

Case Report

Cavernous sinus tuberculoma mimicking a neoplasm: Case report, literature review, and diagnostic and treatment suggestions for tuberculomas in rare locations

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Abstract

Background: Cavernous sinus tuberculomas are extremely rare, but the increasing incidence worldwide of central nervous system (CNS) tuberculosis, mostly due to human immunodeficiency virus and poor sanitary conditions, and the ability of tuberculomas to mimic a brain neoplasm makes cavernous sinus tuberculomas a suspicious pathologic finding in the differential diagnosis of a brain space-occupying lesion.

Case Description: We present an immunocompetent patient with no signs of systemic tuberculosis and an isolated right cavernous sinus space-occupying lesion. A skull base approach was performed and tumor resection achieved. The postoperative course was uneventful. Pathologic findings consisted of a tuberculoma and antituberculous treatment was immediately begun with total tumor regression after a 12-month regimen. After reviewing the literature, we propose suggestions to orient the diagnosis and a treatment algorithm for tuberculomas in rare locations.

Conclusion: Tuberculomas in rare locations, as the cavernous sinus, are a challenging pathology as they have the ability to mimic a brain neoplasm. Although first line treatment are antituberculous therapy (4 drugs for at least 12 months) and adjuvant steroids, in inconclusive cases, surgical biopsy or excision is recommended for histopathologic confirmation and to reduce the mass effect, always following with antituberculous therapy and adjuvant steroids.

Key Words: Brain tumor, cavernous sinus, meningioma, skull base, tuberculoma, tuberculosis

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INTRODUCTION

Tuberculosis (TB) has reemerged as a public health problem worldwide, mostly due to human immunodeficiency virus (HIV) and poor sanitary

conditions. Central nervous system (CNS) involvement with TB ranges from 0.5% to 10%, most commonly affecting immunodeficient patients and developing countries.^[8,12,21,23] Meningoencephalitis is the most frequent CNS manifestation of TB, while tuberculomas represent

only 10-30% of cases, being mostly hemispheric.^[3,6] Unusual reported locations are the hypothalamic region, Meckel's cave, sellar and suprasellar regions, cerebellopontine angle, and intraventricular spaces.^[7,9,11,15,18] Cavernous sinus (CS) tuberculomas are extremely rare, with only eight^[2,4,5,8,13,14,16,23] cases published. Furthermore, isolated CNS tuberculomas without systemic TB, as our case, are exceptional and commonly misdiagnosed. Current treatment of tuberculomas in rare locations, as CS, is controversial.

We present a case of an isolated right CS tuberculoma with no signs of systemic TB operated on with a skull base approach, review the literature to propose suggestions to orient diagnosis, and provide a treatment algorithm for tuberculomas in rare locations.

CLINICAL CASE

History and examination

A 42-year-old immunocompetent female patient presented with a 6-month history of severe intermittent right hemicranial headaches. Four months later she developed a right eye ptosis and ophthalmoplegia. She had benign medical and epidemiologic histories. A neurologic examination revealed gaze limitations in all directions, ptosis of the right eye and right hemifacial hypoesthesia, with no signs of meningeal irritation. The general examination, routine hematologic examination, and chest radiography were normal with no history of fever or respiratory tract infections. Orbital computed tomographic scans and magnetic resonance imaging (MRI) were normal. Brain MRI revealed a right CS tumor [Figure 1a]. Erythro sedimentation, HIV serology,

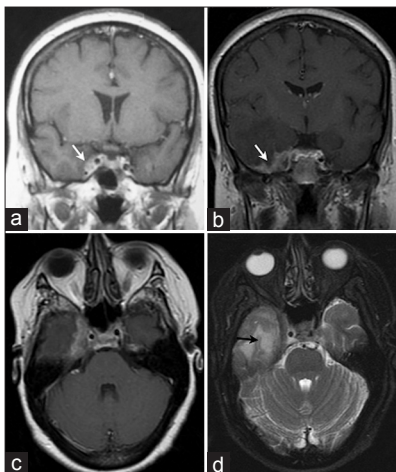


Figure 1: First T1-weighted coronal magnetic resonance images (a) with contrast enhancement of a right cavernous sinus tumor (white arrow). Six months later, preoperative T1-weighted coronal (b) and axial (c) MRI with gadolinium showing progression of the tumor involving the right cavernous sinus with dura-arachnoid thickening and intense pachymeningeal enhancement with mesial temporal infiltration (white arrow); T2-weighted axial MRI (d) showing temporal lobe edema (black arrow)

VDRL, C3, C4, ANA, ANCA, thyroid profile, and PCR for Epstein-Barr virus and TB all yielded negative results. Cerebrospinal fluid (CSF) testing was normal.

