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Intracranial tuberculoma: a rare complication of extrapulmonary tuberculosis. Illustrative case

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BACKGROUND Intracranial tuberculomas are rare entities commonly seen only in low- to middle-income countries where tuberculosis remains endemic. Furthermore, following adequate treatment, the development of intracranial spread is uncommon in the absence of immunosuppression.

OBSERVATIONS A 22-year-old man with no history of immunosuppression presented with new-onset seizures in the setting of miliary tuberculosis status post 9 months of antitubercular therapy. Following a 2-month period of remission, he presented with new-onset tonic-clonic seizures. Magnetic resonance imaging demonstrated interval development of a mass concerning for an intracranial tuberculoma. After resection, pathological analysis of the mass revealed caseating granulomas within the multinodular lesion, consistent with intracranial tuberculoma. The patient was discharged after the reinitiation of antitubercular medications along with a steroid taper.

LESSONS To the best of the authors' knowledge, this case represents the first instance of intracranial tuberculoma occurring after the initial resolution of a systemic tuberculosis infection. The importance of retaining a high level of suspicion when evaluating these patients for seizure etiology is crucial because symptoms are rapidly responsive to resection of intracranial tuberculoma masses. Furthermore, it is imperative for surgeons to recognize the isolation steps necessary when managing these patients within the operating theater and inpatient settings.

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KEYWORDS tuberculoma; intracranial; extrapulmonary tuberculosis

Intracranial tuberculomas are rare and represent a serious form of tuberculosis caused by hematogenous spread of *Mycobacterium tuberculosis*. Intracranial tuberculomas are exceedingly uncommon in the United States and are most frequently seen in low- to middle-income countries where tuberculosis is endemic.[1–3] The clinical picture of intracranial tuberculomas is nonspecific and can often lead to delayed diagnoses; accurate diagnosis requires a high level of suspicion. Commonly reported presentations include new-onset partial or general seizures, evidence of systemic tuberculosis, and various focal neurological deficits. Radiologically, intracranial tuberculomas classically appear isointense to gray matter with vasogenic edema on T2-weighted magnetic resonance imaging (MRI) with ring enhancement after contrast administration.[4] Although most patients with intracranial tuberculomas can be managed nonoperatively, surgical excision is indicated when medical therapy fails. Due to the rarity of this entity, medical and surgical failure rates are unknown.[5] Our report highlights the importance of retaining a high level of suspicion for the presence of intracranial tuberculomas in a patient who had documented control of a previous tuberculosis infection. We discuss the presentation, differential diagnosis, and role of surgical management for intracranial tuberculomas.

Illustrative Case

A 22-year-old Micronesian man with a medical history significant for miliary tuberculosis status post 9 months of pharmacological therapy, exploratory laparotomy for a pelvic abscess with enterocutaneous fistula, and severe malnutrition with ascites presented to an outside hospital following a first-time seizure event. The patient had completed the

ABBREVIATIONS CNS = central nervous system; CSF = cerebrospinal fluid; CT = computed tomography; DWI = diffusion-weighted imaging; MRI = magnetic resonance imaging.

