Acknowledgment

We thank Lawrence Crapo, MD, Tom Kelsey, MD, Robert Archibald, MD, John Hamilton, MD, and Ramona Desai, MD, for their support and advice in the production of this report.

REFERENCES


High-Dose Praziquantel With Cimetidine for Refractory Neurocysticercosis: A Case Report With Clinical and MRI Follow-Up

THOMAS YEE, DO
Stanford, California

JEROME A. BARAKOS, MD
San Francisco, California

ROBERT T. KNIGHT, MD
Davis, California

NEUROCYSTICERCOSIS is an infection of the central nervous system by the larval forms, or cysticerci, of Taenia solium, the pork tapeworm,1 which is prevalent primarily in the rural areas of Latin America, Asia, and Africa.2–5 The number of cases of neurocysticercosis diagnosed in the United States is rising as a result of the increasing number of immigrants from endemic areas.6


because the condition may spontaneously resolve without antihelminthic therapy.9–10 Most clinicians, however, recommend treating active neurocysticercosis with antihelminthic agents,11–16 using either praziquantel (50 mg/kg/d)15–21 or albendazole (15 mg/kg/d).11,15,18,22–24 Praziquantel was the first agent used in the United States and is usually the first drug prescribed for this condition. If a patient does not respond to praziquantel, either a repeat course of praziquantel17,25 or a trial of albendazole1,15,18,22–24 is recommended. No consensus has been reached, however, as to the next course of treatment for patients unresponsive to the standard regimens of praziquantel and albendazole.

Several case reports25 suggest the use of high-dose praziquantel (100 mg/kg/d) in treating refractory neurocysticercosis. We report a case of neurocysticercosis in which a patient failed to respond to conventional treatments but improved after treatment with high-dose praziquantel. This improvement was assessed during follow-up, using clinical observation, brain magnetic resonance imaging (MRI), and cerebrospinal fluid (CSF) studies.

Report of a Case

A 36-year-old Hispanic man presented in 1990 with a headache secondary to neurocysticercosis. Brain MRI revealed multiple parenchymal cysts and calcifications, and CSF studies demonstrated findings consistent with neurocysticercosis. The patient was treated with praziquantel (50 mg/kg/d) and corticosteroids for 15 days, which resulted in the subsequent resolution of his headache. Three months after treatment, a repeat brain MRI showed a reduction in the size of the parenchymal cysts.

In 1993, the patient had a recurrence of headache with diplopia and vertigo. A brain MRI revealed new parenchymal cystic lesions, and CSF studies, using the enzyme-link immunosorbent assay, detected the presence of antiglycercerical antibodies. The patient was again treated with praziquantel (50 mg/kg/d), this time without corticosteroids, for 21 days. His symptoms, however, persisted three months after treatment. A repeat brain MRI did not reveal a significant reduction in the size of the parenchymal cystic lesions, and communicating hydrocephalus was now found. A ventriculoperitoneal shunt was placed, and some of the patient’s symptoms subsequently improved, although his headache persisted. One year later, a follow-up brain scan showed new parenchymal cystic lesions with normal-sized ventricles. As a result, he was placed on a 30-day regimen of albendazole (15 mg/kg/d) without corticosteroids. This treatment was discontinued after 28 days, owing to a sudden onset of left hemiareness and hemi-anesthesia associated with slurred speech and dysphagia. The patient was subsequently started on dexamethasone (12 mg/d), and these symptoms improved gradually over 4 to 7 days. A brain MRI revealed new parenchymal cystic lesions, hydrocephalus, an increase in basilar leptomeningeal disease, and evidence of subcortical infarcts in the lenticulostrate arterial distribution (Figures 1 and 2).
Three months after albendazole treatment, such symptoms as headache, mild dysphagia and left-hand weakness persisted. A repeat brain MRI revealed minimal change in the parenchymal cystic lesions and basilar leptomeningeal disease. The patient was started on a 21-day regimen of high-dose praziquantel (100 mg/kg/d) with aspirin (325 mg/d), cimetidine (800 mg/d), and dexamethasone (12 mg/d). Dexamethasone was tapered off over 2 months. The patient tolerated the treatment well, without any complications. Three months after treatment, his headache had improved greatly. A brain MRI showed that both the mesial temporal parenchymal cystic lesions and basilar leptomeningeal disease had improved. CSF studies demonstrated an increased glucose level, a decreased protein level, and a lowered white blood cell count after high-dose praziquantel treatment (Table 1).

