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Case Report

Extrapulmonary tuberculosis presenting as a cavernous sinus syndrome: Case report with review of existing literature

Shashi Kapadia M.D.*, Amee Patrawalla M.D.

Rutgers New Jersey Medical School, Newark, NJ, United States

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ABSTRACT

Tuberculoma involving the cavernous sinus is a rare presentation of CNS disease, with only twelve cases reported in previous literature. We report a case of a 48 year old woman who presented with a right cavernous sinus syndrome of 2 months duration. MRI showed a mass in the right cavernous sinus, and serologic workup revealed an elevated sedimentation rate and positive Quantiferon®-GOLD testing. 18-FDG PET-CT demonstrated a hypermetabolic 3 cm subcarinal lymph node, and lymph node biopsy showed caseating granuloma. Culture of lymphatic tissue grew drug-sensitive *M. tuberculosis*. The patient was treated with a non-standard 4-drug regimen and prednisone, with rapid improvement of symptoms and radiologic abnormalities. Total length of treatment was 12 months. In addition, we review the 12 cases found in literature, and discuss clinical features, diagnostic dilemmas, and approaches to treatment.

Introduction

Tuberculosis is capable of a wide variety of intracranial presentations including meningeal and intracerebral or parenchymal disease. Tuberculomas are usually found in the cerebral hemispheres, and thought to arise by hematogenous spread [1].

Cavernous sinus involvement is rare; only 12 cases have been reported in the English language literature since 1992 [2–14]. The presentation may mimic meningioma, and has often been found only after surgical resection of the lesion. Diagnosis without biopsy is often based on the finding of *Mycobacterium tuberculosis* in other sites.

We report a case of presumed tuberculoma of the cavernous sinus that was diagnosed by biopsy of another extrapulmonary site, identified by PET-CT scanning, in a previously healthy, U.S. born individual.

Case report

A 48 year old woman presented to her ophthalmologist with complaints of headache and double vision. She first noticed diplopia two months prior to evaluation, which waxed and waned in intensity. One month later, she had recurrent severe diplopia, most prominent on rightward gaze, accompanied by nausea, headache, and photophobia. Her symptoms persisted and progressed to include and right-sided eyelid heaviness. The patient was previously healthy, born in New York City, and had worked in maintenance.

Neurologic exam revealed right ptosis, sluggish pupil, lateral gaze palsy, and diminished medial as well as downward gaze. She also had hypoesthesia in the V2 distribution. The patient was afebrile and had no meningeal signs. She had no pulmonary symptoms.

Results of complete blood count, routine chemistry, complement testing, and serum ACE were normal. Sedimentation rate was elevated at 49. MRI of the brain was performed, showing an enhancing lesion in the right cavernous sinus (Fig. 1). A Quantiferon®-GOLD test was performed as part of the initial work-up, and returned positive (Nil 0.046, TB Ag > 10, Mitogen > 10, TB-Nil > 10).

Result of chest X-ray and HIV testing were negative. 18-FDG PET-CT was performed to assess for additional disease sites that would be more amenable to biopsy. PET-CT cuts in the chest revealed a subcarinal mass with intense uptake (SUV of 11). Biopsy of the subcarinal lymph node was performed using a robotic VATS procedure. Lymph node pathology revealed both necrotizing and non-necrotizing granulomas, and cultures subsequently grew *M. tuberculosis*, susceptible to all first-line drugs. The patient was started on therapy with INH 300 mg daily, rifampin 600 mg daily, pyrazinamide 1500 mg daily, and levofloxacin 750 mg daily. Ethambutol was not given because of concern for potential ocular toxicity, given her cranial nerve deficits and diplopia. She was also treated with daily prednisone. Pyrazinamide was discontinued in

* Corresponding author.
E-mail address: shk9078@nyp.org (S. Kapadia M.D.).

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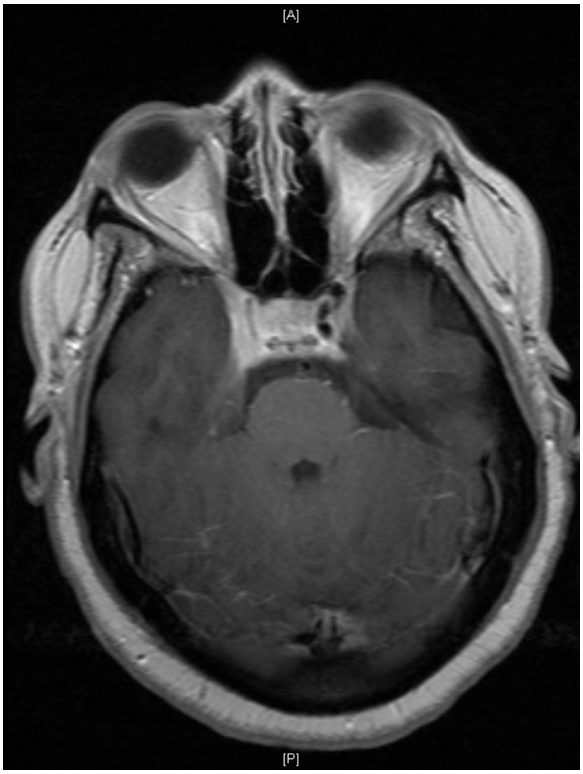

Fig. 1. Initial MRI showing an enhancing lesion in the right cavernous sinus exerting mass effect and narrowing the cavernous segment of the right internal carotid artery.

