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Brain lesions in a long-term kidney transplant recipient: Primary cerebral lymphoma or cerebral toxoplasmosis?☆,☆☆

Lesiones cerebrales en trasplante renal de larga evolución, ¿linfoma cerebral primario vs. toxoplasmosis cerebral?

Introduction

Infection with the obligate intracellular protozoan parasite *Toxoplasma gondii* is asymptomatic in more than 90% of the immunocompetent adult population.[1] Cerebral toxoplasmosis (CTx) mainly affects untreated HIV-immunocompromised patients with a CD4+ T cell count <100 mm^3. It is an extremely rare finding in other patients except for transplant recipients.[2,3] Toxoplasmosis after solid organ transplantation is generally diagnosed after the first month post-procedure. It is more frequent in heart transplant recipients and rarely affects kidney transplant recipients.[4] We present the case of a patient with cerebral toxoplasmosis 18 years after transplantation.

Clinical case

Our patient was a 74-year-old woman with a history of arterial hypertension, obesity, and severe chronic kidney disease secondary to nephroangiosclerosis and analgesic nephropathy. She underwent transplantation of the right kidney in 1996 and was treated for acute rejection with OKT3. Since then, she has been treated with ciclosporin, prednisone, and mycophenolic acid as immunosuppressants. The patient was assessed by the neurology department due to acute-onset symptoms of dysarthria and right hemiparesis with spontaneous recovery. While hospitalised, she experienced 3 similar episodes that remitted with levetiracetam and increasing the dose of corticosteroids.

A cranial computed tomography (CT) scan showed diffuse hypodense lesions with effacement of convexity sulci on the right frontal-parietal-temporal area and the left frontoparietal area, as well as multiple subcortical hyperenhanced lesions. A brain MRI showed vasogenic oedema in the subcortical frontoparietal area and left posterior temporal area, plus 3 subcortical nodules (Fig. 1). The electroencephalography revealed no abnormalities. Results for tumour markers and a CT scan of chest, abdomen, and pelvis were normal. The positron emission tomography (PET) revealed that lesions were hypermetabolic and suggestive of malignancy.

A brain biopsy was performed. The first histopathological study yielded non-specific results consisting of presence of lymphoproliferative infiltrate. We requested a second assessment of the same sample, which revealed trophozoites; we diagnosed CTx. The PCR test for *T. gondii* was positive.

The patient showed good clinical and radiological progress (Fig. 2) after starting treatment with pyrimethamine and clindamycin.

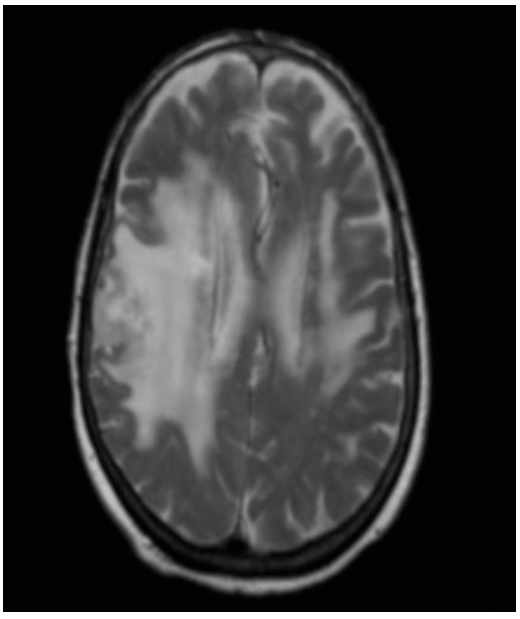

Figure 1 Brain MRI T2-weighted sequence. Hyperintense lesions on the right temporoparietal area and the left temporal area with associated vasogenic oedema.

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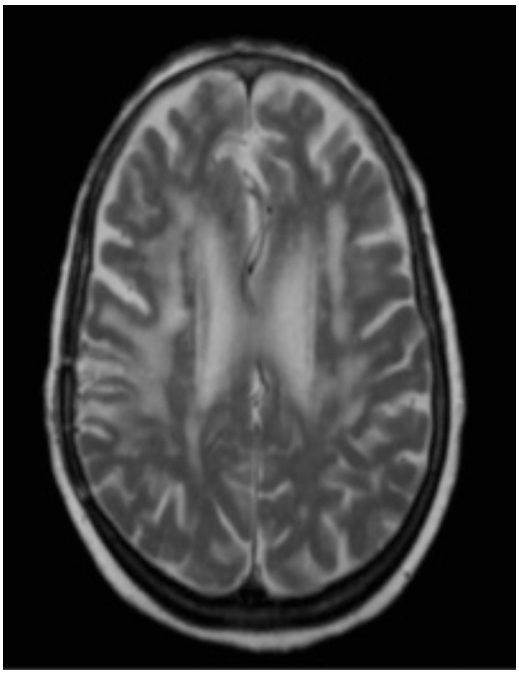

Figure 2 Brain MRI. T2-weighted sequence. Significant decreases in the volumes of lesions and associated oedemas after 4 months of CTx treatment.

Discussion

We described the case of a non-HIV immunocompromised patient in whom cerebral toxoplasmosis was diagnosed and treated specifically 18 years after she had undergone a kidney transplantation.

