CASE PRESENTATION

Tuberculoma of the brain

Mohammad Yahya Abdulrazaq,[a] Hiba Adnan Hameed,[b] Hussein Alwan Hussein,[c]

ABSTRACT

Tuberculosis (TB) is a significant infectious disease that poses a major global health challenge and stands as one of the leading causes of death from infectious diseases worldwide. Although TB primarily targets the respiratory system, it can also affect other parts of the body. A rare manifestation of TB is its impact on the central nervous system, particularly the brain, where it can form a space-occupying lesion known as a brain tuberculoma. Diagnosing brain tuberculoma is challenging but crucial to prevent severe complications. In this report, we present a rare case of brain tuberculoma documented at the National Tuberculosis Institute. This case highlights the unusual form of extrapulmonary tuberculosis and discusses the diagnostic and treatment approaches.

Key words: tuberculosis, tuberculoma, caseated granulomas.

INTRODUCTION

Central nervous system (CNS) tuberculosis (TB) represents about 1%–2% of all TB cases globally, causing considerable morbidity and mortality.[1] Although it is one of the rarer forms of human mycobacterial infection, CNS-TB is among the most severe and devastating.

Clinically, CNS infections are categorized into three types: subacute or chronic meningitis, intracranial tuberculoma, and spinal tuberculosis.[2] Tuberculoma is the second most frequent manifestation of CNS tuberculosis and makes up a significant portion of intracranial space-occupying lesions (SOL) in developing countries where tuberculosis remains widespread.[3]

CNS tuberculosis progresses through two stages. Initially, tubercule bacilli seed to form "Rich foci" primarily within the brain parenchyma following hematogenous dissemination during the primary or post-primary phase of the infection. The second stage begins after a latent period of months or a few years. In this stage, either the bacilli or their antigenic components are released into the subarachnoid space, leading to tuberculous meningitis, or the intracranial tubercles enlarge within the brain parenchyma, forming a space-occupying lesion (SOL) known as a tuberculoma that separated from the brain parenchyma by a thick fibrous capsule.[4] Unlike the rapid onset of tuberculous meningitis, brain tuberculoma has a slow progression, although both conditions can sometimes occur simultaneously in the same patient.[5]

Several risk factors for CNS tuberculosis have been identified. Children and HIV-coinfected patients are particularly susceptible to developing this condition.[6] Other risk factors include malnutrition and recent measles in children, as well as alcoholism, malignancies, and the use of immunosuppressive agents in adults.[7]

The clinical symptoms of tuberculomas vary based on their location and size, with the most

a: CABM, FIBMS, FRCP; Consultant pulmonologist & Internist, National Tuberculosis Institute. Baghdad, Iraq. b: MBChB, FIBMS; Family physician. National Tuberculosis Institute. Baghdad, Iraq c: MBChB, DTM. Pulmonologist. National Tuberculosis Institute. Baghdad, Iraq.

*Corresponding Author: **Mohammad Yahya Abdulrazaq**, E mail: **ntp.mohammad@gmail.com**.*

common symptoms being headache, epileptic seizures, neurological deficits, and papilledema.[8,9] Tuberculomas are firm, avascular, spherical masses ranging from 2 cm to 10 cm in diameter. They are well-circumscribed, and the surrounding brain tissue often shows signs of oedema and gliosis.[10]

Distinguishing tuberculomas from other infectious and non-infectious intracranial lesions is challenging. A biopsy of the lesion is the diagnostic gold standard, and stereotactic techniques have significantly improved the safety of this procedure. In one series, a stereotactic biopsy provided a diagnosis in 75 out of 80 (94%) patients, with only one patient experiencing complications. The obtained tissue should be examined for classical caseating granulomas and the presence of acid-fast bacilli.[11] On computed tomography (CT) and magnetic resonance imaging (MRI), tuberculomas typically appear as ring-enhancing or hyperdense lesions with associated oedema.[3] Sometimes, a combination of clinical symptoms, a family history of TB, and a positive response to treatment strongly indicate the presence of TB.[12] The duration of treatment of tubercuolosis involving CNS extended to 1 year instead of 6 months with steroid coverage for the first 2 months.[13]

CASE PRESENTATION

A 39-year-old hypertensive man from Baghdad was referred to the National TB Institute by a neurosurgeon for treatment and follow-up of brain tuberculoma.

