Case Report

Circulating Antigen Levels Follow Post-Treatment Evolution of Subarachnoid Neurocysticercosis

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Abstract Subarachnoid neurocysticercosis carries poor prognosis and high mortality. Besides neuroimaging, there are no available monitoring tools. We examined antigen levels in sequential serum samples of a patient who required four courses of antiparasitic treatment. Antigen levels decreased in parallel to parasite resolution. Antigen detection may contribute to monitoring treatment of subarachnoid neurocysticercosis.

Keywords Taenia solium; cysticercosis; neurocysticercosis; albendazole; antigen detection

Taenia solium neurocysticercosis (NCC) is associated with a significant proportion of seizure cases in endemic areas [5,11]. Humans are infected by ingestion of Taenia eggs via fecal-oral contamination. The infective embryos penetrate the intestinal mucosa, are distributed by the circulatory system throughout the body, and encyst as metacestode larvae or cysticerci. Outside the nervous system, cysticercosis causes few symptoms, and cysts are almost invariably destroyed by the host’s immune response. Symptoms and signs usually result from parasites located in the eye or the nervous system.

Clinical manifestations of NCC vary according to the number, size, stage and localization of lesions, and the host’s immune response [9]. Whenever NCC is in the brain parenchyma, it is usually associated with good prognosis. The parasites go through a degeneration process that ends with the formation of a calcified scar [9]. In contrast, parasites located in the basal subarachnoid spaces tend to grow and infiltrate the neighboring spaces and are surrounded by a marked chronic inflammatory response. Initially, the growing membranes resemble a bunch of grapes, hence this form of disease was called “racemose” cysticercosis. Basal subarachnoid NCC is associated with disease progression, intracranial hypertension, and mortality of over 20% of cases [1,15].

In 1992, Brandt et al. developed an IgM monoclonal antibody-based antigen detection ELISA directed to a secretory-excretory antigen from Taenia saginata [3]. This assay has been improved by using IgG monoclonal antibodies and pretreatment of the sera by trichloro acetic acid (TCA) [6,16]. It has been applied to CSF, serum, and urine samples for the diagnosis of human and porcine T. solium cysticercosis before [4,7,14]. In order to assess whether specific antigen levels could serve to monitor the evolution of basal subarachnoid cysticercosis, we assayed all archive samples from a successfully treated patient to compare circulating antigen levels. All samples had been obtained under appropriate consent for another IRB-approved research study whose written consent form specifically requested permission for further use of stored samples in immunodiagnostic studies.

A 30-years-old male Peruvian patient presented to our unit in September 2003 with a history of six months of headache and episodic numbness of the left hemibody. Clinical examination demonstrated bilateral papilledema and altered gait. Brain CT demonstrated distortion of the normal brainstem anatomy with profuse cysticercal infiltration of the basal cisterns, mainly in the left side. Serology by enzyme-linked immunoelectrotransfer blot assay (western blot, immunoblot) was strongly positive for specific antibodies to T. solium. The patient improved on steroids (prednisone 30 mg/d) and admission for anti-parasitic treatment was indicated but not executed. He
continued with sporadic symptoms until February 2004 when he was admitted for a 60-day course of albendazole (15 mg/kg/day divided in two daily doses) after which he was released from hospital with marked improvement in symptoms. His first imaging control (MRI three months after treatment onset) showed a decrease of approximately 40% of the parasite area which continued to improve at month 6. In early October 2004, he had to be readmitted because of an episode of acute intracranial hypertension. A noncontrast CT at this time showed mild hydrocephalus and regrowth of the parasite, and the patient had a ventriculoperitoneal shunt placed. A new course of albendazole was initiated at this time but suspended at treatment day 15 because of increased liver enzyme levels. A new scan on January 2005 showed further decrease in the previous lesion areas but new areas of parasite growth in the contralateral side. Despite not having returned to normal GPT levels, albendazole was reinitiated and continued for 60 days. Brain MRI taken three months after the onset of this third course of antiparasitic treatment showed a marked decrease in parasite extension. The patient was released with mild episodic dizziness and headache. A new symptomatic episode occurred in July 2005, associated to CSF transit blockage due to a pseudocystic CSF collection at the abdominal end of the DVP catheter. This was corrected by surgery and the patient became asymptomatic again. Brain MRI at this time showed a localized increase of parasite area in the right side. Antiparasitic treatment was prescribed again but only initiated by the end of September 2005 with marked radiological response. The patient evolved well and continued asymptomatic until his last control visit in early 2010. Comparison images showing the changes in the parasite area along the patient follow up are shown in Figure 1.

The antigen-detection ELISA assay was performed with slight variation from the original report as follows: plate coverage with trapping MoAb (158C11) was performed by agitation during 30 minutes at 37°C, then washed with PBS Tween-20 at 0.05%. After adding blocking buffer (PBS Tween-20 at 0.05%, 1% NBCS), the plate is incubated for 15 minutes at 37°C before washing 5 times with PBS Tween-20. A 100 µL volume of previously TCA-treated serum sample, equivalent to 50 µL of untreated serum, was then added to the well and incubated for 15 minutes at 37°C before washing 5 times with PBS Tween-20 at 0.05%. Biotinylated MoAb B60 H8 A4 (125 µg, at 1.25 µg/µL in blocking buffer) is then added and again incubated for 15 minutes at 37°C under gently shaking. After washing, streptavidin (1/10,000, 100 µL) is added and incubated for another 15 minutes at 37°C. The plate is then washed again.
and o-phenylenediamine was used as chromogen. Optical densities were read at 492 nm. All samples were run in duplicate in the same plate.

Results from our patient are presented in Figure 1. Baseline circulating antigen levels were extremely high, in the range of 300 times the usual levels in patients with parenchymal neurocysticercosis [13]. This is probably due to the extensive and hypertrophic membrane surface characteristic of basal subarachnoid cysticercosis. Circulating antigen levels decreased parallel to parasite resolution on brain imaging. Interestingly, an early peak in antigen levels seems to develop soon after the onset of each antiparasitic treatment. Prolonged and repeated antiparasitic treatment courses have been shown useful in patients with giant cysts [12] and may be helpful in basal subarachnoid NCC. Early reports of the use of serum antigen levels for follow up purposes [2,8,17] had not been subsequently replicated or expanded. Currently, this type of patients is only monitored by expensive neuroimaging [10]. Longitudinal follow up of serum antigen levels can provide a way of titrating patients effectively for continuation or interruption of antiparasitic treatment, a largely expected need in the management of patients with this deadly form of neurocysticercosis.

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References