The patient was empirically treated with steroids suspecting a granulomatous disease with partial clinical improvement; however, she did not take the medications regularly and missed physician follow-up evaluations. Five months later she was readmitted with a clinical relapse and a new cerebral MRI revealed marked tumoral progression with adjacent right mesial temporal involvement [Figure 1b-d].

With no definitive diagnosis and tumoral progression, the patient was referred to our Neurosurgery Department and a surgical excisional procedure was recommended.

Operation

We considered it an inconclusive case and with the suspicion of a brain neoplasm, under general anesthesia, a right crano-orbito-zygomatic with extended middle fossa approach was performed. The extradural anterior clinoidectomy and the CS and middle fossa peeling, allowed to identify both dural layers (dura propia and dura periostica). The inner layer of the lateral wall of the CS was not infiltrated by the tumor. The basal temporal and CS dura propia with an infiltrative tumoral mass, invading the mesial temporal lobe, was resected. The tumor had a firm, white appearance [Figure 2]. Subtotal tumor resection was achieved as the intraoperative pathologic impression was of an inflammatory disease. The CS was not opened. Dural closure was achieved with fascia lata.

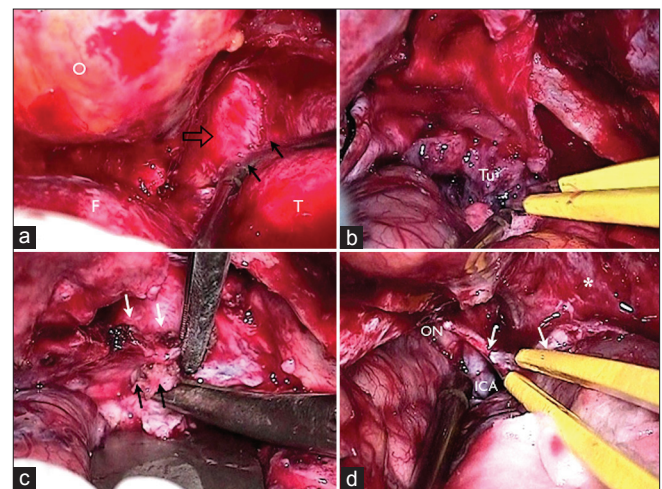


Figure 2: Intraoperative photos. (a) Right crano-orbito-zygomatic with extended middle fossa approach, exposing the orbit (o), frontal (f), and temporal (t) lobes extradurally. Peeling of the lateral wall of the cavernous sinus and middle fossa floor identifying both dural layers (dura propia [black arrows] and dura periostica [open arrows]); (b and c) resection of tumor (Tu) with cavernous sinus and basal temporal dura propia infiltration (black arrows). Inner layer of cavernous sinus lateral wall without tumoral involvement (white arrows); (d) subtotal resection showing the optic nerve (ON), internal carotid artery (ICA), and dura mater (white arrows)

Pathologic findings

Microscopy revealed a caseous necrotic centre surrounded by a granulomatous reaction that included Langhans giant cells, epithelioid cells, and lymphocytes. In addition, there was abundant fibrosis [Figure 3c and d]. Immunological test were performed and definitive pathologic findings consisted of a tuberculoma, although Ziehl Neelsen and PAS stains did not demonstrate acid-fast bacilli and bacteriologic cultures were negative.

Postoperative course

Antituberculous treatment was immediately begun with a four drug (rifampin, isoniazid, ethambutol, and pyrazinamide) 2-month regimen followed by a two drug (rifampin and isoniazid) regimen for 10 months, and dexamethasone for the first 8 weeks.

The postoperative course was uneventful with no surgical morbidity and clinical improvement in the weeks thereafter. The 1-year postoperative follow-up MRI showed complete regression of the lesion [Figure 3a and b] and complete resolution of the symptoms.

