Case report

Intracerebral tuberculomas: A rare cause of seizure in an immunocompetent young male

Khiem Vu¹,a,*, Hannah Adlera, Erica Gibbonsb, Jennifer Pearsona, William Betza

A¹ Grand Strand Medical Center, United States  
T² The Edward Via College of Osteopathic Medicine–Carolinas, United States

A R T I C L E   I N F O

Article history:
Received 4 July 2019
Received in revised form 12 July 2019
Accepted 12 July 2019

Keywords:
Tuberculosis  
Tuberculoma  
Meningitis  
Seizure  
Central nervous system  
Intracerebral

A B S T R A C T

Central nervous system (CNS) involvement occurs in about 1% of all tuberculosis (TB) cases, classically presenting as a meningitis. Intracerebral tuberculomas are a much rarer manifestation. We describe the case of a young black male who presented with new-onset seizure. Cerebral computerized tomography from an outside hospital reportedly showed findings concerning for septic emboli. Brain magnetic resonance imaging at our institution confirmed the presence of multiple, peripherally enhancing lesions in the right frontal and temporal lobes, cerebellum, and pons. Thoracentesis was performed for a concomitant pleural effusion, which contained elevated levels of adenosine deaminase and ultimately grew Mycobacterium tuberculosis. After ruling out other causes, we reached a diagnosis of CNS TB manifesting as cerebral tuberculomas. The patient was initiated on a course of rifampin, isoniazid, pyrazinamide, and ethambutol for two months, followed by rifampin and isoniazid to complete at least twelve months of antimicrobial therapy. We present this case to highlight this unusual manifestation of CNS TB and review the challenges in diagnosis.

© 2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Tuberculosis (TB) is a chronic granulomatous disease caused by Mycobacterium tuberculosis (MTB). It primarily affects the lungs, but may also involve any extrapulmonary organ and may rarely present with potentially debilitating central nervous system (CNS) manifestations. CNS TB occurs in about 1% of all patients with TB, and typically manifests as meningitis [1–4]. Intracranial tuberculomas are the least common presentation of CNS TB, and usually affects immunocompromised patients [1,3]. The radiographic characteristics of tuberculomas often mimic those of other infectious and non-infectious conditions, and the clinical manifestations are diverse and nonspecific. Although the definitive diagnosis of intracerebral tuberculomas technically involves intracranial biopsy and histopathology, this approach is often impractical due to its invasive nature, close proximity of lesions to life-critical structures, and the risk of meningitis from accidental seeding of the subarachnoid space [4,5]. This very challenge underscores the importance of detecting adjunctive, extracranial evidence of active TB supporting the diagnosis of intracranial tuberculomas [3–8].

Case report

A 23-year-old black male with past medical history of chronic cough presented for a witnessed, new-onset seizure. He was initially brought to an outside emergency department where a head CT showed possible septic emboli to the brain, then transferred to our institution for higher level of care. He reported diaphoresis, muscle aches, and a 20-lb weight loss over the last three months. Other than the above, review of systems was negative for confusion, headache, vision changes, slurred speech, focal weakness, numbness, urinary incontinence, bowel incontinence, rashes, or arthralgias.

Upon further history, the patient had undergone a recent workup for chronic cough and fevers one month ago. He was found to have right-sided hilar and mediastinal adenopathy by chest CT and underwent bronchoscopy. Bronchoalveolar lavage at the time was negative for TB, but positive for Streptococcus viridans and methicillin-susceptible Staphylococcus aureus. Multiple transbronchial biopsies were negative for malignancy or granulomas. He also had negative serologies for human immunodeficiency virus (HIV), cytomegalovirus (CMV), Bartonella, and syphilis, and was discharged with a course of antimicrobials for presumed bacterial pneumonia. Travel history was significant for a visit to Key Largo, Florida eight months ago. The patient was a college student and denied alcohol, tobacco, recreational drug use, or exposure to recent sick contacts.

