



Case report

Intracranial tuberculomas: A case report of clinical, radiological, and pathological characteristics[☆]Ahoud Alharbi^{a,b,c,*}, Sami Khairy^{a,b,c}, Fahd Al Sufiani^{b,c,d}, Ahmed Alkhani^{a,b,e}^a Division of Neurosurgery, Department of Surgery, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia^b King Abdullah International Medical Research Center, Riyadh, Saudi Arabia^c King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia^d Department of Pathology and Laboratory Medicine, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia^e Alfaisal University, Riyadh, Saudi Arabia

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ABSTRACT

Background: Intracranial tuberculomas are uncommon yet devastating forms of extrapulmonary tuberculosis with a high mortality rate and morbidity risk. A high level of suspicion is required for a prompt diagnosis and treatment.**Case description:** A 67-year-old male, medically free, presented at the Emergency Department with a 1-day history of nausea and vomiting, and a 15-day history of imbalance and dizziness. Radiological imaging demonstrated right well-defined ring-enhancing lesions. He underwent a sup-occipital craniotomy with lesion resection. The diagnosis of an intracranial tuberculoma was confirmed histopathologically. Anti-tuberculosis therapy was prescribed, and the patient was discharged with mild cerebellar dysfunction.**Discussion:** Intracranial tuberculomas have a high rate of mortality and morbidity. It is critical to consider tuberculoma in the differential diagnosis of intracranial lesions with such clinico-radiological characteristics, especially in developing countries.**Conclusion:** In this article, we are reporting an interesting case with multiple intracranial tuberculomas with an extensive review of the literature.

1. Introduction and importance

Intracranial tuberculomas are uncommon forms of extrapulmonary tuberculosis, yet they are dangerous with a high risk of mortality. They require a high level of suspicion to establish a prompt diagnosis and treatment [1]. The incidence of intracranial tuberculoma is 5–30% of all intracranial lesions in developing countries [1]. The mean age was reported from 24 to 42 years, rendering young adults the most susceptible [2]. The initial clinical presentation of intracranial tuberculomas is variable and depends on the location, size, and number of lesions [3]. The delay of an early diagnosis and treatment can be explained by the absence of a previous history of tuberculosis in more than half of the patients, the indistinct initial clinical presentation, and the prevalent radiological characteristics [1]. Anti-tuberculosis therapy is pivotal for the treatment of intracranial tuberculoma.

Reviewing the literature, intracranial tuberculomas remain under-reported, especially in such rare locations. The present report highlights the clinical presentation, biochemical investigations, as well as the radiological and pathological characteristics of an interesting case of multiple intracranial tuberculomas in a community tertiary care center. The work has been reported in line with the SCARE and PROCESS criteria [4,5]. We believe this report can support healthcare providers to consider tuberculoma in the differential diagnosis of intracranial lesions with such clinico-radiological characteristics.

2. Case description

2.1. Clinical presentation

A 67-year-old male, medically free, presented at our Emergency

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Department with a 1-day history of nausea and vomiting, and a 15-day history of imbalance and dizziness. He reported a history of weight loss and night sweats. He denied any history of fever, seizure, or loss of consciousness. The patient took no daily medication, had no surgical history, or significant family history. He was immunocompetent with no history of recurrent infections or use of immunosuppressive medication.

On the physical examination, he was vitally stable, afebrile (T 36.8 C), with a Glasgow coma scale (GCS) of 15/15. The pupils were 3 mm, equally reactive bilaterally. Power was 5/5 in all muscle groups. The sensory examination was unremarkable. The cerebellar examination showed an ataxic gait. All other examinations were unremarkable.

2.2. Biochemical investigations

Routine biochemical investigations were done during the initial presentation to the Emergency Department. The hemoglobin was 150 g/L (reference range: 135–180), platelet count 252/1L (reference range: 150–400 × 10⁹), white blood cells count 4.77/L (reference range: 4.00–11.00 × 10⁹), lymphocyte count 2.67/L (reference range: 1.00–4.00 × 10⁹), lymphocyte percentage 56%, erythrocyte sedimentation rate was 67 mm/h (reference range: 0–15), and the C-reactive protein was 14 mg/L (reference range: ≤ 8). The HIV investigation was negative.

