Albendazole and praziquantel treatment in neurocysticercosis of the fourth ventricle

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The purpose of this study was to determine the therapeutic efficacy of albendazole and praziquantel administration in the treatment of neurocysticercosis of the fourth ventricle. The authors report the results obtained in 10 patients with cystic neurocysticercosis of the fourth ventricle who were treated with albendazole at a dosage of 15 mg/kg/day for 2 weeks. Because of the failure of albendazole treatment, two of the patients received an additional course of praziquantel at a dosage of 100 mg/kg/day for 2 weeks. A total of 16 courses of albendazole and two courses of praziquantel were administered to the 10 patients. In seven patients (70%), there was complete disappearance of the cyst, in two others (20%) there was an important decrease in the size of the cyst, and in one (10%), no change was seen. None of the patients had complications during the follow-up period of between 6 and 26 months (average 15.7 months). The authors postulate that a regimen of albendazole is the treatment of choice for this type of neurocysticercosis, although praziquantel may also be useful.

Key Words * cysticercosis * neurocysticercosis * albendazole * praziquantel * fourth ventricle

Neurocysticercosis is caused by an infestation of the larval stage of *Taenia solium*.^[16] It is the most frequent parasitosis of the central nervous system (CNS) worldwide. An estimated 50,000,000 people are infected, and approximately 50,000 die annually of this disease.^[20] It is prevalent in developing countries^[17] and its incidence is on the rise.^[22] The costs of treating neurocysticercosis are high, and it is an important public health problem in countries in Asia, Africa, and Latin America.^[3,4] It is also the primary cause of epilepsy in endemic countries.^[23]

The fourth ventricle is the most frequent site of parasitic invasion in intraventricular neurocysticercosis, probably due to the effect of gravitational forces that favor migration of the cysts from superior cavities to the inferior ones. This results in entrapment in this cavity because of the reduced size of the foraminae of Lushcka and Magendie.^[15]

Surgery is currently considered the therapeutic procedure of choice for intraventricular neurocysticercosis,^[5,13,14] including the form located in the fourth ventricle. However, isolated reports of patients with parasites in this location that have been successfully treated by a regimen of praziquantel

or albendazole have raised some controversy.[1,7,11] The latter is the drug of choice for the treatment of the cerebral parenchymatous type of neurocysticercosis and has an efficacy rate of 85% after one course.[21] Multiple studies corroborate an approximate efficacy rate of 60% [8] for praziquantel. There are only two isolated reports of the disappearance of a cyst located in the fourth ventricle after treatment with praziquantel. However, the usefulness of albendazole treatment in neurocysticercosis of the fourth ventricle remains unknown. We report our experience with the use of this drug in the treatment of cystic neurocysticercosis of the fourth ventricle.

CLINICAL MATERIAL AND METHODS

The current study was designed to comply with the rules of the Helsinki Declaration and was approved by the hospital ethics committee. Before entry into the study, patients received detailed information about the surgical procedures available for this type of cysticercosis. All patients signed an informed consent letter.

Summary of Patient Characteristics and Treatment

The group of 10 patients consisted of six women and four men aged 27 to 61 years (average 39.1 years). In six patients, the initial symptomatology was that of acute hydrocephalus requiring immediate ventriculoperitoneal (VP) shunting, which resulted in complete remission of their symptomatology. Three patients suffered seizures: one had generalized seizures caused by the coexistence of cysts in both brain hemispheres and the other two had partial seizures caused by the coexistence of cysts in cerebral parenchyma in one, and a 15-year history of epilepsy caused by a left parietal calcification in the other. The latter patient underwent CT scanning because of poor control of the complex partial seizures, which showed dilation of the fourth ventricle. The remaining patient in this group experienced occasional dizziness. Two patients had previously undergone surgical cyst removal from the fourth ventricle, one of them twice. One patient had Bruns' syndrome[6] and later developed acute confusional status. This patient had a generalized headache for 3 days, after which he developed vertical diplopia in the downward gaze as well as changes in his eye movements, with bilateral saccadic pursuit, spontaneous third-degree nystagmus on the right side, bilateral abnormal optokinetic reflex, and optovestibular reflex with asymmetry to the right side.

