Diffuse "encephalitic" cerebral toxoplasmosis in AIDS

Report of four cases

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Summary. Four patients with AIDS presented with a rapidly fatal global neurological illness. CT did not show any focal lesion and gross post mortem examination of the brain was normal in three of the four cases. Microscopic examination revealed numerous widespread microglial nodules in the brain parenchyma, most containing central toxoplasma cysts or free tachyzoites. Such diffuse, non-necrotic, "encephalitic" forms of cerebral toxoplasmosis appear unique to AIDS and, to our knowledge, have not been documented previously. They represent a treatable, often misdiagnosed cause of diffuse neurological involvement in AIDS patients.

Key words: Acquired immune deficiency syndrome (AIDS) – Toxoplasmosis – Encephalitis

Introduction

Opportunistic infections, secondary to T-helper lymphocyte depletion, at present account for the majority of central nervous system lesions in adult patients with AIDS [11]. Of these, cerebral toxoplasmosis is the most frequently encountered in French series [6, 9] and represents the most common cause of focal lesion in other studies [12, 22].

The characteristic lesions of toxoplasmosis in AIDS, as in non-AIDS patients [13], are abscesses, frequently multiple and easy to diagnose by CT or MRI [16]. On the other hand, asymptomatic widely disseminated toxoplasma cysts without parenchymal reaction [1, 9, 16] may also be found in AIDS.

In contrast, dissemination of parasites in the brain parenchyma with an inflammatory "encephalitic" reaction and little or no necrosis, may be responsible for diffuse encephalopathy. This represents an unusual finding which, to our knowledge, has not previously been reported. We report four cases of such "encephalitic" toxoplasmosis in AIDS patients.

Case reports

Case 1 (HM 6840)

This patient was a 42-year-old homosexual male who was admitted to Henri Mondor Hospital with a fever of unknown origin of 4 months duration, which was associated with a weight loss of 10 kg and altered mental status. One year previously he had been found to be HIV positive. On admission, he presented with mutism rather than true aphasia, severe dysarthria, but no localizing neurological signs. Neurological examination revealed signs of meningitis, mental dullness and dysarthria, but no localizing neurological signs. CT showed a very small contrast-enhancing area in the right internal capsule and thalamus just below the level of the caudate head (Fig. 1a, b). Serology for toxoplasmosis was positive in low titres. The patient was treated with sulfonamide (Adiazine) and pyrimethamine (Malocid). Two days following admission, corticosteroid therapy was started because of pancytopenia. The patient died 3 days after admission from acute respiratory insufficiency.

Post mortem examination revealed diffuse bronchopneumonia with numerous disseminated toxoplasma cysts (Fig. 1c). Encysted parasites were also found in the liver (Fig. 1d) and adrenal medullae.

Neuropathological study. The central nervous system was examined after 1 month of 10% formalin fixation. Gross examination of the central nervous system was performed on coronal sections of the cerebral hemispheres, sections of the brainstem and cerebellum perpendicular to their axes, and horizontal sections of the spinal cord. Twenty systematic blocks from both cerebral hemispheres, cerebellum, brain stem and spinal cord were embedded in paraplast; 6 blocks (4 hemispheric slices and 2 from brain stem and cerebellum) were embedded in celloidin. The sections were stained with haematoxylin and eosin, Loyez stain for myelin, Bodian silver impregnation combined with Luxol fast blue, Masson trichrome, Periodic Acid-Schiff (PAS), Alcian blue, and the method of May-Grünwald-Giemsa, Gram, Ziehl-Nielsen and Grocott.

Small (2 mm in diameter) necrotic lesions with central coagulation necrosis characteristic of toxoplasmosis, surrounded by an inflammatory reaction containing numerous toxoplasma cysts, were found in the basal ganglia bilaterally. There were widespread microglial nodules, most containing toxoplasma cysts or free tachyzoites, in both cerebral hemispheres, brainstem and cerebellum. They were more numerous in the grey matter, but the white matter was also involved. A few nodules showed central necrosis and a few others were devoid of parasites. Toxoplasma cysts were also present in the
There were no viral inclusion bodies and no multinucleated giant cells; no microorganisms were detected in sections stained for bacteria, acid-fast bacilli or fungi.

Case 2 (HM 7077)

This patient was a 25-year-old bisexual male, known to be HIV positive since the onset of a Kaposi’s sarcoma 10 months beforehand. He was admitted to Tenon Hospital with a fever of 40°C, associated with general malaise, a productive cough and episodes of amnesia without objective neurological signs. The only abnormal finding on physical examination was the presence of retinal nodules bilaterally, which was consistent with CMV retinitis. Chest radiographs revealed diffuse bilateral interstitial pneumonia, and arterial PO2 was reduced. Bronchiolo-alveolar washings showed occasional *Pneumocystis carinii*. Serology for toxoplasmosis was negative. CT scan was normal. The patient’s general condition deteriorated very rapidly, and he died of irreversible shock 3 days following admission.

Post-mortem examination was restricted to the brain, which was macroscopically normal.

Microscopic examination was performed according to the same methods as previously described.

There was fulminant involvement of both white and grey matter with microglial nodules (Fig. 2a). Some nodules showed central necrosis (Fig. 2b), while a few others were haemorrhagic, and many contained toxoplasma cysts. Multiple disseminated parasitic cysts without inflammatory reaction or neighbouring gliosis were also observed in the cerebral parenchyma (Fig. 2c). There were no focal lesions, no viral inclusion bodies, no multinucleated giant cells; micro-organisms were not detected in sections stained for bacteria, acid-fast bacilli or fungi.

Case 3 (HM 7086)

This patient was a 69-year-old male who was admitted to Henri Mondor hospital for diarrhoea and general decline of health. One month prior to admission he was found to be HIV positive. The only risk factors were blood transfusions in 1984 and 1985 for a hip prosthesis.

On neurological examination, the patient was apathetic. He had no motor or sensory deficit; deep tendon reflexes were