CASE REPORT

Isolated cerebellar tuberculoma mimicking posterior cranial fossa tumour

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SUMMARY

Isolated central nervous system (CNS) tuberculoma is a rare disease. This disease is associated with high morbidity and mortality, despite modern methods of detection and treatment. CNS tuberculosis can present as meningitis, arachnoiditis, tuberculomas or the uncommon form of tuberculous subdural empyema and brain abscess. We present the clinical, radiological and pathological findings of cerebellar tuberculoma in an Iranian immunocompetent patient mimicking a malignant tumour.

BACKGROUND

Tuberculosis (TB) is an infectious disease that continues to be a significant public health concern in some developing countries such as Iran. Although TB is primarily considered as a pulmonary disease, it can affect any organ system. TB has been found in the lymphatic system, pleura, genitourinary system, bones and joints, mastoid, gastrointestinal system, peritoneum, skin, heart, eye, thyroid, tongue and the central nervous system (CNS).[1] Although extrapulmonary TB is more often found in immunocompromised persons, otherwise healthy patients can also be infected by it. In the CNS, TB is usually a meningeal infection or a tuberculoma; it is rarely an abscess.[2] Diagnosis is frequently quite delayed in CNS involvement. Usually, patients with intracranial TB are immunocompromised. Among immunocompetent patients, children and the elderly are most commonly affected, but our patient did not fit into either category. She was an immunocompetent woman with a diagnosis of cerebellar tuberculoma with no history of primary pulmonary TB. In this era of resurgent TB, we must remain alert to the uncommon manifestations of this disease, as inclusion of TB in the differential diagnosis of intracranial space occupying lesions requires a high index of suspicion.

CASE PRESENTATION

A 42-year-old Iranian woman was admitted to our hospital with nausea, vomiting, headache and convulsion. In her medical history, she was hypertensive and had personality disorder, but she did not have any history of lung disease. The neurological examination revealed confused speech, truncal ataxia and impaired finger to nose test. She had neither nuchal rigidity nor abnormality in cranial nerve examination. Lymph nodes, liver and spleen were not palpable.

INVESTIGATIONS

On admission, the patient was found to have a body temperature 37°C, pulse rate 80/min, respiratory rate 21/min and blood pressure 160/90 mmHg. Laboratory examination showed normal serum electrolyte levels, renal and liver function tests, and complete blood count showed haemoglobin 14 g/dL, white blood cell count $7\times10^3/\mu L$ (66% neutrophils, 18% lymphocytes, 12% monocytes and 4% eosinophils). Erythrocyte sedimentation rate (ESR) was 35 mm in the first hour (normal range 0–30 mm/h). Cranial axial CT without contrast (is not available) revealed no specific abnormality. MRI of the brain without contrast showed a partially well defined and irregular mass-like lesion in the right brachium pontis without significant mass effect. There was mild extension to the right perimedullary cistern which showed inhomogeneous signal intensity. The mentioned lesion caused signal abnormality in the right posterolateral side of pons and medulla (figure 1). Above findings were more compatible with an intra-axial type neoplastic lesion such as glioma. She underwent a suboccipital craniotomy to excise the lesion. On the first postoperative day she regained full consciousness. On physical examination, previous neurological deficits remained but there was no new neurological deficit. Microscopic examination of the excised mass showed granulomatous inflammatory reaction with central caseating necrosis. The granulomas were composed of epithelioid histiocytes, lymphocytes and multiple multinucleated giant cells, both of Langhans and foreign body type (figure 2). We were not able to demonstrate acid-fast bacilli in the specimen. A chest X-ray did not show any abnormality and purified protein derivative (PPD) was negative. Sputum examination revealed negative result for acid-fast bacilli and anti-HIV antibody was also negative. The diagnosis was compatible with primary cerebellar TB. The primary focus of infection in this case remained in doubt.