At follow-up, 18 months after treatment, the patient continued to do well clinically. A brain MRI demonstrated further improvement in the parenchymal cystic lesions and a marked reduction in the basilar leptomeningeal disease (Figure 3).

### Discussion

Praziquantel is generally the first agent employed in the treatment of neurocysticercosis, with dosages varying from 5 to 75 mg/kg/d. Most authorities recommend a dose of 50 mg/kg/d for 15 or 21 days. If a patient fails to respond to an initial course of praziquantel, the literature suggests either a repeat course or a trial of albendazole at 15 mg/kg/d for 8 or 30 days. Albendazole has proven as effective as, if not superior to, praziquantel in the treatment of neurocysticercosis. There is very little data in the literature, however, indicating the next course of treatment for refractory neurocysticercosis in the event that these standard treatments fail.

### Table 1.—Cerebrospinal Fluid Profile Before and After High-Dose Praziquantel Treatment

<table>
<thead>
<tr>
<th>Time</th>
<th>Glucose (45-80 mg/d)</th>
<th>Protein (15-45 mg/d)</th>
<th>WBC (&lt;6 mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Three days before</td>
<td>47</td>
<td>143</td>
<td>62</td>
</tr>
<tr>
<td>Five days after</td>
<td>53</td>
<td>115</td>
<td>40</td>
</tr>
<tr>
<td>Three months after</td>
<td>57</td>
<td>87</td>
<td>48</td>
</tr>
<tr>
<td>WBC = white blood cell</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1.—Post-contrast enhanced T1-weighted images (TR = 500, TE = 30 mseconds) taken prior to high-dose praziquantel treatment reveal mild hydrocephalus evidenced by enlargement of the temporal horn (arrowhead). Extensive leptomeningeal enhancement is noted within the basilar cisterns (black arrows). Two intraparenchymal cysts are evident in the right mesial temporal region (white arrows).

Figure 2.—Post-contrast enhanced T1-weighted images (TR = 500, TE = 30 mseconds) obtained one day after the onset of stroke symptoms reveal two contrast enhancing lesions within the right corpus striatum. These lesions are secondary to ischemia in the territory of the lenticulostrate branches.
Although our patient is a resident of California, he had traveled to the rural areas of Mexico in the past. His travel history after his initial treatment for neurocysticercosis in 1990 was unclear. The stool specimens of both the patient and his family members tested negative for tapeworm infection. Thus, the patient’s recurrence of neurocysticercosis could have resulted from repeated visits to an endemic area. Recurrent neurocysticercosis has been observed, however, in patients without any travel history to endemic areas,17 which suggests that there may be sequestration of the larval forms in an unidentified location. During his recurrence of neurocysticercosis, the patient failed to respond to either a repeat course of standard praziquantel therapy or an additional course of albendazole. In addition, he had a lacunar stroke involving the territory of the lenticulostrate branches during one of these antihelminthic treatments (Figure 2).

Ischemic cerebrovascular disease has been reported as a complication in untreated neurocysticercosis patients and in patients receiving anticysterceral drugs.36-39 In most cases, the stroke involves vessels of small diameter in the territory of the lenticulostrate branches of the anterior or middle cerebral artery and results in a lacunar syndrome.36 A cerebral infarct is caused by occlusive endarteritis secondary to the intense inflammatory reaction triggered within the subarachnoid space by meningeal cysticerci.36 Anticysticercal drugs may enhance the inflammatory reaction and increase the likelihood of cerebral infarcts.36,37 Because the patient’s stroke during antihelminthic treatment was likely the result of an inflammatory arterial occlusion, he was given dexamethasone, in addition to praziquantel, during the high-dose praziquantel treatment. Furthermore, because plasma levels of praziquantel decrease with concomitant dexamethasone treatment,40 cimetidine, which has been reported to increase the bioavailability of praziquantel, most likely by inhibiting cytochrome P-450 hepatic metabolism, was also included in the regimen.41 Although praziquantel concentrations were not measured in our patient, cimetidine may have played an important role in the success of his treatment by minimizing the variations in plasma concentration that result from extensive first pass metabolism of praziquantel.41 The regimen of high-dose praziquantel, dexamethasone, and cimetidine was well tolerated.

