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SEIZURES AND PRAZIQUANTEL. A CASE REPORT.

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SUMMARY

A 27 year old male developed seizures after receiving a single 20 mg/kg dose of praziquantel for the treatment of an intestinal **Hymenolepis nana** infection. On further clinical and laboratorial evaluations, he was found to suffer from an until then asymptomatic parenchymal brain cysticercosis. Praziquantel must be used with caution in those areas where cysticercosis represents a mayor public health problem. The occurrence of unexpected seizures in an individual being treated with the compound, must prompt clinicians to rule out cysticercosis of the CNS.

KEY WORDS: Praziquantel; Seizures; Neurocysticercosis.

INTRODUCTION

Praziquantel (PZQ), an acylated isoquinoline-pirazine derivative, is a broad spectrum antitrematode drug originally developed to treat schistosomiasis, that has proved highly successful in the treatment of diverse cestode infections.

In human intestinal cestodiasis, cure rates as high as 94% for **Hymenolepis nana** and 95% for **Diphyllobothrium latum** have been obtained after single oral doses of 25 mg/kg of PZQ. Furthermore, 100% cure rates with the administration of 10 mg/kg of the compound are usual in **Dyphyllobothrium pacificum** infections as well as in taeniasis due to either **T. saginata** or **T. solium**[5]

Cysticercosis is caused by infections with the larval stages of the porcine tapeworm, **T. solium.** It is believed that ingestion of food contaminated with ova, is the most common mechanism of infection. Once ingested, eggs hatch in the small bowell, burrow into the venules and travel to distal sites, usually subcutaneous tissue, muscles and brain (parenchyma, sub-aracnoid space or ventricular system), where they develop into mature larvae or cysticerci after few months.

The clinical manifestations of CNS cysticercosis depend on the location, pathological process produced by the parasite, patient's inflammatory response to larvae, and alterations of CSF dynamics. Parenchymal lesions have the tendency to cause seizures, visual tract damage, hemiparesis and cranial nerves involvement. Diffuse parenchymal cysts often result in acute cerebral edema with intracranial hypertension, visual impairment, and mental changes. Meningeal locations produce an aseptic, chronic meningites syndrome; while cysts obstructing the fourth ventricle may cause severe headache, vertigo, vomiting and flaccid quadriplegia following sudden head movements, which is known as Burn's Syndrome[3, 7].

PZQ, at a dose of 50 mg/kg per day for 14 days, permits the treatment of most cases with intraparenchymal cysts and to a lesser degree,

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of those with chronic meningitis due to basal arachnoiditis. The drug has not proved effective in the treatment of intraventricular cysts[8, 9].

When given in single doses, PZQ is well tolerated, with frequent though usually mild and reversible side effects, such as abdominal pain (17 to 54%), malaise (0.3 to 14%), diarrhea (10 to 25%), fever (11 to 21%) and headache (6 to 17%)[5].

We report herein, the case of a young man in whom the administration of PZQ at a low single dose for the treatment of an intestinal infection by **H. nana**, triggered the occurrence of repeated episodes of seizures. A thorough clinical evaluation showed that he was suffering from an until that moment asymptomatic brain cysticercosis.

CASE REPORT

A 27 year old male accountant had been in study at the Gastroenterology Service, because of left flank tenderness over a period of one year. Clinical and laboratorial evaluations revealed only a mild eosinophilia of 7% and the presence of **Hymenolepis nana** ova in the stools. He was given 20 mg/kg of PZQ as a single oral dose. Six hour later, he noticed spontaneous toni-clonic movements of the right hand during 10-15 minutes, followed by tonic contracture of the right upper limb lasting 15 seconds approximately. Afterwards, he complained of severe diffuse headache and had a generalized seizure. The following week, he suffered from similar convulsive episodes, on the account of which he was evaluated at the Neurology Service of the same hospital. A brain CAT scan revealed two cystic lesions, 1 2 cm in diameter with ring enhancement and mild surrounding edema on the left parietal cortex (Figure 1). The EEG showed a normal pattern without epileptiform activity. A spinal tap failed to reveal any CSF abnormality. A new hematology revealed an eosinophils count of 11%. A complement fixation (Weimberg's) test performed on the CSF was negative.