https://doi.org/10.1016/j.idcr.2019.e00599
2214-2509/© 2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Vitals on admission were significant for elevated heart rate of 98 beats per minute. Physical exam revealed a tongue laceration and decreased right-sided breath sounds, but no neurological abnormalities. Labs were notable for microcytic anemia with low percent iron saturation, ESR 78 mm/hr, and CRP 5.59 mg/dL. Immunoglobulin (IgG, IgM, IgA) levels showed no evidence of humoral immunodeficiency. Quantiferon-TB Gold was positive. CT chest showed predominantly right-sided pleural effusion and mediastinal lymphadenopathy (Fig. 1). Brain MRI with and without contrast showed multiple, peripherally enhancing lesions in the right frontal and temporal lobes, cerebellum, and lower pons (Fig. 2). Thoracentesis was performed and pleural fluid studies revealed an exudative pleural effusion with white blood cell (WBC) count of 3,559/mm³, red blood cell (RBC) count of 49,234/mm³, glucose of 4 mg/dL, and lactate dehydrogenase (LDH) of 1860 U/L. Pleural fluid studies were negative for bacterial or fungal growth, but culture-positive for Mycobacterium tuberculosis (MTB) and contained elevated levels of adenosine deaminase 18.7 U/L (reference range 0.0–9.4 U/L). A Genexpert assay revealed no MTB resistance to rifampin. The patient also underwent lumbar puncture and cerebrospinal fluid (CSF) studies revealed WBC 2/mm³, RBC 11/mm³, total protein 47 mg/dL, and glucose 47 mg/dL. His CSF showed negative growth for bacteria, virus, fungus, or acid-fast bacilli (AFB). Blood cultures were negative for bacterial growth and a transthoracic echocardiogram was negative for vegetations. Electroencephalogram was normal.

A rheumatologic laboratory workup was also performed. Although the patient tested positive for anti-nuclear antibodies (ANA) and antibodies against chromatin, he had negative antibodies against Smith (Sm), double stranded DNA (dsDNA), Jo-1, ribonucleoprotein (RNP), rheumatoid factor (RF), cyclic citrullinated peptide (CCP), Sjögren’s-syndrome-related antigens A and B (SSA/Ro and SSB/La), and centromere. He also tested negative for cytoplasmic and perinuclear-antineutrophil cytoplasmic antibodies (c-ANCA and p-ANCA).

On hospital day four, the patient received the diagnosis of active CNS TB manifesting as tuberculomas after his pleural fluid tested AFB smear-positive, and after alternative etiologies were ruled out as the cause of his seizure. He was promptly started on rifampin, isoniazid, pyrazinamide, ethambutol (RIPE), and vitamin B6. Levetiracetam was also initiated the day of admission for seizure prophylaxis. Throughout his stay, the patient remained hemodynamically stable and had no additional seizures nor neurological deficits. After two weeks of inpatient monitoring, the patient was discharged to undergo RIPE therapy for two months, followed by rifampin and isoniazid maintenance therapy. Repeat brain MRI at 6 months showed nearly complete resolution of most of the lesions; the pontine lesion decreased in size from 12 mm to 0.4 mm.

**Discussion**

Tuberculosis is a major public health concern recognized for its pulmonary manifestations. However, disseminated forms of TB are possible, such as those involving the central nervous system. CNS TB occurs in about 1% of all cases of active tuberculosis and disproportionately affects children and HIV-infected individuals. Other risk factors for CNS TB include malignancy, malnutrition, alcoholism, and use of immunosuppressive agents. Given the absence of these risk factors in our patient, the diagnosis of intracerebral tuberculomas was unexpected, but reached with a high degree of certainty after a comprehensive workup for alternative etiologies. Although the patient did not recall any close contact with individuals with active TB or productive cough, we speculate as to the role, if any, played by his recent travel to Florida several months prior to presentation.

Meningitis is the classic presentation of CNS TB. Cerebral tuberculomas are a much rarer manifestation. They originate from the hematogenous spread of MTB from the lungs into the brain parenchyma, creating well-circumscribed granulomatous foci. These foci can enlarge and exert local mass effects without necessarily rupturing into the subarachnoid space [1,4,6–10]. The symptoms of tuberculomas are nonspecific, which may include headache, seizures, cranial nerve palsies, or other clinical signs of increased intracranial pressure [1,3,4,6,7,9–11]. Such symptoms are essentially indistinguishable from any other space occupying lesion, making it necessary to evaluate for alternative noninfectious and infectious etiologies such as malignancy, sarcoidosis, pyogenic abscess, toxoplasmosis, bartonellosis, or syphilis. Patients may sometimes present with these various neurological deficits, but without the classic constitutional symptoms typical of active tuberculosis.