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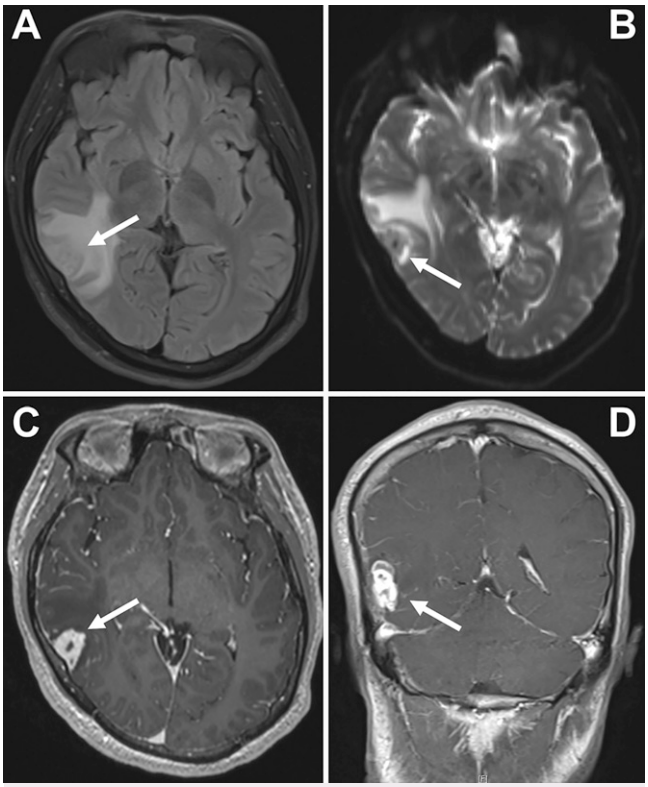

FIG. 1. A: Axial T2-weighted MRI sequence demonstrating a small, lobulated mass broadly abutting the dural margin along the right posterior superior temporal convexity without an enhancing dural tail (*white arrow*). **B:** Diffusion-weighted image demonstrating a small region of diffusion restriction centrally located within the lesion (*white arrow*). **C:** Axial postcontrast T1-weighted sequence demonstrating contrast enhancement of the lesion (*white arrow*). **D:** Coronal postcontrast T1-weighted sequence demonstrating contrast enhancement of the right posterior superior temporal convexity mass (*white arrow*).

recommended 9 months of pharmacological tuberculosis therapy, and his tuberculosis was assumed to be controlled. He was considered to be in remission for 2 months prior to his current presentation with new-onset tonic-clonic seizures with loss of consciousness.

On initial evaluation, computed tomography (CT) revealed a contrast-enhancing, extraaxial, right-sided temporal lobe mass. MRI of the brain revealed a superficial mass without an enhancing dural tail along the right posterior superior temporal convexity that demonstrated partial calcification of the contrast-enhancing lobulated components (Fig. 1). Based on the cranial MRI findings, concern for intracranial tuberculoma was raised. MRI of the complete neuroaxis was performed. Newly developed T1 hypointense, peripherally enhancing lesions were noted in the C5 vertebral body along with endplate destruction in the thoracic and lumbar spine. CT of the chest, abdomen, and pelvis revealed development of multiple small parenchymal and capsular hepatic and splenic masses. Admission laboratory results revealed a white blood cell count of 8.1 K/μL, hemoglobin level of 14.0 g/dL, and platelet count of 265 K/μL (Table 1). On examination, the patient was neurologically intact. From a neurosurgical standpoint, acute intervention for this intracranial mass was deferred pending results from planned hepatic biopsies. Biopsy of two separate hepatic lesions revealed caseating granulomas that were acid-fast bacteria smear negative. Because

TABLE 1. Admission results on initial presentation

Variable	Value	Reference Range
Hemoglobin, g/dL	14.0	13.5–16.5
Hematocrit, %	42.4	40–50
White blood cells, K/μL	8.1	4.5–11.0
Platelets, K/μL	265	150–400
AST, U/L	38	7–40
ALT, U/L	22	7–56
Blood culture, AFB	Negative	–
Liver biopsy, AFB	Negative	–
Urine culture, AFB	Negative	–

AFB = acid-fast bacteria; ALT = alanine transaminase; AST = aspartate transaminase.

of the patient's initial presentation with an appearance of severe malnutrition and a recent 30-lb weight loss and ascites, the concern of poor drug absorption was raised. For this reason, rifampin peak serum concentration studies were undertaken, which revealed a rifampin level 2 hours postdrug administration of 3.1 μg/mL following 750 mg of rifampin (expected to be approximately 10 μg/mL following a 600-mg dose). Given pathological confirmation of tuberculosis recurrence, antituberculosis therapy with moxifloxacin 400 mg daily, isoniazid 300 mg daily, rifampin 1,200 mg daily, pyrazinamide 1,500 mg daily, trimethoprim/sulfamethoxazole 160/800 mg daily, and prednisone 60 mg daily was started prior to discharge. Additionally, for seizure prophylaxis, levetiracetam 500 mg twice daily was begun. The patient was subsequently discharged with instructions to follow up with the neurosurgery department on an outpatient basis.

