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Case Report

Single thalamic localization of brain toxoplasmosis mimicking brain tumors: Radiological and clinical findings

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ABSTRACT

Background: Cerebral toxoplasmosis is a relatively rare disorder that usually affects immunocompromised patients. The most common scenario occurs among human immunodeficiency virus (HIV)-positive patients. In those patients, toxoplasmosis is the most frequent cause of expansive brain lesion and continues to cause elevated morbidity and mortality. In typical cases of toxoplasmosis, both computed tomography and magnetic resonance imaging reveal single/multiple nodular or ring-enhancing lesions with surrounding edema. Nevertheless, cases of cerebral toxoplasmosis with atypical radiological features have been reported. Diagnosis can be obtained by finding organisms in the cerebrospinal fluid or in stereotactic biopsy samples of the brain lesion. If untreated, cerebral toxoplasmosis is uniformly fatal, so prompt diagnosis is mandatory. A prompt diagnosis is necessary, as untreated cerebral toxoplasmosis is uniformly fatal.

Case Description: We discuss imaging and clinical findings of a patient – not aware of being HIV-positive – with a solitary atypical brain localization of toxoplasmosis mimicking a brain tumor.

Conclusion: Although relatively uncommon, neurosurgeons should be aware of the potential occurrence of cerebral toxoplasmosis. High index of suspicion is needed for timely diagnosis and prompt initiation of therapy.

Keywords: Brain magnetic resonance imaging, Brain tumor, Cerebral toxoplasmosis, Stereotactic biopsy

INTRODUCTION

Acute *Toxoplasma gondii* infection is typically subclinical in the vast majority of immunocompetent subjects and it is very seldom associated with serious clinical events. In contrast, cerebral toxoplasmosis is caused almost exclusively by reactivating latent cerebral cysts and can have devastating consequences in host immunocompromised patients, particularly in people living with human immunodeficiency virus (HIV) disease or acquired immune deficiency syndrome (AIDS). In these patients, toxoplasmosis is the most common cause of expansive brain lesions and continues to cause high morbidity and mortality.[10] If untreated, cerebral toxoplasmosis is uniformly fatal, so a prompt diagnosis is mandatory.

In an HIV-positive patient, the discovery of single or multiple brain lesions should immediately lead to a suspicion of cerebral toxoplasmosis to rapidly begin the treatment and reduce the risk of progression.[4,9]

A difficult problem to solve is represented by patients who are unaware or unwilling to report that they are infected with HIV/AIDS. In these cases, the risk of diagnostic delay is high with potentially serious consequences for the patient.

We discuss imaging and clinical findings of a 25-year-old patient – not aware of being HIV positive – with a single right thalamic localization of toxoplasmosis mimicking a brain tumor.

CASE DESCRIPTION

A 25-year-old woman was admitted to our emergency department with a subacute onset of mild confusion and left hemiparesis (Medical Research Council grade 4/5). She was fully alert and orientated, complaining about headaches (Visual Analogic Scale 7/10). She had no history of drug abuse or cigarette smoking.

Pre- and postcontrast computed tomography (CT) scans of the brain [Figure 1] revealed a 2 cm diameter hypodense nodular lesion in the right thalamus with perilesional edema causing moderate mass effect, with colliquative features inside. Brain magnetic resonance imaging (MRI) pre and post contrast [Figure 2] confirmed a right thalamic nodular lesion measuring 25 × 22 mm, with perilesional edema. The nodule appeared hypointense on T2-weighted and fluid-attenuated inversion recovery sequences, isointense on T1-weighted and reg-diffusion-weighted imaging (DWI) sequences. The nodule and associated edema resulted in ipsilateral ventricular compression. In the coronal sections [Figure 3], there was an irregular postcontrast enhancement, especially along the nodule walls. Was also visible an inner enhancing nodule, which should have raised the suspicion of parasitic infection [Figure 3, Panel C].

The clinical presentation (without any known history of immune suppression) and the neuroimaging features of the solitary brain lesion primarily suggested a brain tumor, even if other diagnostic hypotheses could not be rejected.