The diagnosis of intracranial tuberculosis can be challenging and is typically made by the combination of clinical history, imaging studies, and labs. Imaging alone is insufficient due to the lack of specific radiologic features. Brain MRI findings of peripheral ring enhancement are valuable for supporting the diagnosis but not necessarily pathognomonic, for such findings can be similarly found in multiple other disease processes. CSF analysis is usually

![Fig. 1. Tuberculoma chest CT.](image-url)
not helpful, although our patient was found to have a mildly elevated CSF protein. In certain cases where there is no evidence of active TB elsewhere, a brain biopsy can be confirmatory. However, such an invasive procedure comes with inherent risks and is not ideal in all scenarios. In our case, the neurosurgical service deemed a stereotactic brain biopsy too hazardous given the proximity of the central lesions to the brainstem and the diminutive size of the more peripheral lesions. However, CT imaging demonstrated mediastinal lymphadenopathy and a right-sided pleural effusion that contained elevated levels of ADA and eventually grew MTB. Thus, the pleural fluid studies were the key surrogate evidence to reach our diagnosis in expedited fashion but with high degree of clinical confidence.

In conclusion, the symptoms and radiologic features of tuberculomas are nonspecific and variable. Our patient was found to have active tuberculosis infection outside of the CNS, which supported the diagnosis of tuberculoma over other intracranial pathologies. In cases that do not present with increased intracranial pressure, treatment is predominantly medical in nature and is extrapolated from the standard RIPE regimen used for pulmonary TB. In some cases, duration of treatment may need to be prolonged for up to 18–24 months, depending on clinical or radiological improvement, as well as expert opinion [1,3–7,9–12].

We present our case to highlight the diagnostic approach towards intracranial tuberculoma and to review its current understanding.

**Declaration of Competing Interest**

We declare no conflicts of interest.

**Acknowledgements**

We thank the service of our resident physicians, teaching faculty (infectious disease, neurology, and pulmonary subspecialties), and nursing staff at Grand Strand Medical Center in the care of this patient. Lastly, we thank the patient for consenting to the presentation of his case.

**References**

[1] Rock RB, Olin M, Baker CA, Molitor TW, Peterson PK. Central nervous system tuberculosis: pathogenesis and clinical aspects. Clin Microbiol Rev 2008;21 (2):243–61.

[2] Phypers M, Harris T, Power C. CNS tuberculosis: a longitudinal analysis of epidemiological and clinical features. Int J Tuberc Lung Dis 2006;10 (1):99–103.

[3] Monteiro R, Carneiro JC, Costa C, Duarte R. Cerebral tuberculomas - a clinical challenge. Respir Med Case Rep 2013;9:34–7.
Venter F, Heidari A, Galang K, Viehweg M. An atypical presentation of tuberculomas in an immunocompetent host. J Investig Med High Impact Case Rep 2018;6:2324709618798407.

Sahaiu-Srivastava S, Jones B. Brainstem tuberculoma in the immunocompetent: case report and literature review. Clin Neurol Neurosurg 2008;110(3):302-4.

Idris MN, Sokrab TE, Arbab MA, et al. Tuberculoma of the brain: a series of 16 cases treated with anti-tuberculosis drugs. Int J Tuberc Lung Dis 2007;11 (1):91–5.

Kheir AEM, Ibrahim SA, Hamed AA, Yousif BM, Hamid FA. Brain tuberculoma, an unusual cause of stroke in a child with trisomy 21: a case report. J Med Case Rep 2017;11(1):114.

Survashe PT, Guthe S, Velho V, Naik H. Tectal tuberculoma: an unusual cause of parinaud’s syndrome. Asian J Neurosurg 2018;13(2):400–2.

Chatterjee S. Brain tuberculomas, tubercular meningitis, and post-tubercular hydrocephalus in children. J Pediatr Neurosci 2011;6(Suppl 1):S96–S100.

Salway BJ, Sangani S, Parekh S, Bhatt S. Tuberculoma-induced seizures. West J Emerg Med 2015;16(5):625–8.

Helmy A, Antoun N, Hutchinson P. Cerebral tuberculoma and magnetic resonance imaging. J R Soc Med 2011;104(7):309–13.

Thwaites GE, Macmullen-price J, Tran TH, et al. Serial MRI to determine the effect of dexamethasone on the cerebral pathology of tuberculous meningitis: an observational study. Lancet Neurol 2007;6(3):230–6.

HCA Disclaimer

This research was supported (in whole or in part) by HCA and/or an HCA affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA or any of its affiliated entities.