Approximately 1.5 months after the patient's initial seizure event, he experienced a breakthrough seizure event while on consistent levetiracetam 500 mg twice-daily therapy. Neurological examination was unremarkable. Repeat MRI of the brain demonstrated evolution of the mass lesion, with increased size and corresponding vasogenic edema causing early entrapment of the ipsilateral temporal ventricular horn. Following discussion with the patient, a decision to resect the mass was made.

Preoperatively, there were no external defects on the scalp. Right-sided parietal craniotomy was conducted in normal fashion. Dura was opened in a cruciate fashion. Using intraoperative navigation, the lesion was identified, and corticectomy was conducted to expose the lesion (Fig. 2). Intraoperative pathology was consistent with intracranial tuberculoma, with multiple nodules on frozen and permanent sections demonstrating caseating/necrotic contents. No acid-fast bacilli were present, likely because of the prior extended antitubercular therapy (Fig. 3). The mass was removed en bloc without any intraoperative complications, and the patient was transferred postoperatively to the intensive care unit for close monitoring. There were no postoperative neurological deficits. The patient was subsequently discharged on postoperative day 2. Discharge medications included a 2-week dexamethasone taper, levetiracetam 500 mg twice daily, and his prior antitubercular therapy.

At a 2-week postoperative follow-up, the patient remained neurologically intact and had not experienced any further seizure events. Antiepileptic drug therapy with levetiracetam was discontinued. Per infectious disease recommendations, antitubercular medications were continued.

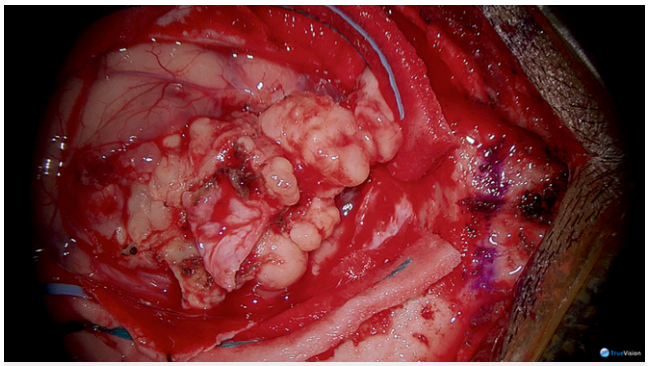

FIG. 2. Intraoperative image of the right posterior superior temporal convexity mass lesion demonstrating amenability to en bloc resection.

Discussion

Observations

The involvement of the central nervous system (CNS) in a tuberculosis infection is rare and represents a severe form of tuberculosis due to *M tuberculosis*. CNS involvement can present as meningitis, calvarial osteomyelitis, abscess, or, in rare cases, tuberculomas. Although not established in the literature, tuberculomas have been reported to occur in ∼1% of all CNS tuberculosis cases.[6] CNS involvement in tuberculosis is theorized to occur as a result of hematogenous spread from other infected organs. A two-stage pattern of development for cerebral tuberculoma has been described. Initially, tuberculous lesions develop during the phase of fulminant bacteremia during the initial tuberculosis infection. Subsequently, in the second stage, the rupture of one of these intracranial lesions leads to the development of CNS tuberculosis with potential tuberculoma development.[7]

