MRI FINDINGS IN TOXOPLASMOSIS CEREBRALIS

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ABSTRACT

We present the case of a 25 years-old HIV infected patient with low CD4 count who presented seizures and receptive language disturbances. The MRI findings were highly suggestive for cerebral Toxoplasmosis. An empirical treatment for Toxoplasma gondii was started, with favorable outcome. We discuss the MRI findings in cerebral toxoplasmosis in immunocompromised patients.

Key words: Toxoplasmosis Cerebralis, HIV, MRI, ring enhancing lesion.

BACKGROUND

Toxoplasma gondii is a single-cell protozoa that exists as oocysts, bradyzoites and tachyzoites. Humans acquire the infection via the oral or transplacental route. The oral route consists in consumption of raw or undercooked meat that contains viable cysts, direct ingestion of oocysts from contaminated soil and water or consumption of unwashed vegetables (Hai & Hutchinson 1983). In adults, most Toxoplasma infections are subclinical, but severe infection can occur in immunocompromised patients (eg. HIV, malignancies). The parasite may invade multiple organs, including nervous system, retina, lungs, heart and skeletal muscles. In immunocompromised patients the brain infection usually represents the reactivation of previously dormant disease when the CD4 count drops below 100 – 200 cells/µl. It manifests as cerebral abscesses or encephalitis, toxoplasmosis being the most common cause of a focal brain lesion in patients with AIDS. The clinical signs consist in neurologic deficits, seizures, headache, altered mental status or signs of raised intracranial pressure. Any HIV infected patient with focal neurological signs, particularly when associated with seizures and fever, should be suspected of toxoplasmosis cerebralis. Serologic tests for Toxoplasma gondii are unreliable in HIV infected patients; most of the patients do not present IgM antibodies because the disease represents reactivation of a chronic infection (Luft et al., 1984). Rising IgG titers indicate the reactivation of toxoplasmosis, but the infection may also reactivate with minimal changes in antibody titers due to severe immunosuppresion (Derouin et al, 1996). Polymerase chain reaction testing demonstrates the presence of circulatory organisms, but parasitemia may be present without encephalitis. Neuroimaging studies are indispensable for the diagnosis and management of cerebral toxoplasmosis. MRI is more sensitive than CT, revealing one or multiple lesions that have predilection for the grey-white interface and the basal ganglia. Often the lesions present surrounding edema and contrast enhancement of the rim (Simon et al, 2009). A definitive diagnosis of toxoplasmosis cerebralis can only be

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made by brain biopsy but it is now in standard practice to treat any HIV infected patient with low CD4 and mass lesions on neuroimaging with Pyrimethamine and Sulfadiazine or Clindamycin. A response, clinically and radiologically, confirms the diagnosis (Howard & Manji, 2009). Up to 90% of the patients have a favorable response to therapy within the first few weeks (Simon et al, 2009).

CASE REPORT

We present the case of a 25 years – old male that was admitted in the Neurology Clinic for 3 grand mal seizures and motor jacksonian seizures in the right side of the body. He presented an advanced HIV infection (stage C3), with a poor adherence to therapy, stopping his antiretroviral treatment 2 months prior to the admission.

The neurological examination at hospital admittance revealed a conscious but obnubilated patient (postcritical state), with receptive language disturbances, no motor deficits, brisk tendon reflexes and bilateral Babinski sign, cranial nerves – unremarkable.

The cerebral CT scan done in the same day showed 2 left temporal lesions with ring enhancement and surrounding edema. The MRI scan revealed 3 relatively well-delimitated intracranial expansive processes of a round shape, with mixed signal, hypointense on T1-weighted sections and hyperintense on T2-weihgted images. There was a moderate surrounding edema and ring enhancement. The lesions were situated in the left parietal, left temporal and right temporal lobes (see Figure 1).

As the clinical and neuroimaging studies were highly suggestive for cerebral toxoplasmosis, the patient was transferred to the Infectious Diseases Clinic for appropriate management.

The CD4 cell count was 44 cells / µl and his viral load was of 12.600 copies / ml, with a severe immunosuppresion. The serological tests revealed an IgM titer of 0.093 (negative) and an IgG titer of 446 UI/ml (positive).