Considering the deep location in an eloquent area, it was decided to perform a neuronavigated stereotaxic biopsy [Figure 4]. Preoperative planning was conducted using three-dimensional reconstruction to simulate the surgical trajectory and avoid functional areas and tracts (StealthStation S8; Medtronic, Minneapolis, Minnesota, USA) [Figure 4].[3,5-7] A coronal trajectory was used passing lateral to the lateral ventricle wall. Histopathology revealed extensive areas of necrosis, vascular thrombosis phenomena and aspects of vasculitis with lymphohistiocytic and granulocytic infiltrate at the level of the vascular walls. Rounded structures containing eosinophilic corpuscles inside the infiltrate were found, suggesting a protozoal infection, and allowing the diagnosis of cerebral toxoplasmosis [Figure 5].

The immediate postoperative course was uneventful without complications. Nevertheless, in the following days, the patient presented with fever and abdominal pain with rapid clinical worsening and septic shock. Therefore, the patient was then

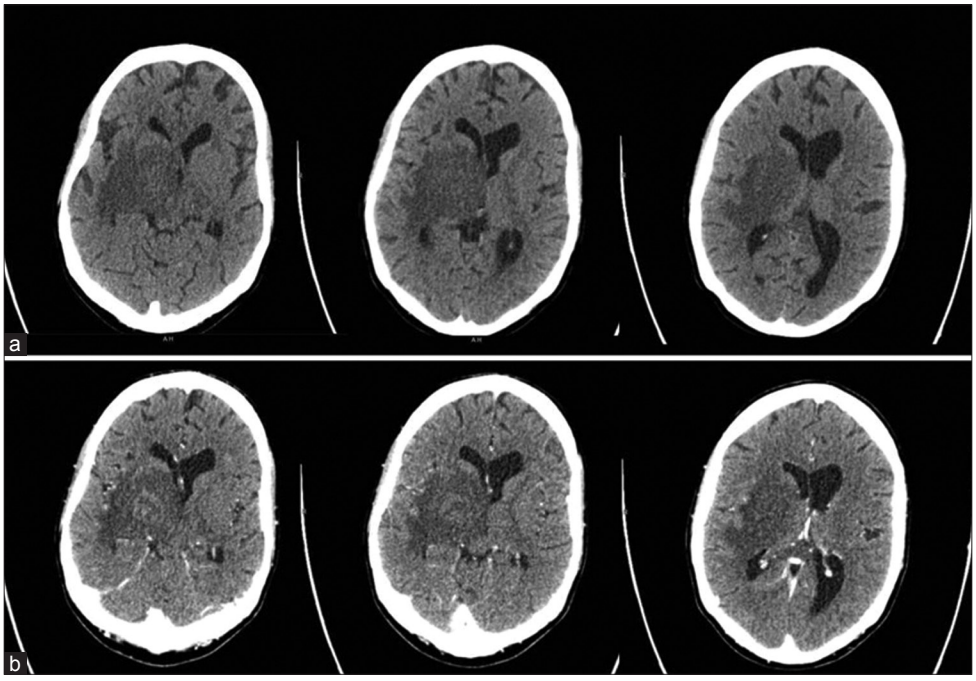

Figure 1: Pre- (a) and postcontrast (b) computed tomography scan of the brain revealed a 2 cm diameter hypodense nodular lesion in the right thalamus with perilesional edema causing moderate mass effect, with colliquative features inside.