Ten patients with neurocysticercosis of the fourth ventricle were prospectively studied. The neurocysticercosis was diagnosed by computerized tomography (CT) scanning and magnetic resonance (MR) imaging of the brain. All patients underwent cerebrospinal fluid (CSF) cytochemical tests and enzyme-linked immunosorbent assays for the determination of anticysticercal antibodies in both CSF and serum.

Six patients developed hydrocephalus before the cestocidal treatment was administered, and each received a VP shunt; two of them required shunt revision due to dysfunction; one of them required a second revision.

All 10 patients received an initial course of 15 mg/kg/day albendazole for 2 weeks; six patients also received a second identical course of albendazole. Two patients did not respond to albendazole and were given one course of 50 mg/kg/day praziquantel for 2 weeks: one of them after the first course of albendazole and the other after the second course.

Six patients who developed adverse effects from the albendazole treatment were given corticosteroids between Days 3 and 4 of the first cestocidal treatment. Two patients received 8 mg/kg dexamethasone

intravenously, which was reduced to 4 mg/kg at Day 7 and progressively tapered thereafter. Prednisone was later substituted for dexamethasone, which was also gradually reduced. The other four patients received 0.5 mg/kg/day of prednisone with the same tapering scheme. Three of these patients also required prednisone during the second cestocidal treatment. Finally, one patient received steroids only during the second cycle of treatment with albendazole; he did not develop adverse effects during the first cycle of the drug.

Laboratory Tests and Imaging Studies

The CSF was examined in all patients before treatment; in four cases, inflammation was found with pleocytosis from 19 to 29 cells and protein levels from 90 to 100 mg/dl. Enzyme-linked immunosorbent assay demonstrated that all patients had anticysticercal antibodies in their CSF sample and also in the serum of seven patients.[10] Computerized tomography scanning showed a rounded and enlarged fourth ventricle in all cases. Magnetic resonance imaging demonstrated the presence of cysts inside the cavity in all patients. In three patients there was additional abnormal enhancement after administration of gadolinium contrast material, which suggested endyemitis. Magnetic resonance imaging in five patients showed additional cysts in other locations or basal arachnoiditis.

The follow-up period ranged from 6 to 26 months (average 15.7 months). Clinical evaluations were performed monthly. Magnetic resonance imaging was obtained every 3 months (a total of two times), except in one patient in whom three MR images were obtained. The response to treatment was considered good when MR studies demonstrated disappearance of the cyst or a decrease in its size together with clinical improvement. Treatment was considered a failure when the MR studies revealed no change with respect to posttreatment images, regardless of an apparently stable symptomatology.

RESULTS

Clinical Manifestations

Nine of the 10 patients experienced improvement in their symptoms after treatment. Bruns' syndrome and the acute confusional state disappeared in patient one; however, diplopia persisted during the entire follow-up period (26 months) although it did not disable the patient and he was able to return to his normal activities. In the three patients with epilepsy, seizures were controlled with antiepileptic drugs: two received phenytoin 300 mg per day and the other carbamazepine 800 mg per day. The patient who did not respond to the treatment continued to experience dizziness; however, this did not interfere with her normal activities. She underwent exploratory endoscopic surgery of the fourth ventricle that showed ventricular entrapment secondary to endyemitis, but there was no cysticercal vesicle. None of the patients in whom a VP shunt was placed showed any sign of dysfunction after treatment. No relapse or reinfection has been documented to date.

Fig. 1. Magnetic resonance T₁-weighted images, sagittal views. Upper: The arrow shows a cellulose-type cysticercal cyst with a vesicle and scolex inside. Lower: The arrow shows a large, lobulated cysticercal racemose cyst without scolex.

Magnetic Resonance Follow-Up Studies

Magnetic resonance imaging revealed that five patients had cellulose cysts (Fig. 1 upper) and five had racemose cysts (Fig. 1 lower). The three patients whose cysts disappeared after the first course of treatment had cellulose cysts, and the only patient who did not respond to treatment had a cystic racemose image with an abnormal perilesional enhancement that suggested ependymitis (Fig. 2).