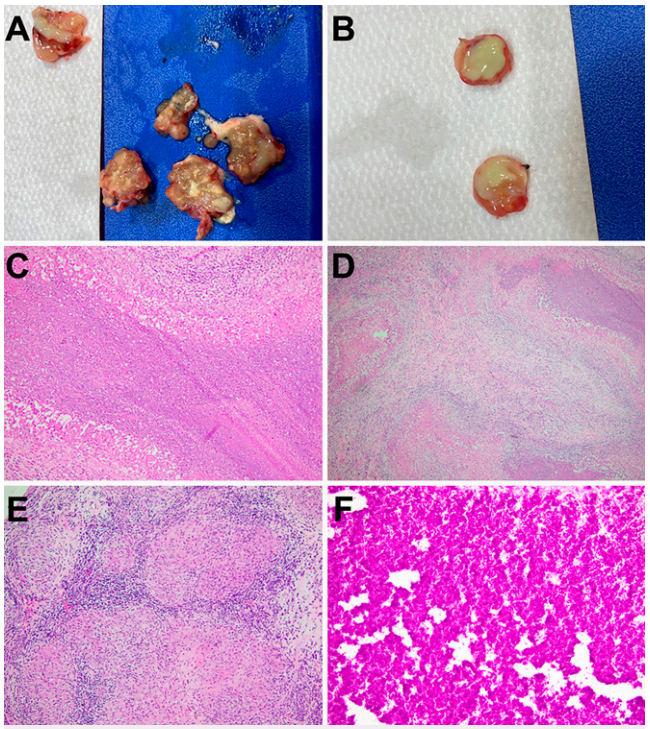

FIG. 3. A and B: Gross pathological sections of the mass lesion showing "caseating" necrosis. **C and D:** Low-power microscopic views of the large confluent granulomas with central necrosis. **E:** Well-formed granulomas. **F:** Smear of necrotic granuloma material at the time of intraoperative consultation. C–F: Hematoxylin and eosin stain. Original magnification ×20 (C and E), original magnification ×10 (D), and original magnification ×40 (F).

Tuberculomas are infrequently identified in patients with tuberculosis. Patients affected by CNS tuberculomas are often young and immunosuppressed.[8–11] Although our patient was young, after a thorough evaluation, no coexisting medical conditions were identified that predisposed this patient to a fulminant tuberculosis infection. Furthermore, in the literature, to our knowledge, all cases of cerebral tuberculoma were in patients who had not undergone a full cycle of antitubercular antibiotic therapy and demonstrated resolution.[2,3,6,8,10–13] In this case, we report a young, immunocompetent patient who developed an intracranial tuberculoma despite a presumed full course of antibiotic therapy. However, with the worsening of the patient's condition, there was concern that gastrointestinal absorption of the antitubercular drugs may be reduced given the severe state of malnutrition observed initially. This patient's rifampin level 2 hours post drug administration was 3.1 μg/mL following 750 mg of rifampin. When compared to the known clinical pharmacokinetics of rifampin, a 600-mg dose of rifampin should correlate to a peak serum concentration around 10 μg/mL.[14] Although there is speculation as to the root cause for this relapse, a potential explanation could be the patient harboring a tuberculosis infection within one of his organs as a result of the initial miliary tuberculosis infection.

A high degree of suspicion is crucial in the diagnosis of intracranial tuberculomas due to the nonspecific neurological symptomatology. Radiographically, tuberculomas are often isointense to gray matter on T1- and T2-weighted MRI sequences and demonstrate significant vasogenic edema on T2-weighted imaging. Following contrast enhancement, they classically exhibit peripheral ring enhancement or may simply appear as a conglomerate enhancing mass, as in our case. Furthermore, diffusion-weighted imaging (DWI) often does not exhibit diffusion restriction; however, if there is central liquefactive necrosis within the tuberculoma, high signal may be present on DWI, representing diffusion restriction.[4,7] In our case, MRI revealed features associated with intracranial tuberculoma; however, given its nonspecific radiographic findings, it could have represented a superficial primary glial neoplasm such as a ganglioglioma or pleomorphic xanthoastrocytoma. Along with gliomas, the differential diagnosis includes meningioma, intracranial abscess, cerebral metastases, and other CNS infectious etiologies.[12]