DISCUSSION

CNS *Mycobacterium tuberculosis* dissemination is hematogenous, generally from a primary lung infection, developing subpial, subependymal, or subcortical foci. The time from primary lung infection to CNS tuberculoma is age- and immune-dependent,^[12] and the tuberculoma may lie latent for years with activation from Rich's focus.^[5]

Tuberculomas represent 10-30% of cases of CNS TB, and in developing and endemic countries nearly 20% of brain

masses have a tuberculous origin.^[8] CS infections are extremely rare. We performed a PubMed search and found only eight cases of CS tuberculomas published.^[2,4,5,8,13,14,16,23]

Most cases of CS tuberculomas presented with variable degrees of CS syndrome, no history of TB, and nonspecific laboratory and chest radiographic findings, thus, not considering this diagnosis. Four reported patients presented with extra-neural TB.^[2,4,8,16] The proposed diagnosis was meningioma in five cases^[5,8,13,14,23] and an intradural transylvian or subtemporal approach was performed. In all cases, tuberculous bacilli were absent in the CSF, and cultures from the excised mass were negative. Medical treatment was empiric in two cases^[2,4] with satisfactory resolution. All patients received a three or four drug regimen for a 12-month period; only two patients^[2,14] were administered steroids. Resolution was achieved in all patients [Table 1].

CNS tuberculomas have the ability to mimic a brain neoplasm and can develop in any region of the CNS, including extremely rare locations, such as the CS. Can even occur in immunocompetent patients with no history of TB (Gonzalez Ericsson P, Álvarez C, Nobili C, Jaimovich SG, Figurelli S: TB and CNS. Our Experience. Poster presented at the 44th Argentinean Congress of Pathology, Buenos Aires, Argentina, November 15-17, 2012). Brain imaging is not characteristic and clinical manifestations are consistent with a CS syndrome, making the diagnosis a difficult task, and thus the importance of surgical biopsy of the lesion to obtain anatomopathologic confirmation of the tuberculoma so to immediately initiate antituberculous chemotherapy.^[12,23]

Unusual locations, reported in the literature, are the hypothalamic region, Meckel's cave, sellar, suprasellar and CS regions, cerebellopontine angle, intraventricular spaces.^[7,9,11,15,18]

After reviewing the literature we propose suggestions to orient the diagnosis:^[3,6,12,17,20,21,22]

- Extensive epidemiologic and medical history interrogatory;
- Infectious disease serologic testing;
- Erythro sedimentation (generally elevated);
- Blood and CSF tests;
- TB PCR;
- Chest X-rays;
- Mantoux tuberculin skin test (not specific in endemic areas);
- Search for extra-CNS TB (adenitis, pulmonary infection, bone, joint or kidney infections);
- Brain MRI (high sensitivity, but low specificity); and
- Rule out other differential diagnoses. For CS location rule out meningiomas, lymphomas, metastases, giant cell tumors, or inflammatory diseases (sarcoidosis, Tolosa Hunt syndrome, Wegener granulomatosis, aspergillomas, and mucormycotic lesions)

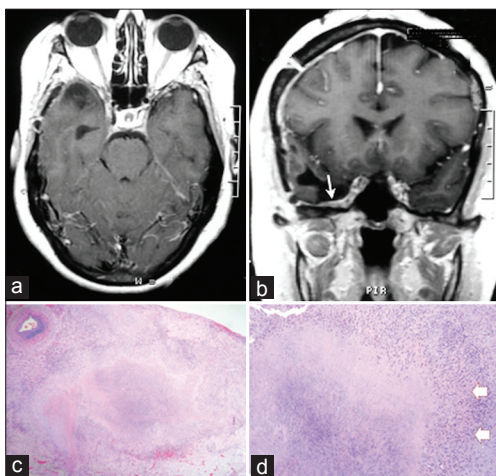


Figure 3: (a and b) Postoperative T1-weighted axial (a) and coronal (b) MRI with contrast injection showing the dural closure with fascia lata (white arrow). c and d: Photomicrograph H and E. (c) (original magnification ×100): Fibrosis and thickening of the dura with granulomatous inflammation and caseous necrosis; (d) (original magnification ×200): Granuloma with Langhans cells (arrows)