The patient presented with headaches, dizziness, vertigo, blurred vision, and tinnitus. He also reported a mild fever and generalized weakness. He had no history of smoking or alcohol use and no history of pulmonary TB or contact with TB patients. His hypertension was well-controlled with medication, and he had a long history of nasal polyps for which he had received medical and surgical treatments. Initially, his physician attributed his symptoms to nasal polyps and prescribed various medications, which failed to alleviate his symptoms. Upon further examination, bilateral papilledema was observed, prompting an MRI with contrast and MRV to investigate the cause.

MRI results revealed a dura-based enhancing mass measuring 60x57x26 mm in the right anterior part of the brain, with surrounding edema causing significant mass effect and a 15 mm midline shift of the ventricular system, suggestive of meningioma or dural lymphoma. Additionally, the left lateral ventricle was mildly dilated, with no lesions detected in the posterior fossa and no signs of sinus venous thrombosis. **(Figure1, A, B and C)**

The patient was referred to a neurosurgeon and admitted for surgical management of a frontal skull base lesion compressing both optic nerves and extending from the crista galli to the optic foramina and sphenoid wings, predominantly on the right side. Bilateral papilledema was confirmed on examination.

Under general anesthesia, the patient underwent a craniotomy and durotomy via a right-sided lateral supra-orbital approach. Total micro resection of the lesion, which appeared grossly similar to tuberculoma or meningioma, was performed. Coagulation was secured, and a watertight dural closure was achieved using TachoSil, without applying a drain.

The early postoperative period was uneventful, with no complaints of CSF leakage, anosmia, headache, weakness, or personality changes. The patient experienced full improvement in vision. Pending histopathology results, he was discharged on paracetamol 1000 mg twice daily, kappa 500 mg twice daily, dexamethasone 8 mg intramuscularly for 5 days, omeprazole 20 mg twice daily, and antibiotics.

Gross pathology showed multiple grayish tissue pieces measuring 10 cm in aggregate. Microscopic examination revealed confluent epithelioid caseating granulomas with multiple Langhans multinucleated giant cells and necrosis with fibrosis, consistent with tuberculosis. No neoplastic cells were detected. Consequently, the clinical diagnosis

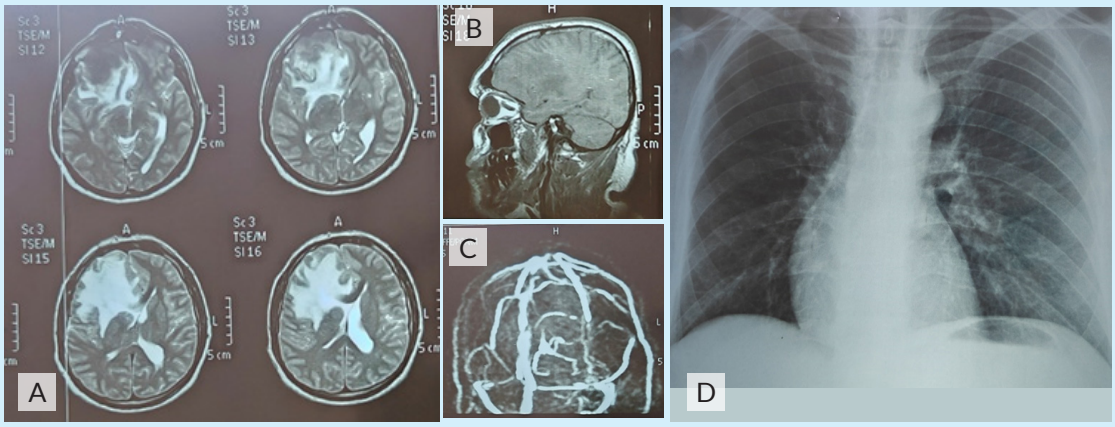

Figure 1 | (A) & (B) MRI pictures show an enhancing right frontal dural-based lesion measuring 60*57*26mm associated with vasogenic oedema in the right frontal lobe, causing a mass effect on the ipsilateral lateral ventricle with a midline shift of 15 mm and mild dilatation of the contralateral lateral ventricle with normal posterior fossa. **(C)** Normal MRV study. **(D)** Normal posteroanterior view chest X-ray of the same patient.

was tuberculoma of the brain.