The importance of definitive diagnosis was urgently pursued in this case due to the interval progression of radiographic features along with the persistence of breakthrough seizures while on consistent first-line antiepileptic therapy. Other indications for resection of these masses includes rising intracranial pressure and mass effect leading to cerebral herniation. It is important to note the location of the intracranial tuberculoma, with most located in the frontoparietal region, basal ganglia, cerebellopontine angle, corpus callosum, suprasellar region, and ventricular regions. In the event of ventricular involvement, gelatinous exudates have been reported on the choroid plexus, leading to ependymitis and hydrocephalus developing due to the formation of adhesions within the ventricular system.[15] Minimal evidence is present regarding outcomes after resection. In 2020, Vemula et al. proposed a set of criteria that warranted surgical therapy. In patients who fail medical therapy, resection decreases the duration of lesion presence while also reducing the total length of antitubercular therapy.[16] On resection, tuberculomas are often firm, avascular, lobulated masses that are

amenable to en bloc resection (Fig. 2). However, while resection is considered to be the gold standard for tuberculomas, other nonsurgical options that may be considered include cerebrospinal fluid (CSF) diversion for hydrocephalus and endoscopic or stereotactic biopsy for initial tissue diagnosis.[15] Prior published cases have presented with features of hydrocephalus, and some describe success with solitary CSF diversion and antitubercular therapy. Care must be taken to ensure close follow-up in these patients to rapidly identify a patient exhibiting neurological decline.[17]

After resection of these lesions, histopathological evaluation demonstrates central necrotic regions of caseation with the potential for tubercule bacilli to be found.[7] Importantly, the lack of tubercule bacilli on histopathological and microbiological analysis does not exclude the diagnosis of cerebral tuberculoma.[18] Tissue in our case did not demonstrate acid-fast bacilli, likely due to long-term antitubercular therapy prior to procurement of tissue.

When treating patients with tuberculosis or complications associated with tuberculosis, the health and safety of the healthcare team is paramount. Guidelines for airborne infection control vary based on country of practice and clinical setting; however, basic guidelines are as follows. For patients with active tuberculosis that has not been treated with a full course of antibiotic therapy, full airborne precautions must be undertaken by all staff members, including isolation of the patient in an airborne infection isolation–equipped room. In situations in which the patient has been deemed not infectious by the hospital's infectious disease team following a full course of antitubercular therapy, the patient can be roomed without full airborne precautions. In any situation in which tuberculosis-containing tissue may be encountered, full airborne precautions must be followed, including housing the patient in an airborne infection isolation room.[19] In our case, the patient was deemed noninfectious, but in the operating theater, given the aerosolization of bone and manipulation of a potential infectious lesion, full airborne precautions were practiced by all members of the healthcare team.

Lessons

We discuss the development of an intracranial tuberculoma in a patient who was initially presumed to have undergone a full course of antitubercular therapy and was in remission for 2 months. Given radiographic findings, the differential diagnosis included intracranial tuberculoma, meningioma, cerebral metastases, or other CNS infections. It is important to note that MRI findings of intracranial tuberculomas can vary depending on the stage of the lesion and surgical excision, with histological diagnosis being the only way to confirm an intracranial tuberculoma. This case demonstrates the efficacy of resection after the appropriate diagnosis, highlighting the need for all clinicians to retain a high suspicion for the presence of intracranial tuberculoma despite prior antitubercular therapy. Furthermore, we highlight the isolation steps necessary when managing these patients within the operating theater and inpatient settings to ensure the safety of all healthcare workers involved in each patient's care.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Letchuman, Lundy, Camarata. Acquisition of data: Letchuman, Lundy, Lakis. Analysis and interpretation of data: Guillotte, Letchuman, Dharia, Lakis. Drafting the article: Guillotte, Letchuman, Dharia. Critically revising the article: all authors. Reviewed submitted version of manuscript: Guillotte, Letchuman, Lundy, Camarata. Approved the final version of the manuscript on behalf of all authors: Guillotte.

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