Table 1: Summary of CS tuberculoma cases reported

Authors and year	Age (years)/ gender/ ethnic origin	History/ laboratory/ chest X-ray	Symptoms	Cranial nerve palsies	Immune competent	Extra-neural TB	Proposed diagnosis	Surgical Treatment	Bacteriologic examination	Medical Treatment	Outcome
Morris and Joyce, 1992	42/F/Filippino	Normal	Orbital pain, ptosis, facial numbness, vision blurred	III, V, VI	NR	No	Meningioma	Pterional approach	Negative	HRZ	Complete resolution of eye deficits
Phookan and Towns, 1995	33/M/Asian	Normal	Orbital pain, diplopia, facial pain, ptosis	III, IV, VI	NR	No	Meningioma	Pterional transsylvian approach; CS opened	Negative	HRZE+steroids	Complete resolution of eye deficits
Bafna and Lee, 1997	65/F/NR	Normal	Orbital pain, ptosis	III, IV, VI	Diabetes	Cervical lymph node	TB	Cervical node biopsy	Positive	HRZE	Partial resolution of eye deficits
Grayeli <i>et al.</i> , 1998	48/M/Comoros	Apical macronodular hypodensities	Orbital pain, ptosis	III, V	Yes	Pulmonary	Meningioma	Subtemporal approach	Negative	HRE	Complete resolution
Rebai <i>et al.</i> , 2000	44/F/NR	Encapsulated pleurisy punctured; negative culture	Headache, ptosis, diplopia	III, IV, VI	NR	Pulmonary	Metastasis, TB, sarcoidosis	Subtemporal approach	Negative	HRE	Complete resolution
Al Soub <i>et al.</i> , 2001	44/M/Thai	Negative history; lung infiltrate on chest radiography; sputum culture positive	Orbital pain, ptosis, headache	III, IV, VI	Yes	Pulmonary	TB	No	Sputum culture positive	HRZS+steroids	Complete resolution
Yanardag <i>et al.</i> , 2005	36/M/NR	Normal	Headache, ptosis, diplopia, gaze limitation	III, IV, VI	Yes	No	Meningioma	Pterional transsylvian approach	Negative	HRE	Complete resolution
Boutarbouch <i>et al.</i> , 2009	45/M/NR	Normal	Headache, hemifacial neuralgia, gaze limitation, ptosis	III, IV, V, VI	NR	No	Meningioma	Subtemporal approach	Negative	HRZS	Complete resolution
Jaimovich <i>et al.</i> , 2013	42/F/Argentina	Normal	Hemicranial and orbital pain, ptosis, diplopia, facial numbness	III, IV, V, VI	Yes	No	Meningioma, sarcoidosis	Extradural middle fossa approach	Negative	HRZE+steroids	Complete resolution

NR: Not reported, H: Isoniazid, R: Rifampin, Z: Pyrazinamide, S: Streptomycin, E: Ethambutol, CS: Cavernous sinus

Clinical manifestations are of a CS syndrome, presenting with varying degrees of headaches, periorbital pain, ophthalmoplegia, ptosis, and hemifacial hypoesthesia

Systemic infections and usual laboratory parameters may be absent. Even tuberculous bacilli are not always present in the CSF.^[17,23]

MRI is highly sensitive, but has low specificity for the diagnosis of tuberculomas. T1-weighted images show an area of hypo- or iso-intensity, revealing dural thickening and pachymeningeal contrast enhancement involving the CS, and T2-weighted images show a hypo- or iso-intense tumor with perilesional hyperintensity (edema).^[5,6,22] Currently, proton MR spectroscopy can help orient

diagnosis. Tuberculomas are characterized by a prominent decrease in NAA/Cr and a slight decrease in NAA/Cho, with lipid-lactate peaks usually elevated.^[5]

For a definitive diagnosis, a tissue sample is mandatory for bacteriologic and histopathologic evaluations. However, according to the literature, bacteriologic examinations are positive in only 25% of CSF samples and 35% of tuberculoma tissue samples, and results may take between 10 days and 8 weeks. Consequently, negative bacteriologic samples do not eliminate a diagnosis of tuberculomas.^[17,22] In our case, as in all the cases reported, tuberculous bacilli were absent and cultures from the excised mass were negative.^[5,8,13,14,16,23]