2.3. Radiological findings

A brain computed tomography (CT) scan was done in the Emergency Department which showed diffuse white matter hypodensity involving the right parietal lobe, occipital lobe, and cerebellum, with significant surrounding edema, most likely representing mass occupying lesions. The brain magnetic resonance imaging (MRI) with gadolinium administration showed well-defined lesions on the medial aspect of the right parietal lobe, measuring 1.7 × 1.1 × 1.7 cm and on the medial aspect of the right cerebellar hemisphere, measuring 2.0 × 2.3 × 2.3 cm [Fig. 1]. Both lesions demonstrated a hyperintense rim with a hypointense center on T2-weighted images (T2WI) and FLAIR, without hydrocephalus or a midline shift. The chest and abdomen/pelvis CT were done to rule out primary lesions. The chest CT showed bilateral intermediate non-calcified and calcified pulmonary nodules with prominent reactive thoracic lymph nodes. The abdomen/pelvis CT showed multiple

enlarged abdominal lymph nodes.

2.4. Pathological findings

The patient underwent a sub-occipital craniotomy for biopsy and lesion resection. The surgery was done by the senior author and two assistant surgeons. Intra-operatively, the lesion was firm, yellowish, and with a cheese-like internal content [Fig. 2]. Histopathologically, the cerebellar lesion had a caseous necrotic center [Fig. 3A star]. The necrotic center was surrounded by lymphocytes, epithelioid cells and multinucleated Langhans type giant cells [Fig. 3B arrow]. The tuberculosis polymerase chain reaction (TB PCR) and Acid-Fast-Bacilli (AFB) culture were positive for *Mycobacterium Tuberculosis*.

2.5. Outcome

The patient was diagnosed with disseminated TB and was prescribed anti-tuberculosis therapy. He was discharged in a good condition, following-up at the neurosurgery and infectious diseases clinics. On his recent six-months follow-up, he was independent, ambulatory, with mild cerebellar dysfunction. He was still on anti-tuberculosis medication. The patient was feeling much better.

3. Clinical discussion

Although the risk of mortality and morbidity of tuberculosis has declined significantly after the discovery of anti-tuberculosis medication, central nervous system involvement still carries the burden of mortality and neurological morbidity [6]. The patient in this report is an elderly man, coming from a rural area with a high number of reported tuberculosis cases in the country. He has never received a BCG vaccine. All these factors may have played a role in acquiring the infection. We report an interesting case of multiple intracranial tuberculomas in an immunocompetent patient.

Because the brain is a highly oxygenated organ, it is targeted by the aerobic organism, *Mycobacterium Tuberculosis* [6]. Once the organism is acquired and deposited in the lung alveoli, it interacts with the alveolar macrophages, resulting in the activation of the innate immune system and the formation of granulomas [6]. The organism results in the disruption of the blood-brain-barrier (BBB) which initiates the

