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MULTIPLE INTRACRANIAL TUBERCULOMAS IN AN HIV-NEGATIVE 28 YEAR OLD MALE - A CASE REPORT.

*** A. O. Ogunrin, ** A. A. Adeyekun**
**Neurology Unit, Department of Medicine, **Department of Radiology, University of Benin Teaching, Hospital, Benin City Nigeria*

ABSTRACT
Intracranial tuberculomas are uncommon complications of tuberculosis, especially in immuno-competent individuals with no evidence of extra-cranial foci. We report a case of an HIV- negative young male who presented with presumed cerebral and cerebellar tuberculomas without identifiable extra-cranial focus. The CT scan revealed multiple intracranial ring-enhanced lesions. The remarkable response to antituberculous drugs and steroid (prednisolone) with near complete resolution of clinical and radiological signs was highly suggestive of diagnosis. In the differential diagnosis of intracranial mass lesions in sub-Saharan Africa, a high index of clinical suspicion is needed to avoid misdiagnosis of intracranial tuberculoma.

Key words: intracranial, tuberculomas, diagnosis, treatment *(Accepted 25 October 2006)*

INTRODUCTION
Central nervous system (CNS) tuberculoma is an uncommon complication of tuberculosis, affecting 0.5 to 2 percent of patients with systemic or military tuberculosis[1,2].It usually follows hematogenous dissemination of tuberculous bacilli from an infection elsewhere in the body, usually the lungs[2,3]. The clinical course is usually sub-acute or chronic and they typically occur in immuno-compromised patients. We occasionally encounter immuno-competent adult patients with cerebral tuberculomas without extra-cranial focus of infection[1,4,5] and this call for continuing vigilance for this disease. Recognition and prompt diagnosis of this condition is important because early treatment can lead to clinical improvement[3].

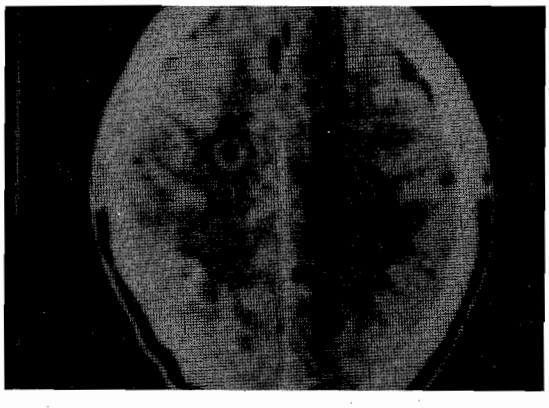
In patients with intracranial tuberculomas, especially when relatively silent sites are affected, there may be paucity of clinical findings[4,5]. A high index of clinical suspicion is needed to make the diagnosis.

We report a case of an HIV- negative young male who presented with intracranial tuberculomas without identifiable extra-cranial focus.

CASE REPORT
Mr. P.A. is a 28 year-old accountant who complained of progressive unsteadiness of gait, dysarthria, weakness of the left extremities and visual blurring of 3months duration. He had enjoyed good health prior to the onset of his complaints. He gave no history of weight loss, cough, night sweats, fever, headaches, diplopia, seizures, personality changes, dysphagia, facial asymmetry or contact with persons with chronic cough. He had no symptoms to suggest, and has never been diagnosed as having, diabetes mellitus. He has never received blood transfusion or steroids. He took alcohol sparingly and smoked cigarettes occasionally.

The general examination was insignificant. The respiratory and cardiovascular systems examinations were unremarkable. Neurologically, he had staccato speech, vertical and horizontal nystagmus, mild hypertonia with intact cranial nerves and normal muscle bulk but grade 3 power in the left extremities. The reflexes were slightly brisk. In addition he had bilateral dysdiadochokinesia with ataxic gait but no Rombergism. The sensory system was normal and there were no signs of meningeal irritation. Fundoscopy was normal. A clinical suspicion of intracranial lesions affecting both the cerebral (pyramidal) peduncles and the cerebellum was made.