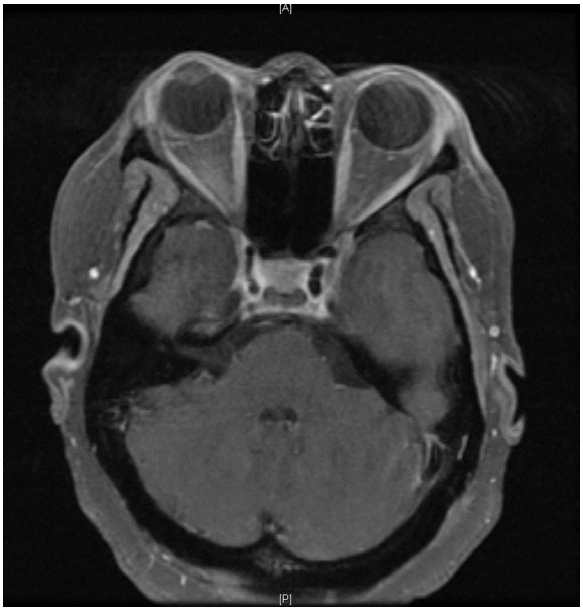

Fig. 2. MRI after completion of therapy showing resolution of the previously described lesion.

3 months, and levofloxacin in four months. She was treated with INH and rifampin to complete a 12 month course.

The patient's gaze palsies improved while on therapy, though her facial hypoesthesia persisted. Repeat MRI 3 months into treatment showed improvement of cavernous sinus lesion. MRI after treatment showed near-complete resolution of the lesion (Fig. 2).

Discussion

While accounting for about 5% of all extrapulmonary TB in the United States, CNS tuberculosis can be among the most challenging and difficult to treat [15]. The clinical syndromes include meningitis, abscess formation or tuberculoma [1]. Tuberculoma accounts for between 10 and 30% of cases of CNS disease, though the reported frequency varies. The majority of cases involve the cerebral hemispheres [1,7,16]. Despite the propensity to affect the hemispheres, unusual locations of CNS tuberculoma continue to be reported, including the cerebropontine angle, the sellar and suprasellar regions, and as in our case, the cavernous sinus [9].

Diagnosis of cavernous sinus tuberculoma is complex. While radiographic features have been described depending on the level of necrosis, differentiating tuberculoma from tumor on imaging alone remains difficult [5]. In a majority of cases of cavernous sinus tuberculosis, the diagnosis was reached only after surgical biopsy of the lesion, often due to suspicion of meningioma [4–14]. Other cases, including our case above, were diagnosed after testing revealed evidence of tuberculosis at extra-CNS sites [2,3]. Molecular methods including PCR testing and potentially GeneXpert MTB/RIF may also have a role in diagnosis, though they have not been used in any of the below cases. Proton MR spectroscopy, diffusion weighted MRI, and dynamic contrast enhanced MRI may also be useful as adjunctive imaging tests that can increase the specificity of the diagnosis [4,5,9].

The need for surgery in diagnosis depends largely on whether or not noninvasive testing yields a diagnosis. The diagnostic approach suggested by the British Infectious Society for suspected tuberculoma recommends a thorough search for AFB in the CSF, as well as PCR and nucleic acid amplification testing. A careful search for extra-CNS sites should be undertaken, and consideration for imaging of chest and abdomen to seek an easily accessible source of tissue [17]. Our case demonstrated the utility of PET-CT in finding an alternative site of disease. In many cases, the diagnosis remains unclear, and histological evaluation is ultimately required [9]. Often, this can be done safely via stereotactic biopsy [18].

Review of literature found 12 reported cases of tuberculosis in the cavernous sinus other than our own, with 2 of those cases localizing to Meckel's cave (see Table 1). Epidemiologic features are inconsistently reported, but 8 of the 13 total cases were found to be HIV negative. Ten cases were diagnosed based on operative removal of the tumor and resultant pathology. It is notable that none of the biopsied intracranial tumors had reported AFB smear positivity and none had culture positivity for *M. tuberculosis*. Of the remaining cases, Al Soub reports diagnosis of tuberculosis based on a positive sputum culture [2], Bafna reports a case based on culture of a cervical lymph node [3], and our case was diagnosed based on culture of a subcarinal lymph node.

Treatment of tuberculoma follows that of CNS tuberculosis in general: 4-drug antituberculous therapy in a 2-month intensive phase followed by 2 drug therapy for a continuation phase to complete a 9–12 month course [17,19]. The choice of drugs for sensitive *M. tuberculosis* infection typically include isoniazid and rifampin as well as pyrazinamide. The optimal fourth drug remains unclear: streptomycin and ethambutol are frequently recommended. The former runs risk of renal toxicity as well as frequent resistance, and the latter may result in concerning ocular toxicity. Both drugs are shown to have poor CNS penetration, making their therapeutic role unclear [20]. Fluoroquinolones are another option; though not as well established, CNS penetration appears