Fig. 2. Magnetic resonance T_1 -weighted images, axial views. Upper: The arrow shows a dilated fourth ventricle and a cyst without an interior scolex; there is annular reinforcement with the contrast medium (gadolinium). Lower: After two treatments with albendazole and one with praziquantel, the image is unchanged.

The first cycle of albendazole induced cyst disappearance in three patients and a reduction in size in five. After the second treatment cycle of albendazole, the cysts disappeared in four of the five patients in whom there was already an initial reduction in size after the first cycle (Fig. 3).

Fig. 3. Magnetic resonance T_1 -weighted images, sagittal views. Upper: The arrows point to racemose cysticercal cysts that dilate and deform the fourth ventricle prior to treatment. Lower: The arrows point to the disappearance of the parasites after two cycles of albendazole.

The remaining patient showed an additional decrease in cyst size. One of the patients in whom no response was obtained to the first cycle of treatment with albendazole showed disappearance of the cysts after treatment with praziquantel. Finally, a patient who received two cycles of albendazole and one of praziquantel showed no change on MR imaging (Table 1).

Case No.	Status of Cysts Posttreatment			Side Effects	Surgery Posttreatment	Follow up (mos)/ Complications
	1st Treatment	2nd Treatment	3rd Treatment			
1	disappearance alb/dex			none	no	26/none
2	80% decrease alb/dex	disappearance alb/pdn		headache	no	25/none
3	90% decrease alb/pdn	disappearance alb/pdn		none	no	24/none
4	90% decrease alb	95% decrease alb/pdn		headache	no	16/none
5	no change alb/pdn	disappearance prz/pdn		headache	no	16/none
6	no change alb	no changes alb	no changes prz	none	yes	16/none
7	disappearance alb/pdn			none	no	12/none
8	90% decrease alb	disappearance alb		none	no	10/none
9	disappearance alb/pdn			headache & partial seizures	no	6/none
10	80% decrease alb	disappearance alb		none	no	6/none
* alb = albendazole; dex = dexamethasone; prz = praziquantel; pdn = prednisone.						

Secondary Effects

Six patients experienced no side effects during treatment; four patients experienced headaches. One of these four patients showed no side effects during the initial treatment cycle, but complained of headaches during the second cycle. Headaches were satisfactorily treated with regular analgesic and corticosteroid medications. One patient transiently lost the control of his seizures and was given a course of corticosteroid agents with an increase in the dose of antipileptic drugs (Table 1).

DISCUSSION

Surgical removal of cysts of the fourth ventricle has been considered the treatment of choice for neurocysticercosis.[14,15] Surgery should be performed as soon as the diagnosis has been established to avoid death due to an acute complication. Surgical removal of the cyst also prevents chronic complications such as ependymitis with ventricular entrapment.[2] Surgical treatment has been used despite knowledge of the efficacy of praziquantel treatment since 1979[18] and albendazole treatment since 1987[9] in other forms of neurocysticercosis. In a series reported by Robles, et al.,[19] they described a follow-up period of more than 5 years in 141 patients treated with praziquantel, five of whom had cysticerci within the fourth ventricle. In that study, parasites located in the fourth ventricle were not affected by this drug, apparently because of its low concentration in CSF. Thus, the authors recommended surgery as the treatment of choice for cysticercosis of the fourth ventricle. This recommendation was not adequately supported, however, because they did not mention the levels of the drug in CSF. In addition, only one cycle of treatment was used and the authors made no reference to whether the cysts were of the cellulose or racemose type.

Important morbidity and mortality risk rates have been documented in surgical series of neurocysticercosis of the fourth ventricle. In one series, there was a 14.8% morbidity rate,[12] and in another series, the mortality rate was 26.3%.[12] These poor results were attributed to inflammatory changes, which made surgical handling of these cases difficult. In recent years, important advances in anesthetic procedures and surgical techniques for examining the fourth ventricle have been developed in concert with the possibility of exploration of this cavity with the flexible ventriculoscope to decrease the rate of complications.