Neurological complications due to toxoplasmosis are rare in solid organ recipients, and even more so in kidney transplantation patients. The literature describes 35 cases.[4,5,7,8]

Infection with *T. gondii* in solid organ transplantation patients results in high mortality rates. In a report of 6 cases of toxoplasmosis following kidney transplantation, the mortality rate amounted to 65.5%, whereas neurological complications were less frequent.[5] Symptom onset after transplantation ranges from the first to the fourth month, but there is also late variants which are exceptionally rare.[6,7] Our patient showed her first neurological symptoms 18 years after the transplantation, and no changes had been made to her immunosuppressant treatment; therefore, late presentation of CTx may be possible in these patients.

Diagnosing toxoplasmosis in non-HIV immunocompromised patients might be difficult; in fact, 30% of these diagnoses are established by autopsy.[7] In an immunocompromised kidney transplant recipient with brain lesions, the main aetiological options to be assessed are infection and neoplasm. The microbes to be considered are *Aspergillus*, *Nocardia*, *Cryptococcus*, *Listeria*, *Tuberculosis*, and *Toxoplasma*. Primary cerebral lymphoma (PCL) is the most frequent of the neoplastic aetiologies.[9] It is often difficult to distinguish between one entity or the other using only radiological findings, and even more challenging in immunocompromised patients who may display PCL as multiple lesions.[7,9] Certain radiological characteristics may help us differentiate them[10]; however, biopsies are generally necessary to determine the aetiology of the lesions histologically. In our case, the first histological study suggested PCL, and it was not until the second study that the trophozoites were detected.

Positive PET findings are thought to suggest a neoplastic aetiology; however, there are no conclusive studies on the effectiveness of this technique in patients with CTx.[11] A previous case of positive PET findings in a patient with CTx has also been described,[12] but the usefulness of this test for distinguishing between PCL and CTx is questionable.

No empirical treatments for toxoplasmosis were started, as would be done with HIV patients, since toxoplasmosis was not initially considered due to the time elapsed (more than 15 years since transplantation).

Conclusion

Firstly, we must underscore that CTx may manifest late in patients with kidney transplants; and secondly, this entity must be included in the differential diagnosis of brain lesions in transplant patients, although the main diagnostic alternative is PCL. Thirdly and fundamentally, an accurate study of the anatomical pathology findings is necessary since the prognosis can change drastically and become favourable.

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Mechanical thrombectomy during ischaemic stroke due to a calcified cerebral embolism☆

Trombectomía mecánica en un ictus isquémico debido a embolia cerebral cálcica

Dear Editor:

Ischaemic stroke due to a calcified embolus is an extremely rare complication of cardiac surgery. Treatment for these cases has not been clearly defined. We present our experience with a patient whose middle cerebral artery (MCA) was occluded by a calcified embolus after aortic valve surgery; the occlusion was successfully managed using neurointerventional techniques.

Our patient was a 77-year-old woman with aortic valve stenosis who had been admitted at our hospital to undergo aortic valve replacement. Four months before admission she began to experience exercise-induced dyspnoea. She had a history of hypertension and diabetes. The echocardiogram showed a normal left ventricular ejection fraction, mild left ventricular hypertrophy, mild bilateral atrial enlargement, and severe aortic stenosis. The patient was treated with acetylsalicylic acid, simvastatin, torasemide, and metformin. During the preoperative assessment, she was alert and oriented with no sensory or motor deficits and displaying normal gait. Laboratory test results were within normal limits. The patient underwent a thoracotomy and aortic valve replacement (porcine valve). An intraoperative transoesophageal echocardiogram revealed no thrombi in the left atrium.

At day 1 after surgery, after extubation and upon waking up at the cardiac postoperative care unit, our patient displayed drowsiness, right hemiparesis, and global aphasia; these clinical symptoms were compatible with ischaemic stroke of the left MCA. In-hospital code stroke was activated. Our patient's NIHSS score at that moment was 18. An emergency brain CT scan revealed a high-density rounded mass in the area corresponding to the proximal segment of the left MCA. A CT perfusion map showed a large ischaemic penumbra in the territory of the left MCA. MR angiography revealed interrupted blood flow distal to the origin of the left MCA (Fig. 1). Thrombolytic therapy was ruled out since our patient had recently undergone surgery. She received endovascular treatment under general anaesthesia: stentriever-based thrombectomy successfully restored circulation with a single pass (Fig. 2). The results of the histology study of the extracted fragment were compatible with a calcium embolus. The patient was discharged after 7 days and the outcome was very favourable: she scored 1 on the mRS at 3 months.

Aortic valve stenosis due to calcification is the most common acquired heart valve disorder in developed countries. Surgery is frequently recommended to treat symptoms and reduce associated mortality in these cases.[1] Aortic valve calcification may be a source of emboli travelling to the brain. Mechanical manipulation of cardiac valves during diagnosis or treatment may predispose patients to calcified cerebral emboli, although these blockages may also appear spontaneously or secondary to endocarditis on rare occasions.[2,3]

Around 20% of patients with prosthetic heart valves will experience a cardioembolic stroke within 15 years after valve replacement.[4] On the other hand, ischaemic stroke due to perioperative thromboembolism or hypoperfusion is a well-known complication of cardiovascular surgery. This type of surgery is associated with a high risk of perioperative stroke, which may be attributed to an increase in particles and the likelihood of air embolisation; calcific embolisation is extremely rare.[5] In a prospective series of more than 16 000 patients undergoing cardiac surgery with a mean of 12 months of follow-up after the intervention, short-term risk of stroke was 4.8% after aortic valve replacement, 8.8% after mitral valve replacement, and 9.7% after multiple valve replacement.[6]

Perioperative stroke can be classified as either early-onset, occurring during extubation (intraoperative), or late-onset, occurring after extubation (postoperative).

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