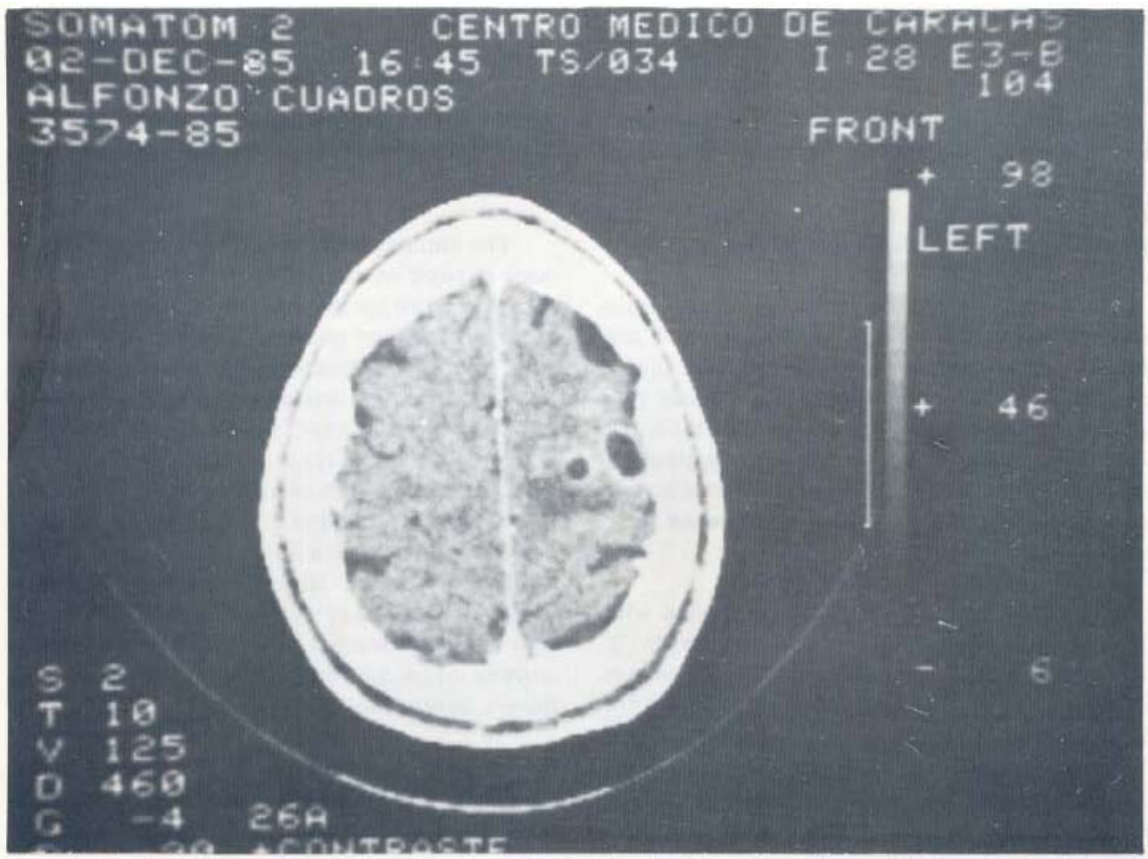

Figure 1 — Brain CAT scan the patient showing two left parietal, cortical, hypodense lesions, 1 to 2 cm in diameter, with mild surrounding edema and ring enhancement after contrast administration.

He was given a 14 days course of 50 mg/kg per day of PZQ orally, in three divided doses, plus 20 mg/day of prednisone. He continued to take 300 mg per day of diphenilhydantoin and 100 mg/day of phenobarbital also.