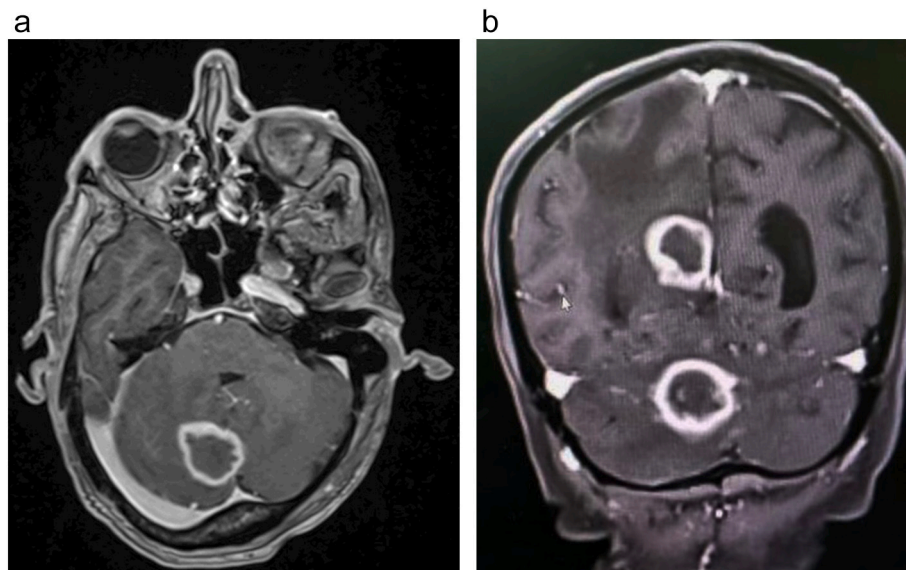


Fig. 1. T1-weighted magnetic resonance imaging (MRI) of the brain with gadolinium administration A. An axial cut showing a ring-enhancing lesion of the cerebellum compressing the fourth ventricle. B. A coronal cut showing supra-tentorial and infra-tentorial (cerebellar) ring enhancing lesions measuring 1.7 × 1.1 × 1.7 and 2.0 × 2.3 × 2.3 cm, respectively.

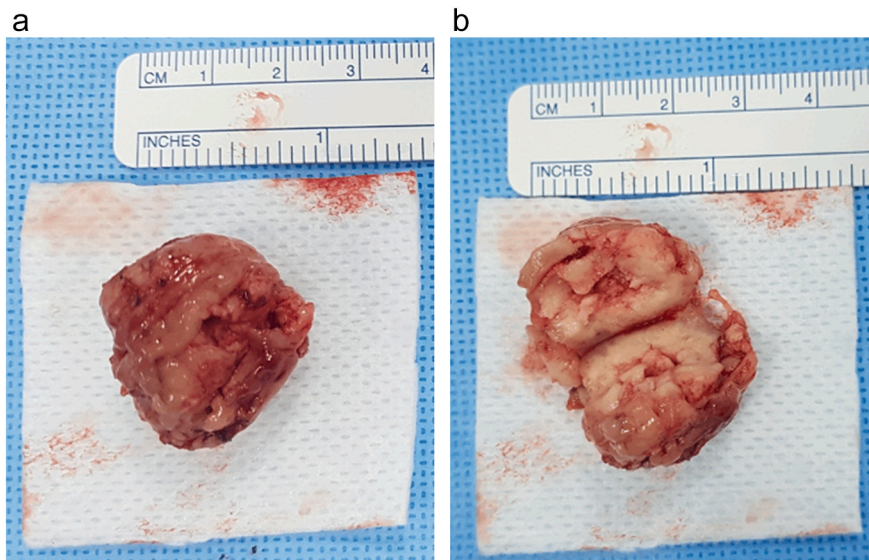


Fig. 2. A: Gross pathological examination of cerebellar tuberculoma showing firm and yellowish lesion. B: The internal content demonstrates a cheese-like appearance.