DIFFERENTIAL DIAGNOSIS

Granulomas are caused by an extremely broad range of disease processes. These can be conveniently divided into infectious and non-infectious causes. The majority of cases of CNS granulomatous diseases are infectious in aetiology, especially TB.[3] Most clinically important fungi are also associated with granuloma formation, including *Aspergillus*, *Cryptococcus*, *Candida* and *Histoplasma* to name a few.[4] *Sarcoidosis* is one of the most common non-infectious granulomatous diseases. Another group of diseases are Wegener's granulomatosis, foreign

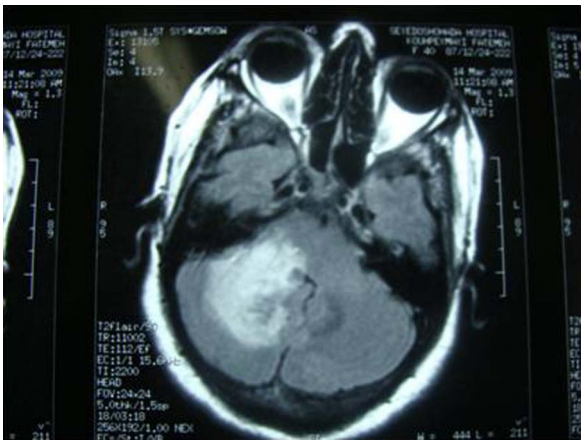

Figure 1 MRI without contrast showed a partially well-defined and irregular mass-like lesion in the right brachium pontis without significant mass effect.

body reaction and Langerhans cell histiocytosis.[5] Imaging features of tuberculomas are known to overlap with those of other intracranial focal lesions, like the healing stage of neurocysticercosis, fungal granulomas, chronic pyogenic brain abscess and lymphomas. Some gliomas and metastases may also have features similar to those of tuberculomas and should be considered in their differential diagnoses.[6]

TREATMENT

The patient received isoniasid (INH), rifampin and ethambutol for 9 months.

OUTCOME AND FOLLOW-UP

The patient followed by clinical examination and MRI after receiving anti-TB drugs. She was better month by month and after 3 months there were some dysmetria in the right limb and also had slurred speech but her gait was normal. After about 5 months, the patient was absolutely normal without any residual disease. Now (2 years after initial presentation) she is in good condition without any neurological deficit.

DISCUSSION

TB remains a public health issue of considerable magnitude, especially in developing countries such as Iran.[7] CNS TB is a rare presentation of active TB and accounts for about 1% of cases.[8] Unfortunately, diagnosis of TB in the CNS remains difficult. The most frequent form of parenchymal TB is tuberculoma. Other less common presentations are tuberculous abscess, focal cerebritis and 'allergic' tuberculous encephalopathy.[9] CNS tuberculoma accounts for 5–10% of intracranial space occupying lesions in the developing world.[10] Cerebellar involvement is slightly more common in children (6 months to 6 years). Aniba *et al*[11] reported a case of a giant cerebellar tuberculoma mimicking a malignant tumour in a 6-year-old girl. Some studies in developing nations showed that the onset of neurotuberculosis is seen with a mean age between 25 and 45 years.[12–14] Our patient was a 42-year-old woman residing in Iran. Risk factors for CNS TB include age (children>adults), HIV-coinfection,[15] malnutrition, recent measles in children[16] alcoholism, malignancies and the use of immunosuppressive agents in adults.[17] But our patient did not have any of these risk factors. Clinical manifestations of tuberculoma or tuberculous brain abscess depend largely on their location, as in our case, she suffered from signs of raised intracranial pressure and cerebellar dysfunction. Routine laboratory studies, such as ESR or differential count of peripheral white blood cells, follow no characteristic pattern. But one study showed, in the case of intracranial tuberculoma, a high ESR that may indicate multiple tuberculomas.[18]

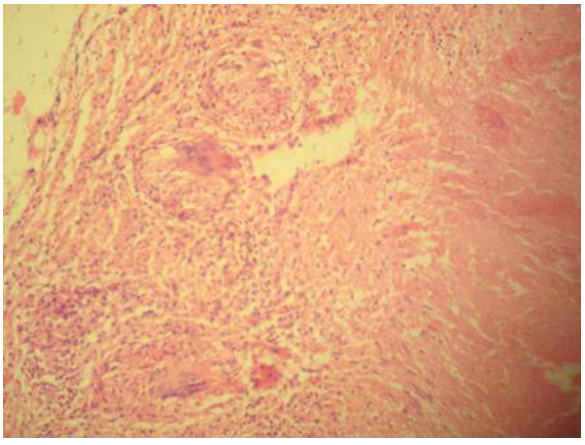

Figure 2 Section showing granulomatous inflammatory reaction with central caseating necrosis (H&E stain ×10).