A new spinal tap, performed after completing treatment with PZQ, revealed a positive complement fixation test for cysticercosis in the CSF at a titer of 1:2. CAT scan films taken two months later did not show any residual lesions.

The patient was discharged on phenobarbital treatment and had remained asymptomatic after 1 year of follow up.

Worldwide, cysticercosis is regarded as the most common parasitic infection of the CNS. It is particularly common in Mexico and other parts of Central and South America, Africa, India, China, Eastern Europe, and Indonesia.

In general, cysticercosis affects communities in which hygienic conditions are poor, although it is occasionally found in middle and upper class inhabitants of urban areas.

Neurocysticercosis may represent a mayor public health problem in some developing regions, where general autopsy series place its prevalence as high as 3.5%, whereas 25% of all intracranial masses recorded at necropsy are due to cysticercosis[1].

The CNS is involved in 60-96% of those with cysticercosis. Less than 20% have solitary cysts and over 200 cysts have been found in some brains. Cerebral involvement may be asymptomatic for long periods. The average interval from initial infection to onset of symptoms is approximately 5 years, with a range from a few months to 30 years[3, 6]. Between 53 to 59% of patients with neurocysticercosis have epilepsy and it is the sole manifestation in 18 to 34%. Focal seizures have been reported in up to 75% of patients[3, 6].

In epileptic patients, the CAT scan is far more useful than serology in stablishing the diagnosis. Lesions suggestive of cysticercosis (multiple calcifications or multiple cystic lesions), are seen in 71.4% of epileptic patients who have CAT scans. On the other hand, only 42.1% of those with meningitis show other neurological manifestation. There appears to be a trend toward decreased frequency and severity of seizures in epileptic patients, even without treatment, after six months of observation[1, 3, 6].

PZQ is well tolerated by humans, and there seems to be no long-term toxicity. The drug is rapidly absorbed after oral administration, and it is excreted with its metabolites through the kidney. Serum concentrations of 1 mcg/ml of the drug are obtained after single oral administration of 50 mg/kg. Half life averages 4 to 5 hours. Once in the blood, 76% of the PZQ is reversibly bound to serum proteins, disappearing rapidly from the intramuscular space as it is concentrated into various tissues. PZQ penetrates blood-brain barrier, reaching CSF concentrations, of 15-20% of those reached in serum[2].

Fever, headache, nausea, vomiting, meningismus, seizures, and increased intracranial pressure are associated with PZQ therapy, suggesting the destruction of cysts and a resulting inflammatory response. Administration of corticosteroids lessens these symptoms but there are not clear guidelines for use of steroids in such conditions[4, 7, 8].

On the other hand, tolerance studies of PZQ in human volunteers did not reveal any relevant abnormality in hematological tests, urinalysis, EKG and EEG, as well as in physical or psychological examination or neurological tests. At the high dose of 75 mg/kg/day, some volunteers complained of mild fatigue, malaise and nausea. However, intense nausea, vomiting, severe gastritis and sinus tachicardia with a heart rate above 140 beats per minute has been reported by us in a patient receiving 40 mg/kg/day of PZQ in six divided doses[2, 10].

RESUMEN

Convulsiones en un individuo tratado con Praziquantel

Un paciente de sexo masculino de 27 años de edad desarrolló convulsiones luego de recibir una dosis única de 20 mg/kg de praziquantel para el tratamiento de una infección intestinal por **Hymenolepis nana.** Ulteriores evaluaciones clínicas y de laboratorio mostraron que el pa-

ciente sufría de una hasta ese momento asintomática cisticercosis del parenquima cerebral. Praziquantel debe ser utilizado con precaución en aquellas areas en las cuales la cisticercosis representa un problema importante de salud pública. La ocurrencia de convulsiones inesperadas en un individuo que este siendo tratado con el compuesto, hace necesario la exclusión de cisticercosis del SNC.

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