Rep Intern Med. 2020 Sep 14;7(12):001931. doi: 10.12890/2020_001931. PMID: 33313004; PMCID: PMC7727626

7) Meegada S, Gyamfi R, Muppidi V, et al. (March 12, 2020) Multiple Intracranial Tuberculomas with an Intra-medullary Spinal Cord Tuberculoma in a Pediatric Patient. Cureus 12(3): e7248. DOI 10.7759/cureus.7248

8) Abu-Abaa M, Arshad H, Ali D, Abdulsahib A. Meningeal Tuberculoma Masquerading as a Brain Tumor: A Case Report. Cureus. 2022 Oct 28;14(10):e30804. doi: 10.7759/cureus.30804. PMID: 36457642; PMCID: PMC9705070.

9) Baykan, A.H., Sayiner, H.S., Aydin, E. et al. Extrapulmonary tuberculosıs: an old but resurgent problem. Insights Imaging 13, 39 (2022). https://doi.org/10.1186/s13244-022-01172-0

10) Marais S, Van Toorn R, Chow FC, Manesh A, Siddiqi OK, Figaji A, Schoeman JF, Meintjes G; Tuberculous Meningitis International Research Consortium. Management of intracranial tuberculous mass lesions: how long should we treat for? Wellcome Open Res. 2019 Oct 31;4:158. doi: 10.12688/wellcomeopenres.15501.2. PMID: 32047859; PMCID: PMC6996525.

11) Chatterjee S. Brain tuberculomas, tubercular meningitis, and post-tubercular hydrocephalus in children. J PediatrNeurosci 2011;6:S96-100.

12) McMahon P, Pisapia DJ, Schweitzer AD, Heier L, Souweidane MM, Roytman M. Central nervous system tuberculoma mimicking a brain tumor: A case report. Radiol Case Rep. 2023 Nov 14;19(1):414-417. doi: 10.1016/j.radcr.2023.10 .042. PMID: 38028299; PMCID: PMC10679855.

13) Perez-Malagon CD, Barrera-Rodriguez R, Lopez-Gonzalez MA, Alva-Lopez LF. Diagnostic and neurological overview of brain tuberculomas: a review of literature. Cureus. 2021;13:e20133. doi: 10.7759/cureus.20133. [PMC free article] [PubMed] [CrossRef] [Google Scholar].