Fig 1 CT brain scan showing intracranial ring-enhanced lesions

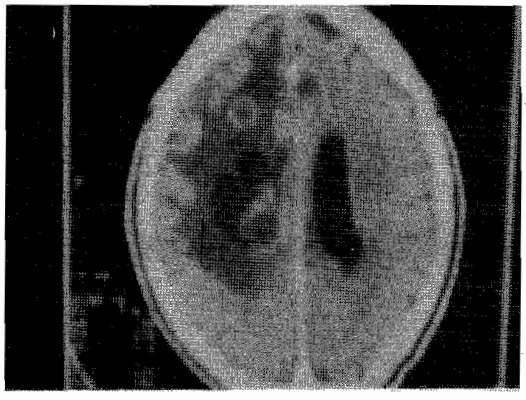


Correspondence: Dr A. O. Ogunrin
Email:bfunmi@uniben.edu

The CT brain scan revealed multiple ring-enhanced cerebral lesions with no appreciable mass effect or edema highly suggestive of intracranial tuberculomas (Fig 1).

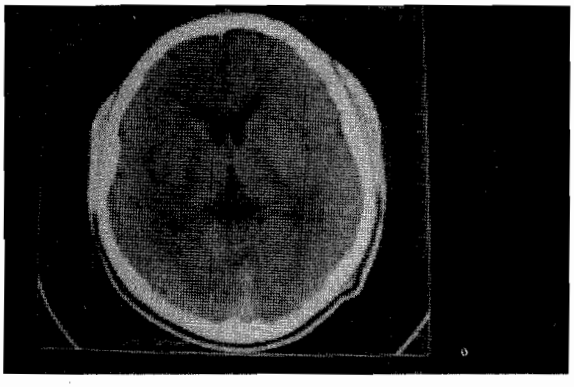
The results of other laboratory investigations are outlined on table 1. He was commenced on oral antituberculous therapy {ATT}- (ethambutol, pyrazinamide, isoniazid and rifampicin) and oral prednisolone (40mg/day).On the seventh day of admission, he developed nausea, vomiting and carpal spasms. His serum calcium was found to be 5.5mg/dl and this was corrected with calcium gluconate. The prednisolone was increased to 60mg/day as repeat CT brain scan revealed worsening of lesions as evidenced by appearance of significant peri-lesional oedema (Fig 2).

Fig 2 — CT brain scan showing initial worsening of lessons following commencement



Subsequently, the patient made remarkable improvement with near complete resolution of all pyramidal and cerebellar signs. He was discharged to follow-up after 28 days of hospitalization. Another CT brain scan done 6months after discharge showed complete resolution of lesions (Fig 3).

Fig 3
CT scan with complete resolution of lesions



He is however to take medication for 18 months with maintenance therapy of isoniazid and rifampicin.

Table 1 - **Results of laboratory investigations**

Tests	Results
Full blood count	
Hematocrit	42%
Hemoglobin	14g/L
White Cell Count	6600/ μL
Neutrophils	56%
Lymphocytes	44%
Erythrocyte Sedimentation Rate	12mm/hr (Westergren)
Mantoux test	9mm
Urea	20mEq/L
Sodium	127mEq/L
Potassium	3.1mEq/L
Bicarbonate	19mEq/L
Chloride	94mEq/L
Creatinine	0.9mg/dl
CSF analysis	
Sugar	60mg/dl
Protein	40mg/dl
Microcopy lymphocytes/cl	11
Gram stain	Negative
AAFB	Negative
Blood Sugar (Random)	110mg/dl
X ray chest	Normal findings
HIV test (ELISA)	Negative
CT Brain Scan	multiple ring enhanced lesions in the cerebral hemispheres.

DISCUSSION

The presumed diagnosis of intracranial tuberculoma is supported in this patient by the insidious onset of symptoms, the appearance of contrast ring-enhanced and target lesions, and the significant improvement in clinical and radiological features following administration of anti-tuberculous therapy (ATT).