Therapy with Pyrimethamine (200 mg on the first day, then 100mg/day), Sulfadiazine (1g 4 times daily), folinic acid (10 mg 4 times daily), Depakine Chrono (500mg 2 times daily) and Dexamethasone (8mg 3 times daily) was started immediately. This regimen was continued for 6 weeks, except the Dexamethasone which was discontinued after 1 week. Afterwards, because his CD4 lymphocytes were < 100 cells/µl, he was recommended to continue suppressive therapy with Pyrimethamine (50mg/day), Sulfadiazine (1g/day) and folinic acid (10mg/day) until immune reconstitution. The antiretroviral medication was reintroduced in the second week of hospitalization.

The clinical status of the patient improved in about 2 weeks. The language disorder remitted and the neurological examination was unremarkable. MRI scan repeated in 3 weeks showed a positive response to therapy with the regression in size of all lesions.

DISCUSSIONS

Toxoplasmosis is the most common cause of focal brain damage in HIV infected patients and MRI plays a major role in the diagnosis and management of the disease. However, the immunocompromised patients are susceptible to various infections and malignancies and identifying the cause of the lesion can be difficult.

On cerebral MRI, toxoplasmosis appears with T1 hypointense and T2 hyperintense lesions; usually they have a diameter of 1 – 3 cm, with surrounding edema. Isointense lesions may also be present; rarely the lesions may be hemorrhagic. Other non-specific MRI patterns are assumed to be related to the patient's altered immune status. Most frequently, the lesions are situated at the corticomedullary junction and in the basal ganglia; leptomeningeal involvement is rare unless it is secondary to a concomitant condition; the involvement of corpus callosum is uncommon, although it has been reported. A characteristic pattern in cerebral toxoplasmosis is the eccentric target sign, characterized by a ring – enhancing abscess made up of an eccentric nodule along an irregular wall (Ramsey & Gean, 1997). This sign is highly suggestive for the disorder but false-positive findings may result from other diseases.

When there are ring enhancing lesions, it suggests a subacute or chronic process. Additionally, the gadolinium enhancement is peripheral because the central area is necrotic and lacks a good blood supply. The main causes for such lesions are infectious (toxoplasmosis, pyogenic abscesses, tuberculosis and fungal infections), primary brain tumors (e.g. lymphoma, glioblastoma) and metastatic tumors. Other causes could be infarction, granulomatous processes, demyelinations (e.g. progressive multifocal encephalopathy) or subacute hematoma (Bhidayasiri et al, 2005).

In HIV infected patients, the most probable cause is considered to be cerebral toxoplasmosis, but it can not be distinguished from primary CNS lymphoma solely on radiological criteria, which is the main differential diagnosis.