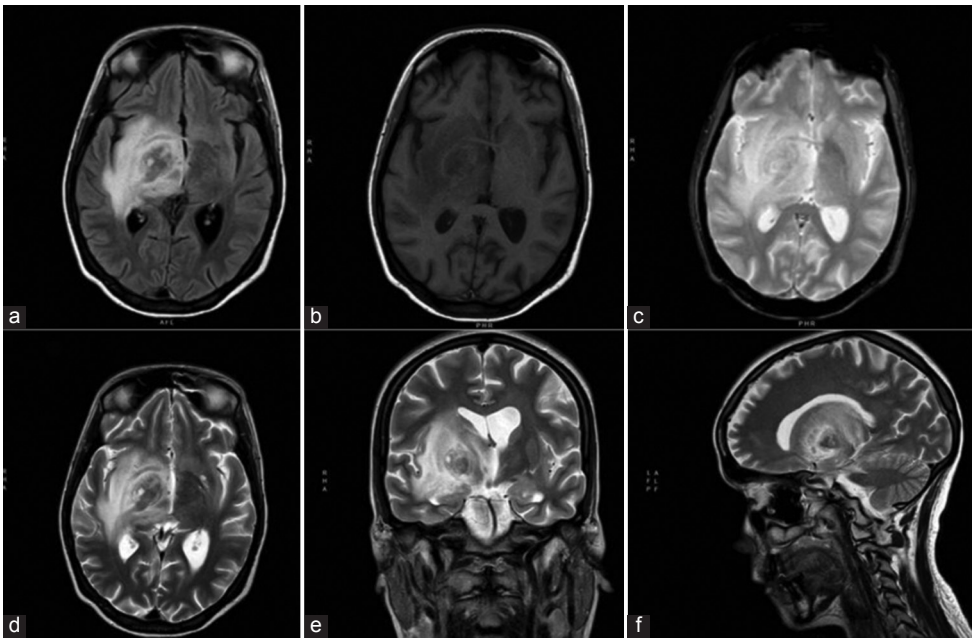

Figure 2: Brain magnetic resonance imaging without contrast showing a right thalamic nodular lesion measuring 25 × 22 mm, with perilesional edema. The nodule appeared hypointense in fluid-attenuated inversion recovery sequences (a), isointense on T1-weighted (b) and reg-diffusion-weighted imaging sequences (c), and hypointense on T2-weighted images (d-f). The nodule and associated edema resulted in slight compression of the ipsilateral ventricle.

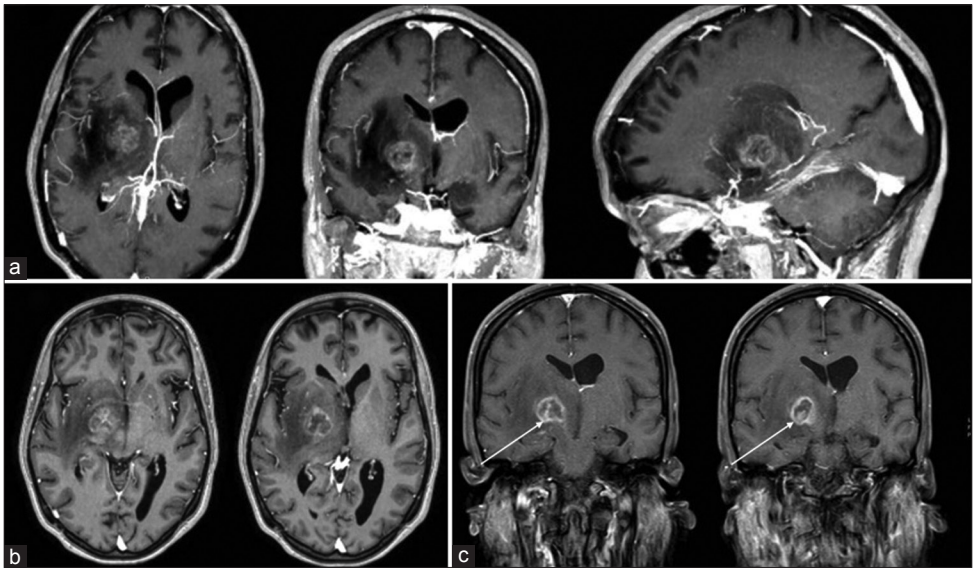

Figure 3: Brain MRI, post-contrast T1 weighted sequences showing irregular post-contrast enhancement particularly along the nodule walls (ring enhancement); white arrows (panel C) indicate an intranodular enhancing component (similar to "eccentric target sign").

transferred to intensive care unit. A total-body CT scan revealed multiple abscesses (liver, kidney, and thyroid gland), intestinal walls thickening, and pleural effusion [Figure 6].

Due to the septic shock and the diagnosis of toxoplasmosis, the patient was evaluated by the infectious disease specialist, who initiated the treatment of toxoplasmosis and performed a serologic test which revealed an HIV infection.

Despite therapy, due to HIV-related immunosuppression, the patient suffered multiorgan failure and died.

