Case report

Cerebral tuberculomas – A clinical challenge

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A B S T R A C T

Cerebral tuberculomas are a rare and serious form of tuberculosis (TB) due to the haematogenous spread of Mycobacterium Tuberculosis (MT). Symptoms and radiologic features are nonspecific, leading sometimes to misdiagnosis. Anti-TB drugs are essential for the successful treatment of cerebral tuberculomas but there is no agreement regarding the duration of therapy.

The authors present a case of a 55 years old male, presented to the emergency room with sudden onset of diplopia. Cerebral computerized tomography revealed multiple brain lesions, with contrast enhancement and peri-lesional oedema. The patient was HIV negative and because of previous malignancy the first suspicion was metastatic disease. Cultural exam of the bronchial wash showed MT sensitive to all first-line drugs. The patient started antituberculosis treatment with 4 drugs (HRZE) for 2 months, followed by maintenance therapy (HR). Treatment was prolonged for 24 months because at 12th and 18th months of treatment one of the brain lesions, although significantly smaller, still showed contrast enhancement.

Even though it is not clear if contrast enhancement lesions represent active lesions or just inflammation, continuing treatment until total resolution of the tuberculomas is probably prudent.

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1. Background

Central nervous system (CNS) tuberculosis (TB) is a serious form of TB, due to haematogenous spread of Mycobacterium Tuberculosis (MT). Manifesting as meningitis, cerebritis and tuberculous abscesses or tuberculomas, it occurs in approximately 1% of all patients with TB, affecting disproportionately children and immunosuppressed patients. Other risk factors include malnutrition, alcoholism and malignancies.

Intracranial tuberculomas are the least common presentation of CNS TB, found in 1% of these patients. They are multiple in only 15%–33% of the cases. Tuberculomas often present with symptoms and signs of focal neurological deficit without evidence of systemic disease. The radiologic features are also nonspecific and differential diagnosis includes malignant lesions, sarcoidosis, pyogenic abscess, toxoplasmosis and cysticercosis.

It is universally accepted that anti-TB drugs are essential for the successful treatment of intracranial tuberculomas but there is no agreement regarding the duration of therapy.

2. Case report

A 55 years old white male, ex-smoker for 19 years (6 pack-years), working as an air conditioning installer, came to the Emergency Room in May 2010 with sudden onset of diplopia. He also complained of headache, loss of weight (about 10% over the last month) and of back pain over the last year, that he thought to be related with an accident. He denied any respiratory symptom or other.

His medical history included a right colon cancer, treated with surgery and chemotherapy 20 years ago (he had abandoned follow-up after 10 years), and pulmonary TB 4 years ago, treated with 2 months of Isoniazid, Rifampicin, Pyrazinamide and Ethambutol (HRZE) follow by 4 months of Isoniazid and Rifampicin (HR) under directly observed therapy (DOT) – after that he went abroad and missed follow-up. He was not on any medication and denied any allergies.

On examination the patient was underweight and walked with difficulty because of the diplopia. His physical examination was...
unremarkable besides an ophthalmoplegia. Cerebral computerized tomography (CT) revealed multiple brain lesions, with contrast enhancement and peri-lesional oedema.

He was admitted for investigation and treatment. Brain magnetic resonance imaging (MRI) confirmed 4 space occupying lesions with central necrosis, irregular outlines with peripheral contrast enhancing and moderate peri-lesional oedema (Fig. 1).

Lumbar puncture was performed but was not diagnostic (cerebrospinal fluid was negative for malignant cells or microorganisms). Biochemical analyses such as nucleic acid amplification or adenosine deaminase measurement were not performed. Chest X-ray was considered normal. Serologies to human immunodeficiency virus (HIV) and toxoplasmosis were negative. Thoracic and abdominal CT revealed peri-centimetric mediastinal lymph nodes,

Fig. 1. Brain MR before treatment: 4 space occupying lesions in the brain with central necrosis, irregular outlines with peripheral contrast enhancing and moderate peri-lesional oedema.
bilateral pulmonary micronodules, a small condensation area in the right middle lobe with discrete air bronchogram and a lytic lesion at the left 8th rib-vertebral joint (Fig 2). Bronchoscopy showed no changes in the bronchial tree besides anthracotic plates. There were no malignant cells in the bronchial wash and direct exam was negative for TB. Endoscopies did not show any sign of malignancy. A positron emission tomography (PET) was performed and revealed abnormal enhancement in multiple small foci in both lung fields, mediastinal and abdominal lymph nodes, bone lesions (3rd and 8th left ribs and right iliac wing), both adrenals and brain (Fig. 3). The biopsy of the rib lesion presented only epithelioid granulomas. TB was confirmed by cultural exam of the bronchial wash that showed MT sensitive to all first-line drugs.

The patient had already started corticosteroids (prednisolone 1 mg/kg) at admission for cerebral oedema and antituberculous treatment was added when TB was found. The patient was discharged but continued treatment with 4 drugs (HRZE) in form of...
DOT and completed 8 weeks of corticosteroids with clinical improvement. After 2 months the patient was completely asymptomatic and treatment was reduced to maintenance therapy with 2 drugs (HR).

Radiologic revaluations were made at 6th, 12th, 18th and 24th months after the diagnosis and beginning of the treatment. The lung micronodules and mediastinal lymph nodes remained stable and some calcified. Bone lesions also stabilized. The brain MRI at the 18th month of treatment one of the lesions, although significantly smaller still showed contrast enhancement so treatment was prolonged for 24 months. In the last brain MRI no contrast enhancement lesions were seen (Fig. 4).

3. Discussion

Due to its rarity, nonspecific symptoms and radiological findings, intracranial tuberculomas remain a clinical challenge. Misdiagnosis of tuberculomas as malignant diseases have been described in literature. Our patient was HIV negative, had a medical history of malignancy and presented with multiple brain lesions so the first suspicion was also metastatic disease. Tuberculomas must however be always included in differential diagnosis of cerebral space occupying lesions.

As the patient missed follow-up after his first TB infection this may be the case of a reactivation but reinfection is also a possibility and genotype was not performed.

Regarding treatment, the Center for Disease Control and Prevention recommends 12 months of treatment for CNS TB when the MT strain is sensitive to all drugs. However numerous variables can affect the response of the disease to therapy and it has been suggested that treatment duration should be tailored to the radiological response. After 12 months of treatment more than two-thirds of the patients still have contrast enhancing lesions. Although it is not clear if this represents an active lesion or just inflammation, continuing treatment is probably prudent. Total resolution of the tuberculoma is observed when scans demonstrate no enhancing lesions or only an area of calcification. Systemic corticosteroids as adjuvant therapy are indicated when there is peri-lesional oedema or paradoxical progression during treatment. Surgical intervention may be necessary in situations with acute complications or when the diagnosis is not ensured.

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