Three months after high-dose praziquantel treatment, a repeat brain MRI showed improvement in the parenchymal cystic lesions and leptomeningeal disease. A follow-up brain MRI at 18 months demonstrated continuing resolution of the parenchymal cysts and a marked reduction of the basilar leptomeningeal disease (Figure 3). Spinal fluid findings also provided evidence of improvement three months after the patient’s treatment with high-dose praziquantel (Table 1). It is unlikely that the improvements evidenced by the brain MRI resulted from prior albendazole treatment. Previous reports have found that in most neurocysticercosis patients who respond to albendazole, lesions disappear on brain MRIs within three to four weeks.42,43 In this case, the patient’s lesions persisted three months after albendazole therapy.

In a report by Bittencourt and colleagues,25 three patients with neurocysticercosis who had previously failed to respond to a standard regimen of praziquantel were subsequently treated with high-dose praziquantel. Although two of these patients died from recurrent shunt complications at 18- and 21-month follow-ups, all three improved initially upon treatment with high-dose praziquantel. Like our patient, they all tolerated high-dose praziquantel. Taken together, the results of Bittencourt and colleagues’ study and the case we are presenting suggest that high-dose praziquantel may be a safe and effective treatment for patients with refractory neurocysticercosis who do not respond to standard regimens of either praziquantel or albendazole. Because the use of antihelminthic agents may lead to cerebral infarction subsequent to angiitis caused by acute inflammatory reaction,35-39 the addition of dexamethasone, with or without cimetidine, may help decrease the risk of untoward vascular events during high-dose praziquantel therapy.

Figure 3.—Post-contrast enhanced T1-weighted images (TR=500, TE=30 mseconds) taken after high-dose praziquantel treatment reveal considerable reduction in the extent of leptomeningeal disease within the basilar cisterns. Hydrocephalus and intraparenchymal cysts have resolved.
Diabetic Ketoacidosis in Pregnancy With a Recent Normal Screening Test

MICHAEL J. O’SHAUGHNESSY, MD
KELLI R. BEINGESSER, MD
WILLIAM U. KHIU, MD
San Francisco, California

KETOACIDOSIS IS A RARE COMPLICATION of diabetic pregnancies. It occurred at a rate of 1.73% in a recent series of pregnancies with preexisting, insulin-dependent diabetes.1 Ketoacidosis is an extremely rare complication of gestational diabetes, as well.2–3 In addition, ketoacidosis has been reported in two patients with previously undiagnosed diabetes.4–5 We report a case of early diabetic ketoacidosis involving a patient who had had a normal glucose tolerance test (GTT) only 10 days before presentation.

Case Report

A previously healthy, 23-year-old, gravida II, para I, Asian woman arrived at the obstetrical service in her 36th-week of pregnancy, complaining of contractions every three minutes and decreased fetal movement. The patient also admitted to polyuria and polydipsia. She denied nausea, vomiting, fever and chills. She had no signs or symptoms of genitourinary, respiratory, or gastrointestinal infectious processes. Her past medical history was unremarkable. Her past obstetrical history was unremarkable.

From the University Medical Center, University of California, San Francisco Fresno-Central San Joaquin Valley Medical Education Program, Fresno, California. Reprint requests to Michael J. O’Shaughnessy, MD, University of California, San Francisco Fresno-Central San Joaquin Valley Medical Education Program, 445 South Cedar Avenue, Fresno, CA 93702.