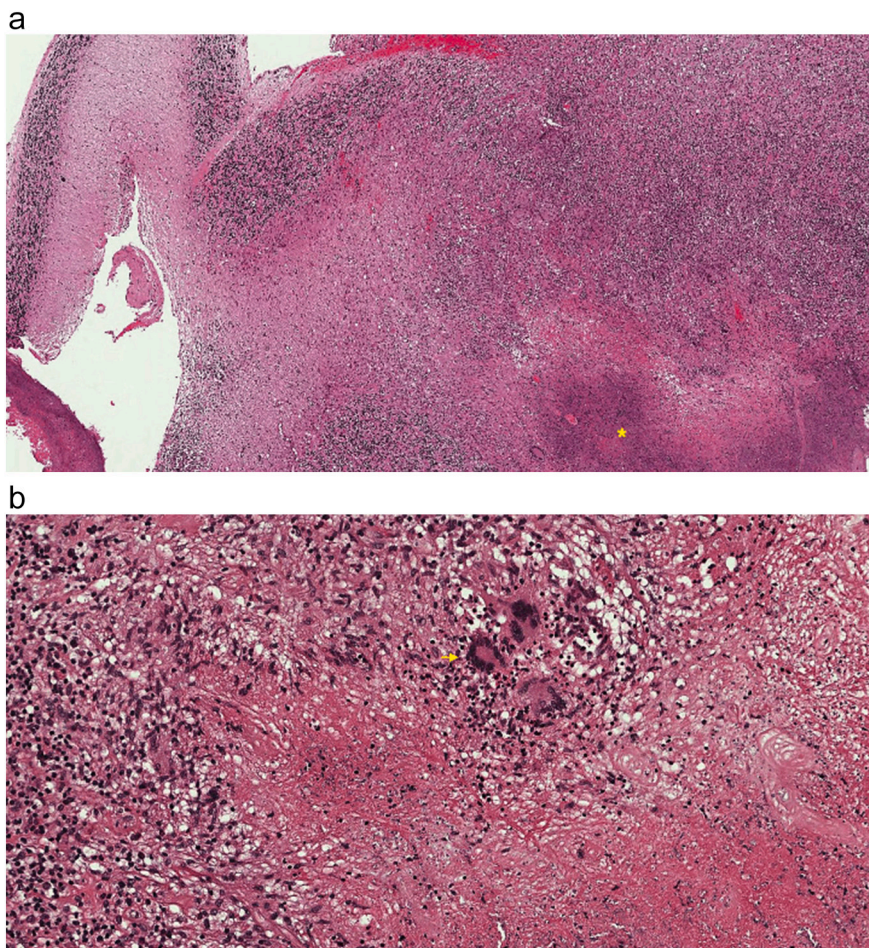


Fig. 3. Histological section from the cerebellar lesion showing A. caseous necrotic center (star). B. The necrotic center is surrounded by lymphocytes, epithelioid cells and multinucleated Langhans type giant cells (arrow). H&E stain.

inflammatory cascade. The vascular endothelial growth factor (VEGF) has been shown to increase the BBB permeability and activate angiogenesis in the acute phase [7]. K^{Trans} is a measure of BBB permeability

that is obtained using dynamic contrast-enhanced MR perfusion [7]. K^{Trans} has been shown to be high in patients with intracranial tuberculoma [7]. The matrix metalloproteinases (MMPs) have been shown to

be responsible for the surrounding tissue destruction in intracranial tuberculoma [8]. Inflammatory cytokines secreted by the monocytes such as IL-1 β and TNF- α have been described to play a role in the upregulation of MMP-9 [9]. MMP-9 may play a role in the destruction of the extracellular matrix adjacent to the BBB. MMP-9 may also result in the destruction of collagen type IV present in the basal lamina [10]. The presence of high K^{Trans} and high diffusion tensor imaging indices correlate with the expression of MMP-9 [7,11]. The organism disseminates to distant organs through the draining lymph nodes [6]. Central nervous system tuberculomas start by the formation of tuberculous foci in the brain parenchyma, meninges, or the spinal cord [6]. Tuberculous meningitis tends to be the primary presentation of central nervous system tuberculosis [6]. Microglial cells are the primary targeted cells in the central nervous system [6].

The initial clinical presentation of intracranial tuberculomas varies depending on the size, number, and location of the lesions. Intracranial tuberculomas tend to be multiple and located in areas with a rich blood supply [12]. The cerebral and cerebellar hemispheres are the most frequent locations [13]. Patients usually present with subacute to chronic signs and symptoms of high intracranial pressure with focal neurological deficits [6]. Intracranial hypertension presenting as headache and papilledema is the most frequent presentation found in more than two-thirds of the patients [14]. Other frequent presentations include vomiting, visual disturbance, confusion, drowsiness, seizure, hemiparesis, paraparesis, and ataxia [15]. Signs of systemic infections are uncommon [12]. Fever is reported in less than 20% of the patients [16]. Less frequent presentations include depression, irritability, anorexia, and a decreased level of consciousness, resulting in constipation and urinary retention [17].