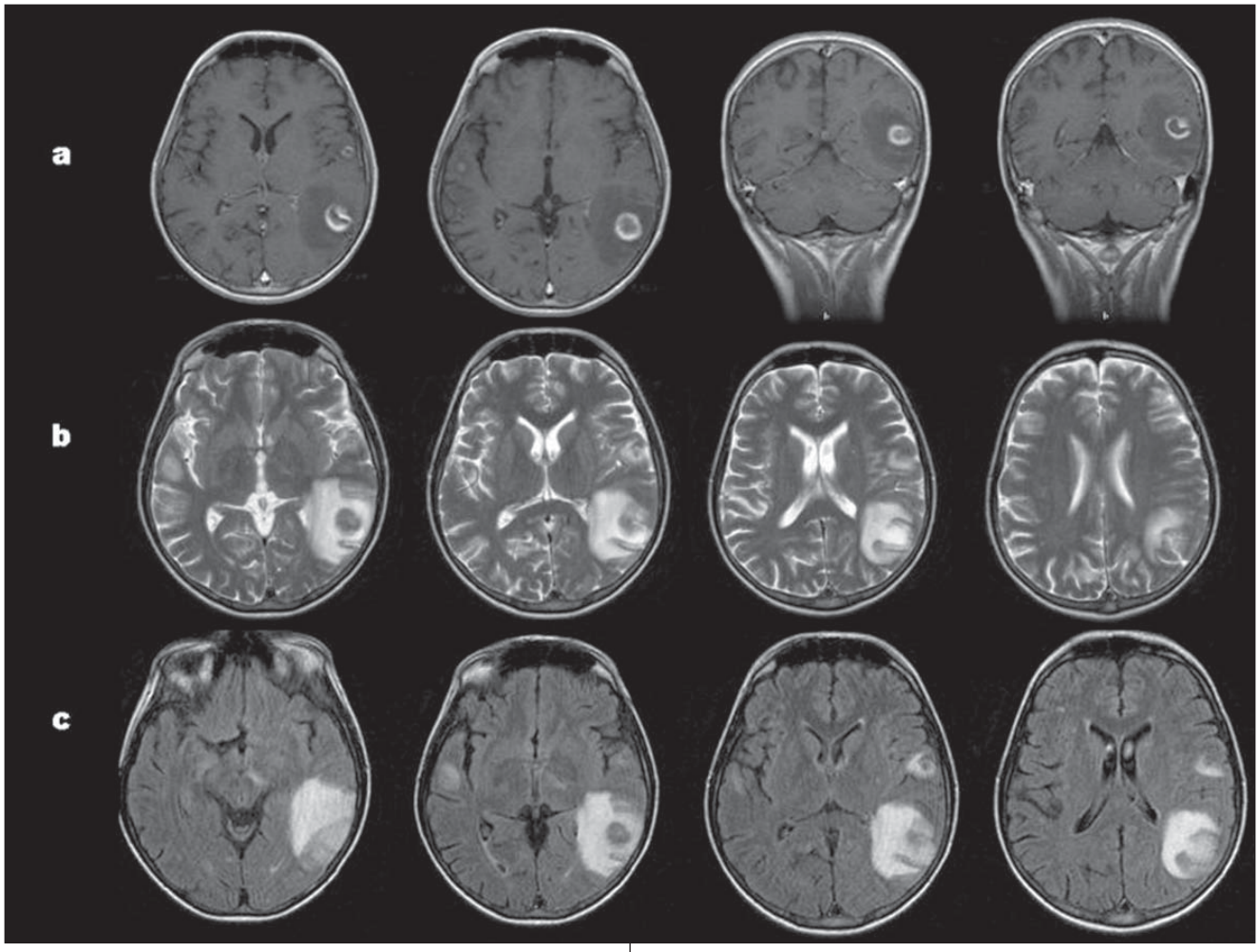

Figure 1. *MRI scan: a. T1 sequences; b. T2 sequences; c. Flair sequences.*

AIDS-related lymphoma causes variety appearances on MRI but usually it is a single supratentorial lesion, located in deep gray nuclei or periventricular white matter. Coating of the ventricles and spread across the corpus callosum is suggestive for lymphoma. Furthermore, on T2-weighten MRI it appears as isointense in about 50% of cases. (Bhidayasiri et al, 2005). Generally, CNS lymphoma has an irregular gadolinium enhancement and lesions are greater than 4 cm.

In HIV infected patients with CD4 lymphocytes count < 100 cells / µl that are not receiving prophylactic therapy for Toxoplasma gondii, finding on MRI multiple ring enhancing lesions is highly suggestive for cerebral toxoplasmosis. In this case, the patients must be treated empirically for toxoplasmosis and if the diagnosis was correct, there should be clinical and neuroimaging improvement in about 2 weeks. If improvement is not noted, brain biopsy is indicated (Davaro & Thirumalai, 2007). In patients on prophylactic therapy or those with a single brain lesion, the differential diagnosis includes CNS lymphoma and other infections (fungal, mycobacterium or cytomegalovirus infection) and Kaposi sarcoma.

In summary, MRI is an essential tool in the diagnosis of cerebral toxoplasmosis in HIV infected patients, being more sensitive than CT scanning. Although there are some MRI findings that are highly suggestive for toxoplasmosis, there are no clear distinctive features from other diseases such as CNS lymphoma. Occasionally in cerebral toxoplasmosis there can be found unusual MRI appearances that make the diagnostic very difficult by standard neuroimaging techniques. Furthermore, the immunocompromised patients may develop a variety of infections that are difficult do differentiate by brain imaging. However, there is a very high probability that the patient's condition is caused by Toxoplasma gondii if the following criteria are met: Toxoplasma IgG is positive, CD4 < 100 cells/µl and the patient is not receiving prophylaxis for Toxoplasma and multiple ring enhancement lesions are found in MRI or CT.

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