The first case of subarachnoid and intraventricular cysticercosis treated with chemotherapy was reported in 1990. The cyst was located in the left lateral ventricle and was successfully treated with albendazole and corticosteroids.[7] In 1991, two more cases were published describing cysticercosis of the fourth ventricle treated with VP shunt placement and praziquantel treatment. In one case, the cyst disappeared, leaving a calcification,[11] and in the second, it decreased in size.[1] No adverse effects were reported in any of the three cases mentioned, and the patients improved. The results led us to believe that the cestocidal drugs were useful in the treatment of intraventricular forms of neurocysticercosis.

Our findings indicate that the cestocidal treatment was efficacious in 90% of the patients. Albendazole was the drug treatment used initially, and its efficacy rate was 80%: in seven patients the cysts disappeared and the remaining patient showed a 95% decrease in cyst size. In one case, despite the fact that the cysts had a racemose appearance and that no changes were seen after the administration of one cycle of albendazole, the cysts disappeared with an additional course of praziquantel. In those patients who received praziquantel, the dose was 100 mg/kg/day, concomitantly administered with prednisone, twice the usual dose for parenchymatous neurocysticercosis. The CSF levels were well within therapeutic range. In four of the 10 patients, there was no need for VP shunt placement before treatment or during the follow-up period. Surgical procedures in the posterior fossa were thus avoided in nine of the 10 cases. The patient in whom no response was obtained underwent ventriculoscopy, which revealed ependymitis with ventricular entrapment. In this patient, the MR imaging did not allow for differentiation between the racemose cyst and the ventricular entrapment, explaining the failure of the cestocidal treatment. The image showed a large oval "cyst," without a nodule occupying the entire ventricular cavity. Contrast medium was administered and the result suggested the possibility of concomitant ependymitis.

The involution of the parasites and the absence of adverse effects indicate that treatment with albendazole and praziquantel is an efficacious, safe, and well-tolerated therapeutic approach. The need for administering steroid agents concomitant with the cestocidal drug in this type of neurocysticercosis should be considered individually and should not to be administered unless side effects are observed.

Our experience suggests that albendazole is the treatment of choice in patients with uncomplicated neurocysticercosis of the fourth ventricle without hydrocephalus. In patients with hydrocephalus, the placement of a VP shunt must be considered before treatment. In patients in whom a VP shunt has already been placed, a very high CSF density with hyperproteinorrachia yields an increased risk of shunt dysfunction; this can be reduced with a cycle of steroid medication prior to the administration of cestocidal drugs or by the selection of surgery as a first choice of treatment.

The risk of inflammatory complications is negligible, even when other types of neurocysticercosis are involved, as in our cases in which parenchymatous or subarachnoid cysts were found. It is very likely that albendazole will be useful in the treatment of intraventricular neurocysticercosis at other levels; its potential efficacy in cysts of the superior cavities of the ventricular system may mitigate the risk of

migration and relapse after the surgical removal of the cyst from the fourth ventricle, as seen in two of our cases. Our findings are in accord with those of Del Brutto, et al.,[7] in this regard. We believe albendazole treatment should be considered the method of choice when a patient experiences a relapse of cysts within the fourth ventricle that have been previously surgically removed. We also advocate assessing its potential use in the treatment of intraventricular neurocysticercosis at other levels. We should continue to define the concomitant use of steroid agents and to compare this treatment with surgical procedures in terms of efficacy, adverse effects, complications, and probability of relapses.

CONCLUSIONS

The results of this study show that: albendazole is the treatment of choice in cases of neurocysticercosis of the fourth ventricle; it reduces the frequency of surgical procedures of the posterior fossa; it decreases the need for VP shunt placement; it is a well-tolerated treatment with very few secondary effects; the treatment shows no medium-term complications; praziquantel constitutes an alternative treatment for this type of cysticercosis and; the MR imaging does not adequately differentiate between cysts and ependymitis with ventricular entrapment.

Surgical procedures and their potential complications can be avoided in a large group of patients who suffer from a condition that previously was considered an absolute indication for surgery.

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