At our institute, the patient, who had no history of TB contact or pulmonary tuberculosis, and a normal chest X-ray **(Figure 1:D)**, was diagnosed with extrapulmonary TB (brain tuberculoma). He began the initial phase of treatment with a daily fixed-dose combination of rifampicin 150 mg, isoniazid 75 mg, pyrazinamide 400 mg, and ethambutol 275 mg for two months, along with prednisolone tablets tapered off after the first month. This was followed by a continuation phase of rifampicin 150 mg and isoniazid 75 mg daily for ten months. The treatment course was uneventful, and the patient's symptoms improved remarkably.

DISCUSSION

Although tuberculosis primarily infects the lungs, it can affect many organs and systems. Early diagnosis and correct treatment are crucial to reducing mortality and morbidity associated with this disease.[15]

A retrospective study conducted over ten years at a tertiary care hospital in Pakistan found that the mean age of patients diagnosed with CNS tuberculosis was 43 years, with a higher prevalence in males.[16] Our patient, a 39-year-old male, presented with headaches, dizziness, vertigo, blurred vision, and tinnitus, symptoms initially attributed to his history of nasal polyps. Literature indicates that brain tuberculoma presents with variable focal signs and symptoms of a subacute or chronic onset.[17] Common early symptoms include headache, fever, and weight loss, while specific symptoms like diplopia may appear later.[18] In a Sudanese case series of 16 patients with brain tuberculoma, all presented with headaches, about two-thirds had generalized seizures, and approximately half had hemiparesis.[19]

In our case, the focal symptom was blurred vision. Despite impaired visual tests, lenses did not improve his vision, leading to a proper fundal examination revealing bilateral papilledema and shifting the diagnostic focus to the brain. Although seizures, hemiplegia, and other signs of raised intracranial pressure are reported in the literature,[20] our patient exhibited only papilledema.

MRI findings of tuberculomas can vary, with lesions demonstrating homogeneous nodular enhancement on contrast-enhanced images and peripheral oedema on T2-weighted images.[21] Adults generally have frontal or parietal lobe involvement, while children have infratentorial involvement.[22] Our patient's brain MRI suggested a frontal lobe skull base lesion compressing both optic nerves, extending from the crista galli to the optic foramina and sphenoid wings on the right side. The radiographic features of tuberculomas are non-specific and often mimic those of various infectious and non-infectious conditions, posing diagnostic challenges. A definitive

diagnosis requires an intracranial biopsy followed by histopathological examination. Differential diagnoses include malignant lesions, sarcoidosis, pyogenic abscess, toxoplasmosis, and cysticercosis.[23] While CT scans are sensitive and specific for detecting CNS tuberculoma,[24] MRI is superior for diagnosis.[25]

Our patient had no history of tuberculosis or contact with infected individuals but had hypertension and a history of nasal polypectomy. These factors initially diverted attention from CNS tuberculosis. The final diagnosis was made through histopathological examination revealing epithelioid caseating granulomas with multiple Langhans multinucleated giant cells. CNS granulomas can be associated with other infectious diseases, immunologic disorders, congenital disorders, and neoplasms.[26,27] Brain biopsy is the most accurate diagnostic method for multiple brain tuberculomas,[28] and surgical intervention is recommended for patients with neurological deficits.[29,30] Brain tuberculomas can develop in rare cases into pus-filled cavities, indicating poor defence mechanisms, and may require surgical excision.[31]

Our patient was diagnosed with extrapulmonary TB (brain tuberculoma) and treated according to WHO guidelines.[32] The initial phase included four tablets daily of a fixed-dose combination of rifampicin 150 mg, isoniazid 75 mg, pyrazinamide 400 mg, and ethambutol 275 mg for two months, followed by a fixed-dose combination of rifampicin 150 mg and isoniazid 75 mg for ten months. The treatment was successful without adverse effects. The patient also received steroids for one month, tapered off in the second month per WHO recommendations.[13] the duration of treatment is recommended to be 12 months; however, some neurologists extend treatment to 18 months or longer in patients with multiple or large lesions.[33]

CNS tuberculosis is a serious health problem, and treatment should not be delayed.[34] Sometimes, the standard 4-drug anti-TB therapy should be initiated based on strong clinical suspicion, even before bacteriologic confirmation.[34] Numerous variables can affect the response of the disease to therapy, and the duration of treatment may need to be tailored to the radiological response.[35]

The prognosis is generally bad, with a mortality rate that can reach as high as 50 %, especially in children. It depends on many factors at presentation, including Glasgow coma scale score, age, protein level in the CSF, presence of complications and others.[36] Fortunately, our patient responded excellently to the treatment without significant adverse events.