Histopathologic evaluation confirms the diagnosis presenting as caseous necrosis, Langhans giant cells, and epithelioid cells, with or without tuberculous bacilli.^[17]

Treatment of tuberculomas in rare locations, as CS, is controversial.^[2,4,5,8,12-14,16,23]

In the presented case, with the suspected diagnosis of a neoplasm without the suspicion of a tuberculoma, we performed an extended extradural middle fossa approach. Although the postoperative course was uneventful, we think that this pathology has to be always considered in inconclusive cases and, as antituberculous therapy is the treatment of choice, a surgical biopsy for histopathologic confirmation via the most minimally invasive approach possible has to be performed. In cases of symptomatic mass effect, the approach may allow partial tumor resection to achieved neural decompression

Thus, after reviewing the literature, we suggest the following treatment algorithm [Figure 4].

When tuberculoma is strongly suspected, empiric antituberculous treatment may be recommended. Regimen should consists of four drugs (rifampin, isoniazid, ethambutol, and pyrazinamide) for a 2-month period, followed by two drugs (rifampin and isoniazid) for a minimum of 10 months, and dexamethasone (0.4 mg/kg/day for 6-8 weeks).^[21] Close follow-up is recommended until complete lesion regression on MRI. If regression is not achieved after 12 months of conservative treatment, lesion biopsy is suggested to obtain histopathologic confirmation

When the diagnosis is not conclusive, a tissue biopsy is recommended to rule out other differential diagnoses (most often meningiomas, lymphomas, metastases, and inflammatory diseases, for CS location). Different approaches are possible according to the involvement of the lesion.^[2,4,5,8,12-14,16,23] However, the most minimally invasive approach possible has to be performed. Always initiate antituberculous treatment immediately with four drugs (rifampin, isoniazid, ethambutol, and pyrazinamide) for a 2-month period, followed by two drugs (rifampin and isoniazid) for a minimum of 10 months, and

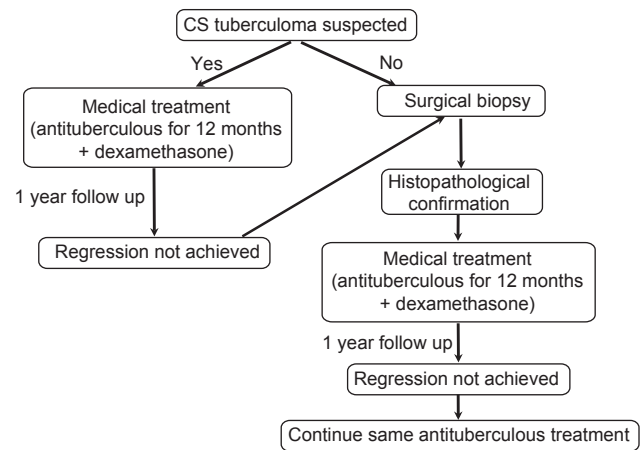


Figure 4: Treatment algorithm suggested (refer to text for details)

dexamethasone (0.4 mg/kg/day for 6-8 weeks).^[21] In cases in which complete regression on MRI is not achieved after a 12-month period, the same regimen must be used for 18 months or until complete regression.

Although there is a lack of prospective and randomized studies on steroid benefits for tuberculomas, its use has been recommended in association with antituberculous treatment to reduce intracranial pressure, prevent paradoxical tuberculoma expansion during treatment and to achieve better outcomes.^[2,10,17,19,21]

Follow-up must be close and for a long-term with MRI, considering the likelihood of recurrence and that the lesion can take more than 18 months to resolve with antituberculous treatment as a function of size. In this situation, the indication is to continue same treatment.^[1,17]

In conclusion, the increasing incidence of CNS TB and the ability of tuberculomas to mimic a brain neoplasm makes tuberculomas an always suspected in the differential diagnosis. In inconclusive cases, surgical biopsy or excision is recommended for histopathologic confirmation and to reduce the mass effect. First line treatment are antituberculous therapy (4 drugs for at least 12 months) and adjuvant steroids, with a long-term follow-up.

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