Radiological imaging plays an important role in the diagnosis and monitoring of the disease, and for assessment of complications. The appearances of tuberculomas on CT usually reveal small rings or nodular-enhancing lesion with only mild oedema and mass effect.[19] Our patient's lesion failed to appear on a CT scan but was readily apparent on MRI scan without contrast media. As a result MRI is the preferred method of initial investigation. Depending on its stage of maturation, appearance of tuberculoma varies on MRI, that is, whether non-caseating, caseating with a solid centre or caseating with a liquid centre. A solid caseating tuberculoma appears relatively isointense to hypointense on both T1-weighted (T1W) and T2W images with an isointense to hyperintense rim on T2W images.[20] Although neuroimaging might be helpful in the diagnosis of TB, histopathological examination is the golden standard in the setting of exact diagnosis. But aetiological agents cannot be identified by Ehrlich-Ziehl-Neelsen (EZN) method in all patients. It was true about the presented case. PPD was negative in our patient. The diagnostic utility of skin testing for CNS TB is highly variable: in some studies only 10–20% of patients with CNS TB have a positive test,[21] others report around 50% are positive.[22] Mention should be made that the performance of the tuberculin skin test for the diagnosis of TB varies according to age, vaccination with BCG, nutritional status, HIV infection and technique of administration.[23] As can be seen that negative test does not always reflect the immunodeficiency and other factors affecting the test result. In addition Delgado *et al*[24] showed that "anergy to PPD is antigen-specific and persistent in a subset of immunocompetent TB patients and is characterised by antigen-specific impaired T cell proliferative responses and a distinct pattern of cytokine production including reduced levels of IL-2."

An extraneural focus of TB should be sought clinically and radiologically in all patients with CNS TB as it may indicate safer and more accessible sites for diagnostic samplings. No evidence of extracerebral TB was found in the presented case and it coincided with the result of another study in which 40% of cases did not have any evidence of extracerebral TB.[25] Since the preoperative and intraoperative diagnosis was tumour cerebrospinal fluid (CSF) was not collected for examination, and we were not able to demonstrate acid-fast bacilli in the specimen by

a histochemical reaction using EZN method. It was compatible with results of some other studies.[26] In addition we did not have the possibility of detecting bacterial DNA using PCR in paraffin-embedded tissue, which is superior to EZN and culture. PCR is a useful and effective adjunct in the diagnosis of CNS TB.[27] Although CSF from patients with tuberculomas without meningitis is usually smear negative, PCR assay on CSF can be used to make a diagnosis and has been recommended as a routine tool for the rapid diagnosis of tuberculoma of the brain. Studies have shown sensitivities of PCR on CSF ranging from 60% to 75% and specificities of 90–95%.[28]

But in countries with high endemic rate of TB, such as Iran the mentioned microscopic findings are compatible with TB and the absence of bacteriological proof, as in this case, however, does not necessarily imply the absence of TB. Our diagnosis was confirmed retrospectively, on the basis of response to anti-TB drug therapy. The outcome in patients with CNS TB depends on the clinical stage and on the age of the patient.[29] The rapidity of diagnosis, surgical resection and the complementary anti-TB treatment have critical roles, and timely initiation of therapy can lead to reduced morbidity and mortality.

In conclusion even in a country where TB is not rarely found, CNS tuberculomas may be misdiagnosed preoperatively according to the clinical and neuroimaging results, mimicking tumours rather than the infectious process. This pathology must be kept in mind when treating patients from countries with a high endemic rate of TB.

Learning points

- Although extrapulmonary tuberculosis is more often found in immunocompromised persons, otherwise healthy patients can also have it.
- Diagnosis is frequently quite delayed in central nervous system involvement.
- The absence of bacteriological proof does not necessarily imply the absence of tuberculosis.
- This pathology must be kept in mind when treating patients from countries with a high endemic rate of tuberculosis.

Contributors All the authors assisted in the preparation of the manuscript.

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