CONCLUSION

Brain tuberculoma is a rare disease but carries serious consequences. The initial clinical features, like headache, malaise and fever, are subtle and non-specific. It has many clinical similarities with other CNS infections, inflammation or neoplasms. MRI and CT scans of the brain may shorten the differential diagnosis list. Histopathology and or bacteriological diagnosis of tuberculosis on brain biopsy is usually needed to confirm the diagnosis.

Treatment with four anti-TB drugs for two months, followed by two drugs for ten months, is needed urgently and without any delay.

REFERENCES

1. Leonard JM. Central nervous system tuberculosis. *Tuberculosis and nontuberculous mycobacterial infections*. 2017 Jun 1:331-41.
2. Lakatos B, Prinz G, Sárvári C, Kamotsay K, Molnár P, Ábrahám A, Budai J. Central nervous system tuberculosis in adult patients. *Orvosi Hetilap*. 2011 Apr 1;152(15):588-96.
3. Bovijn L, Solomons R, Marais S. Neurological TB in HIV. In: Sereti I, Bisson GP, Meintjes G. (eds) HIV and Tuberculosis. Springer, Cham. https://doi.org/10.1007/978-3-030-29108-2_13.
4. Mukherjee S, Das R, Begum S. Tuberculoma of the brain-a diagnostic dilemma: magnetic resonance spectroscopy a new ray of hope. *The Journal of Association of Chest Physicians*. 2015 Jan 1;3(1):3-8.
5. Garg RK. Diagnosis of intracranial tuberculoma. *Ind J Tub.* 1996;43:35-9.
6. Rock RB, Olin M, Baker CA, Molitor TW, Peterson PK. Central nervous system tuberculosis: pathogenesis and clinical aspects. *Clinical microbiology reviews*. 2008 Apr;21(2):243-61.