There have been previous reports of cerebral tuberculomas in Nigerian patients in the pre-HIV era[6,7,8] and in the post-HIV era[4,9], most of which were diagnosed histologically after surgical excision. Before the advent of chemotherapy, tuberculomas constituted approximately 30 percent of intracranial space occupying lesions in adults among the Asian adults[10,11]The introduction of anti-tuberculous agents and the improvement of socio-economic conditions contributed to the epidemiological control of the disease and reduced frequency of intracranial tuberculomas until recently that the HIV pandemic has caused a resurgence of pulmonary and extra-pulmonary tuberculosis (including CNS involvement)[10,11,12]. Nowadays intracranial tuberculomas, though relatively uncommon in the

developed countries[5], is probably becoming more prevalent in sub-Saharan Africa and Asia with the advent of human immunodeficiency virus infection[12,13]. This case is peculiar in that the patient has neither HIV infection nor evidence of military or systemic tuberculosis.

The most common form of presentation of intracranial tuberculomas is seizures, seen in 60-100% of patients[5,11]. Increased intracranial pressure occurs in 56 93% while focal neurological deficits occur in 33-68% of cases[11]. In those who present with seizures, the clinical pattern of convulsive fits can strongly suggest location of lesion.

The diagnosis of intracranial tuberculoma is usually made based on definitive histopathological examination of biopsy obtained with CT-guided stereotactic techniques[14,15], or presumptively on radiological (CT scanning with contrast enhancement or MRI) appearance or clinical response to anti-tuberculous chemotherapy[2,5,11].The computed tomography (CT) ormagnetic resonance imaging (MRI) is useful in suggesting diagnosis as well as monitoring the response to treatment especially when conservative treatment is advised[16,17]. The appearance of the lesion varies on CT and MRI. During the initial phase of disease, oedema and necrosis may appear as a low attenuating area on CT scan, but once the granuloma has begun to organize, there may be high attenuation, contrast enhancement, calcification, as well as variable degree of surrounding oedema[17].

This enhancement may be homogenous or there may be a central zone of necrosis appearing as a radiolucent area. MRI is however more sensitive than CT in detecting cerebral or cerebellar tuberculomas[1,11]. On MRI, the lesions are isotense with grey matter on TI weighted images and show central hyper intensity with hypo intense ring on T2 weighted image[11]. The differential diagnoses of these CT/MRI appearances include pyogenic abscess, cysticercus granuloma, cerebral toxoplasmosis, metastases and sometimes gliomas[11,16]. Therefore accurate diagnosis of intracranial tuberculomas depend on histopathological examination, but in situations where histological confirmation is not possible, the presence of tuberculosis elsewhere or serological evidence of tuberculosis or association with tuberculous meningitis, response to anti-tuberculous treatment (ATT) or the use of newer rapid diagnostic methods (gene amplification by polymerase chain reaction to identify mycobacterial DNA) may be used[11,12,18].

It is important to mention the hyponatremia in this patient which suggests syndrome of inappropriate ADH secretion (SIADH), which has been reported in CNS tuberculosis[13].

Early diagnosis and appropriate therapy with antituberculous drugs and steroids usually result in an excellent or good outcome in most instances. Steroid therapy is usually beneficial[17] though this has not been conclusively proven. The paradoxical response to anti-tuberculous agents has been reported and this usually does not represent failure of therapy[10,18,19]. This phenomenon usually occurs within 3 months of initiation of therapy[19]. The duration of antituberculous therapy (ATT) should be based on the radiological responses of the tuberculomas as larger tuberculomas (maximal size >4cm) have been reported to resolve more slowly than smaller tuberculomas (<4cm)[20]. Most patients however received a 12-18 month course of ATT[18,19]. Surgical excision is necessary in patients who are not responding to medical therapy and with raised intracranial pressure secondary to the lesion[5].

This unusual case underscores the need to keep our index of clinical suspicion of intracranial tuberculoma high when evaluating intracranial mass lesions.

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