Radiological investigations are used to consolidate the clinical presentation. A brain CT scan has a relatively low specificity for the diagnosis of tuberculoma, and false positives have been reported if used alone in 80% of the cases [14]. On the CT scan, tuberculomas appear as isodense or hyperdense calcified lesions with ring enhancement [18]. The presence of calcification with ring enhancement is called the “target sign”, which is specific for tuberculoma [19]. The presence of multiple lobulated or aggregated ring appearance may assist in distinguishing tuberculomas from brain tumors [15]. The appearance of tuberculoma on the MRI depends on the stage of maturation. These include non-caseating, caseating with a solid center, and caseating tuberculomas with a liquefied center [20]. Noncaseating tuberculomas usually appear hypointense on T1-weighted images (T1WI) with homogeneous nodular enhancement when contrasted and hyperintense on T2WI and FLAIR images [21]. Caseating tuberculoma with a solid center exhibit an isointense/hypointense enhancement on both T1WI and T2WI, an isointense/hyperintense rim on T2WI, and a ring-enhancing appearance when contrasted [21]. Caseating tuberculomas with liquefied centers appear hypointense on T1WI, hyperintense with a hypointense rim on T2WI, and with ring-enhancing appearance with contrast [21]. Because of the reciprocal causation relationship between tuberculoma and tuberculous meningitis, radiological evidence of meningitis may also be observed [21].

The definitive diagnosis of the lesion is established through a brain biopsy. Open brain biopsy is a more invasive method compared to a stereotactic biopsy; however, it has a higher chance of obtaining diagnostic tissue [13]. Many surgeons consider stereotactic biopsy as a selected diagnostic method because it has lower chances of obtaining a diagnostic sample rendering the need for an open biopsy [22,23]. Microscopically, typical epithelioid and giant cell granuloma with central caseous necrosis are characteristic [14]. An AFB culture and TB PCR are positive for *Mycobacterium tuberculosis* [17].

The management of intracranial tuberculomas includes symptomatic treatment, medical treatment with anti-tuberculosis medication, and possibly the surgical resection of the lesion. Glucocorticoids, such as dexamethasone, are clinically recommended to reduce the risk of inflammation, alleviate cerebral edema, and decrease the intracranial

pressure [24]. The initial regimen of anti-tuberculosis medication includes isoniazid, rifampicin, pyrazinamide, and ethambutol (Streptomycin or a fluoroquinolone antibiotic can be used as an alternative) for 2–3 months [17]. Isoniazid and rifampicin are then prescribed as consolidation treatment for 12 months [17]. The regimen can be extended to 18 months if necessary [17]. Surgical resection is considered in cases of a mass effect, intracranial hypertension, posterior fossa tuberculomas with hydrocephalus, visual disturbance, and progression of the tuberculoma while on anti-tuberculosis medication [25].

4. Conclusion

Intracranial tuberculomas are rare but serious forms of extrapulmonary tuberculosis. They have a high rate of mortality and morbidity. It is critical to consider intracranial tuberculoma in the differential diagnosis of intracranial lesions with such clinico-radiological features, especially in the developing countries.

CRedit authorship contribution statement

Ahoud Alharbi: Conceptualization, Investigations, Writing – Original Draft, Writing – Review and Editing. **Sami Khairy:** Conceptualization, Supervision, Investigation – Radiological Images, Writing – Original Draft, Writing – Review and Editing. **Fahd Al Sufiani:** Investigation – Pathological Findings, Writing – Original Draft, Writing – Review and Editing. **Ahmed Alkhani:** Conceptualization, Supervision, Investigation – Radiological Images, Writing – Original Draft, Writing – Review and Editing. All authors have critically reviewed and approved the final version of the manuscript.

Declaration of competing interest

No potential conflict of interest relevant to this article.

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Consent

Written informed consent was obtained from the patient's son for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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