7. 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 Dec;13(12).
8. Aniba K, Ghannane H, Jalal H, Belhaj Z, Ousehal A, Lmejjati M, Benali SA. Giant cerebellar tuberculoma mimicking a malignant tumor. *Neuro-chirurgie*. 2008 Sep 25;55(3):337-9.
9. Parihar V, Yadav YR, Sharma D. Giant extra-axial posterior fossa tuberculoma in a three-year-old child. *Neurology India*. 2009 Mar 1;57(2):218-20.
10. Chatterjee S. Brain tuberculomas, tubercular meningitis, and post-tubercular hydrocephalus in children. *Journal of pediatric neurosciences*. 2011 Oct 1;6(Suppl 1):S96-100.
11. Thwaites G, Fisher M, Hemingway C, Scott G, Solomon T, Innes J. British Infection Society guidelines for the diagnosis and treatment of tuberculosis of the central nervous system in adults and children. *Journal of infection*. 2009 Sep 1;59(3):167-87.
12. Said AI, Abdulahi M, Ali AO, Koshin AM, Walhad SA, Muse AH. Left temporal epilepsy unmasking tuberculoma in an immunocompetent adolescent: Case report. *Atención Primaria Práctica*. 2024 Apr 1;6(2):100198.
13. World Health Organization. WHO consolidated guidelines on tuberculosis: module 4: treatment, Drug susceptible tuberculosis treatment. 2022.
14. Wasay M. Central nervous system tuberculosis and paradoxical response. *Southern medical journal*. 2006 Apr 1;99(4):331-3.
15. Talamás O, Del Brutto OH, García-Ramos G. Brain-stem tuberculoma: an analysis of 11 patients. *Archives of neurology*. 1989 May 1;46(5):529-35.
16. Azeemuddin M, Alvi A, Sayani R, Khan MK, Farooq S, Beg MA, Awan S, Wasay M. Neuroimaging Findings in Tuberculosis: A Single‐Center Experience in 559 Cases. *Journal of Neuroimaging*. 2019 Sep;29(5):657-68.
17. DeAngelis LM: Intracranial tuberculoma: case report and review of the literature. *Neurology*. 1981, 31:1133-6. 10.1212/wnl.31.9.1133
18. Monteiro R, Carneiro JC, Costa C, Duarte R. Cerebral tuberculomas–A clinical challenge. *Respiratory Medicine Case Reports*. 2013 Jan 1;9:34-7.
19. Idris MN, Sokrab TE, Arbab MA, Ahmed AE, El Rasoul H, Ali S, Elzubair MA, Mirgani SM. Tuberculoma of the brain: a series of 16 cases treated with anti-tuberculosis drugs. *The international journal of tuberculosis and lung disease*. 2007 Jan 1;11(1):91-5.
20. Harder E, Al-Kawi MZ, Carney P. Intracranial tuberculoma: conservative management. *The American journal of medicine*. 1983 Apr 1;74(4):570-6.
21. Huanjie Ma , Yuan Liu , Caiyu Zhuang ,Yuanyu Shen , Renhua Wu . Clinical features and MRI findings of intracranial tuberculomas. *Radiology of Infectious Diseases* 2018; 154(5):e159
22. Mohammadian M, Butt S. Symptomatic central nervous system tuberculoma, a case report in the United States and literature review. *IDCases*. 2019 Jan 1;17:e00582.
23. Poonnoose SI, Rajshekhar V. Rate of resolution of histologically verified intracranial tuberculomas. *Neurosurgery*. 2003 Oct 1;53(4):873-9.
24. Venter F, Heidari A, Galang K, Viehweg M. An atypical presentation of tuberculomas in an immunocompetent host. *Journal of Investigative Medicine High Impact Case Reports*. 2018 Aug ;6: doi: 2324709618798407.
25. Lwakatare FA, Gabone J. Imaging features of brain tuberculoma in Tanzania: case report and literature review. *African health sciences*. 2003;3(3):131-5.
26. 26. Aquino SL, Gamsu G, Webb WR, Kee ST. Tree-in-bud pattern: frequency and significance on thin section CT. *Journal of computer assisted tomography*. 1996 Jul 1;20(4):594-9.
27. World Health Organization. Framework for collaborative action on tuberculosis and comorbidities. In Framework for collaborative action on tuberculosis and comorbidities 2024.
28. Saleh M, Saeedi AA, Pooran AA. Brain tuberculomas: a case report. *Jundishapur Journal of Microbiology*. 2014 Jul;7(7).
29. Haddadian K, Rezaei O, Samadian M. Multiple brain tuberculomas and role of open brain biopsy: A case report and review. *Internet Jf Infect Dis*. 2005;4(1).
30. Radmanesh F, Nejat F, El Khashab M. Cerebral infarction as the first presentation of tuberculosis in an infant: a case report. *Journal of Microbiology, Immunology and Infection*. 2010 Jun 1;43(3):249-52.
31. Whitener DR. Tuberculous brain abscess: report of a case and review of the literature. *Archives of Neurology*. 1978 Mar 1;35(3):148-55.
32. World Health Organization. WHO consolidated guidelines on tuberculosis: module 6: tuberculosis and comorbidities. In WHO consolidated guidelines on tuberculosis: module 6: tuberculosis and comorbidities 2024.
33. Bijesh Ravindran Nair, Vedantam Rajshekhar; Factors Predicting the Need for Prolonged (>24 Months) Antituberculous Treatment in Patients with Brain Tuberculomas. *World Neurosurgery*, May 2019; 125:e236-e247.
34. Ogbole GI, Bassey OS, Okolo CA, Ukperi SO, Ogunseyinde AO. Testicular tuberculosis presenting with metastatic intracranial tuberculomas only: a case report. *Journal of Medical Case Reports*. 2011 Dec;5:1-5.
35. Lwakatare FA, Gabone J. Imaging features of brain tuberculoma in Tanzania: case report and literature review. *African health sciences*. 2003;3(3):131-5.
36. Wang MG, et al . Treatment outcomes of TB meningitis in adult ; a systematic review and meta analysis. *BMC Pulm Med*.2019 Nov.06;19(1);200.

Abbreviations list: Central nervous system (CNS), Cerebrospinal Fluid (CSF), Computed tomography (CT), human immunodeficiency viruses (HIV), Magnetic resonance imaging (MRI), Magnetic resonance venogram (MRV), Space-occupying lesions (SOL), Tuberculosis (TB), World Health Organization (WHO).

Conflict of interest: Authors have nothing to declare.

Funding: Nothing apart from personal fund.