Ashdin Publishing
Journal of Neuroparasitology
Vol. 1 (2010), Article ID N100804, 3 pages
doi:10.4303/jnp/N100804

Case Report

Circulating Antigen Levels Follow Post-Treatment Evolution of Subarachnoid Neurocysticercosis

Hector H. Garcia,[1,3] Pierre Dorny,[4] Yesenia Castillo,[1] E. Javier Pretell,[1] Silvia Rodriguez,[2] Lizardo Mija,[2] Armando E. Gonzalez,[5] Robert H. Gilman,[1,3] Victor C. W. Tsang,[6] and Jef Brandt[4]

[1]*Department of Microbiology, School of Sciences, Universidad Peruana Cayetano Heredia, Avenida H. Delgado 430, SMP, Lima 31, Peru*
[2]*Cysticercosis Unit (HHG, SR) and Department of Epilepsy (LM), Instituto de Ciencias Neurologicas, Lima 1, Peru*
[3]*Department of International Health, Johns Hopkins University Bloomberg School of Hygiene and Public Health, Baltimore, MD 21205, USA*
[4]*Institute for Tropical Medicine, Nationalestraat 155, 2000 Antwerpen, Belgium*
[5]*School of Veterinary Medicine, Universidad Nacional Mayor de San Marcos, Lima, Peru*
[6]*Department of Biology, Georgia State University, P. O. Box 4010, Atlanta, GA 30302, USA*
Address correspondence to Hector H. Garcia, hgarcia@jhsph.edu

Received 31 August 2010; Accepted 1 October 2010

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 antiparasitic treatment was indicated but not executed. He

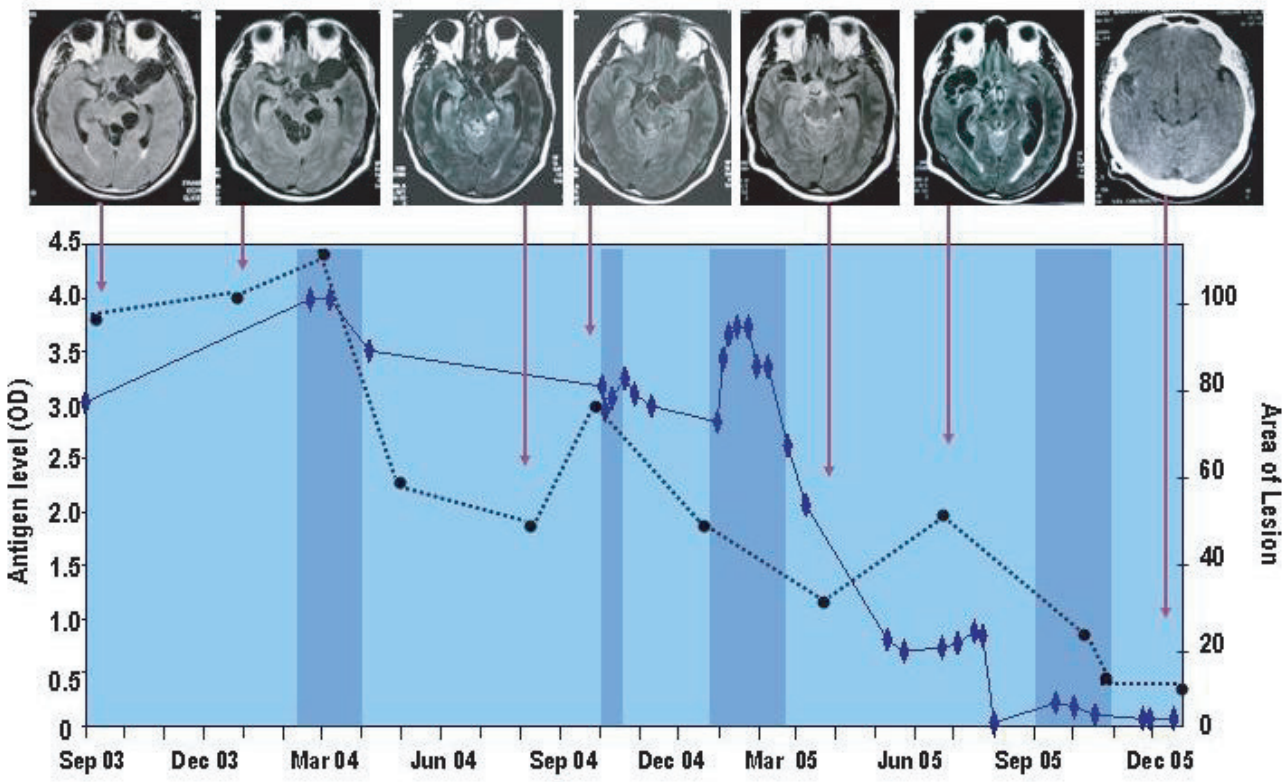

Figure 1: Antigen levels and brain images of the subarachnoid lesions along the follow up. All scans show approximately the same slice level. The dotted line is an estimate of the maximal axial area of cysts in that MRI or CT exam obtained by averaging the axial lesion area in three consecutive slices and adjusted to the immediate pre-treatment lesion area. Shady areas indicate antiparasitic treatment periods.

continued with sporadic symptoms until February 2004 when he was admitted for a 60-day course of albendazole (15 mg/k/d 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 noncontrasted CT at this time showed mild hydrocephalus and regrowth of the parasite, and the patient had a ventricle-peritoneal 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, and the supernatant is discarded. A 100 μL volume of previously TCA-treated [6] 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.

Acknowledgments The authors are indebted to Humberto Zamora who performed most of the immunodiagnostic work reported here. Y. Castillo is partially supported by FIC research training Grant TW001140 from the National Institutes of Health, USA. H. Garcia is a Wellcome Trust Senior Research Fellow in Public Health. The sponsors had no role in the design or writing of this manuscript.

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