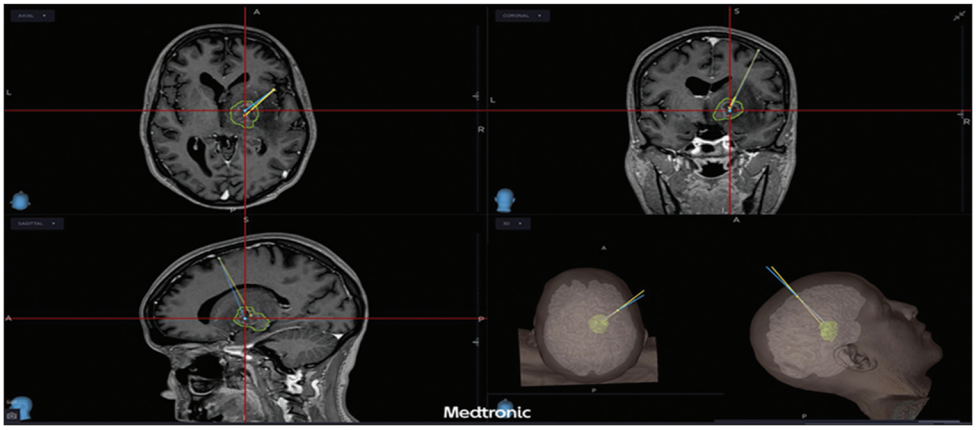

Figure 4: Preoperative planning with 3D reconstruction to simulate the surgical trajectory avoiding functional areas and tracts (Medtronic Stealth S8, Minneapolis). A coronal trajectory was used passing lateral to the lateral ventricle wall.

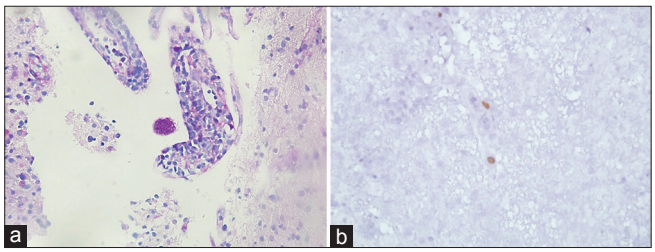

Figure 5: Staining with PAS. ×40. Image of brain tissue with tachyzoites in a Toxoplasma infection (a). Immunohistochemical staining showing cytomegalovirus superinfection in a patient with cerebral toxoplasmosis. Image at ×40 (b).

DISCUSSION

The clinical presentation of cerebral toxoplasmosis is notably heterogeneous, nonspecific, and overlapping. Cerebral toxoplasmosis usually presents neurological subacute manifestations. Nevertheless, the disease may progress rapidly with fatal diffuse encephalitis or ventriculitis, with or without focal brain lesions in imaging studies.[1,2,4,10] The general clinical picture includes rash, myocarditis, and polymyositis; in addition, neurologic symptoms are highly variable. In rare cases with single localization, the disease may cause seizures or neurological deficits (e.g., hemiparesis, aphasia); in the most common cases of multiple brain localizations, patients may develop headache, seizures, confusion, neurological deficits (including cranial nerve deficits), and symptoms of endocranial hypertension (e.g., headache, nausea, and vomiting).

Clinical signs suggesting encephalitis in an immunocompromised patient should raise suspicions of toxoplasma. In contrast, in an immunocompetent patient or in a patient who is unaware of immunosuppression, clinical presentation alone is not sufficient for proper diagnosis and may be confused with other types of meningoencephalitis or brain tumor.[10] Both serum and cerebrospinal fluid (CSF) studies can help determine the cause of central nervous system (CNS) lesions, but there are some caveats. *T. gondii* antibody titers are not very helpful in immunocompromised individuals. Polymerase chain reaction on CSF or serum, in contrast, has good specificity and reasonable sensitivity. The cytological evaluation of CSF occasionally demonstrates the Toxoplasma organisms. Differential diagnosis with tuberculosis, brain tumor, and lymphoma could be challenging. Moreover, a stereotactic biopsy is needed to confirm diagnosis.[1,10]

In typical cases of toxoplasmosis, both CT and MRI reveal varying numbers of nodular or ring-enhancing lesions with surrounding edema. The lesions are scattered throughout the brain, and probably, those adjacent to the subarachnoid space causes the meningitis component in meningoencephalitis.[4] About 15–30% of patients with cerebral toxoplasmosis have a single lesion which revealed by MRI and CT scan.[2,10] The most common localizations are basal ganglia (48%), frontal lobe (37%), and parietal lobe (37%). In addition, occipital lobe (19%), temporal lobe (18%), and brain stem/cerebellum (5-15%) can be affected.

The intensity of enhancement varies and can be weaker in patients with advanced HIV disease and reduced immune response. Lesions occur more frequently at the gray-white matter interface and in the basal ganglia and thalamus. Although signal characteristics vary, the lesions are often hyperintense on T2-weighted sequences. In our case, contrary to the most common cases reported in the literature,[4,10] the nodule appeared hypointense in T2-weighted sequences [Figure 2]. DWI is not specific and usually shows no restriction of diffusion in cerebral localization of toxoplasmosis: the center of the lesion generally appears hypointense on DWI with hyperintense surrounding edema.[4]

One of the most frequently described findings of CNS toxoplasmosis is the postcontrast T1 "eccentric target sign"

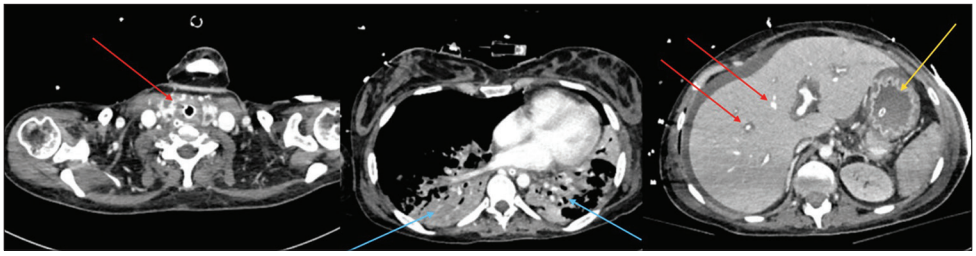

Figure 6: Total-body computed tomography scan showing multiple small abscesses in liver, kidney and thyroid gland (red arrows), intestinal walls thickening (yellow arrow), and pleural effusion (blue arrows).

consisting of three alternating zones: an innermost eccentric enhancing core, an intermediate hypointense zone, and an outer peripheral hyperintense enhancing rim.[8,9]

In our case, there was an enhanced intranodular component that, however, did not show the typical features of the above-mentioned "eccentric target sign" [Figure 3].

In our patient, the intranodular component showed homogeneous enhancement without the intermediate hypointense component, as in certain neoplasms with intracystic nodule. A more specific imaging pattern is the more recently described "concentric target sign" on T2-weighted MR imaging. This focal lesion presents an alternation of concentric layers of hypo- and T2-weighted hyperintensities.[8] The previous literature indicated that "concentric" and "eccentric" signs are rarely seen in the same lesion suggesting that they reflect different pathological states of toxoplasma lesions in evolution.[8]

In our patient, the radiological signs were quite atypical. In the postcontrast T1 sequences [Figure 3], it was possible to identify an intralesional nodule similar to the "eccentric target sign" which should have made us suspect toxoplasmosis. However, there was no "concentric target sign" – that is a more specific but less frequent sign – and in the T2-weighted sequences the nodule appeared hypointense, instead of hyperintense, as more frequently occurs.

Furthermore, the patient was unaware that she was infected with HIV and the remaining clinical and radiological features were indicative of a brain tumor, which delayed diagnosis and treatment. Unfortunately, after surgery, the patient developed severe HIV-related immune suppression that resulted in sepsis and multiple infections leading to death.

Empirical treatment is often initiated in patients with characteristic enhancing mass lesions, due to the high incidence of toxoplasma encephalitis in HIV-infected patients and the difficulty in making a noninvasive diagnosis.

Toxoplasmosis often responds rapidly to therapy with pyrimethamine and sulfadiazine. Radiologic improvement is usually apparent within 2–4 weeks, but, in rare cases, patients may take up to 6 months to respond.[9] A favorable response to medical treatment is considered diagnostic.

When diagnostic uncertainty persists or in patients with radiological lesions suggestive of toxoplasmosis and lack of risk factors as HIV/AIDS and immunosuppression, a biopsy is needed to confirm the diagnosis.

CONCLUSION

MRI findings of single or multiple brain lesions suggesting cerebral toxoplasmosis should lead to screening for immunosuppression, when unknown, and early introduction of specific medical therapy, also for ex adiuvantibus purposes. A biopsy may be needed for differential diagnosis with tumors.

Although cerebral toxoplasmosis is rather rare, this diagnosis cannot be excluded, since an early diagnosis can significantly improve the prognosis of these patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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