

ORIGINAL ARTICLE

The role of mebendazole in the surgical treatment of central nervous system hydatid disease

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Abstract

Although hydatid disease is the most common human disease caused by helminths, cerebral and spinal involvement in hydatid disease is rare. Recurrence is common when cysts rupture during surgical removal. The authors present the results of combined treatment with surgery and mebendazole in four cerebral and five spinal cases of hydatid disease. The patients' ages ranged between 4 and 55 years with a mean of 26 years. In three of the four cranial patients who received mebendazole treatment, the cysts ruptured during surgical removal. Four of the five spinal cases had recurrent disease at the time of admission. Mebendazole was started immediately after surgery and continued over 12 months. All cases but one are stable clinically or radiologically at a mean 27 months follow-up period.

Key words: *Central nervous system, hydatid disease, mebendazole*

Introduction

Echinococcosis or hydatid disease is caused by larvae of *Echinococcus granulosus* and related species, which are small tapeworms found primarily in dogs. The intermediate host is sheep. Infection of humans results from ingestion of the ova usually from close contact with dogs. The larval cysts develop primarily in the liver and lungs, and only rarely involve the central nervous system, with an incidence of 1-2%. The cysts may grow to a large size. The cyst wall is thick, acellular and has a thin germinal layer. Scolices grow in the cyst within which daughter cysts develop.

The disease is more common endemically where sheep are more common, including South America, the Middle East, some Mediterranean countries, Middle Asia, Australia and East Africa.¹⁻⁵

Rupture of the cyst during surgical removal can lead to serious anaphylactic reactions and dissemination of the disease by the formation of additional cysts from further development of protoscolices. Recently, antihelminthic drugs, benzoimidazole carbamate derivatives (albendazole and mebendazole) have been tried in hydatid disease, with and without surgery.⁶⁻⁸ There have been few publications dealing with these medications in central nervous system hydatid disease.

In our department, we have combined surgery with mebendazole secondary to intraoperative rupture or recurrence in a total of nine cranial and spinal cases.

Materials and methods

In Istanbul University, Cerrahpaşa Medical School, Department of Neurosurgery, nine cases of cranial or spinal hydatid disease were treated between 1990 and 1995 with surgery and mebendazole. Clinical and radiological records, mebendazole treatment protocol, operative findings and postoperative complications, and follow-up of nine cases are included here. The mean follow-up period is 27 months.

Results

There were five spinal and four cranial cases of hydatid disease which were treated with mebendazole after surgical removal. Patient's age ranged between 4 and 55 with a mean of 26 years. Six patients had positive serological testing. The ELISA screening method was used in five patients and was positive in three cases only.

TABLE I. Age and sex distribution, initial complaints, neurological and radiological findings and previous surgical procedure of these patients with CNS hydatid disease

Case no.	age/sex (year)	Complaints	Neurological findings	Radiological findings	Previous operations
1	8/M	Right weakness, vomiting	Signs of increased ICP, right hemiparesis, long tract findings	Right frontoparietal cyst compressing lateral ventricle on CT	
2	4/M	Macrocrania, ataxia	Increased ICP, cerebellar signs	Large posterior fossa cyst causing hydrocephalus on CT and MRI	
3	45/M	Epilepsy, headache, vomiting		Right parietal cyst on CT	
4	16/F	Epilepsy, left weakness, stupor	Signs of increased ICP, left hemiparesis	Huge right parietal cyst causing unilateral hydrocephalus and compressing right lateral ventricle on CT	Hydatid disease in the liver
5	24/M	Impairment of leg movements, urinary incontinence, low back pain	Bilateral foot drop, cauda equina syndrome	Multiple lytic lesion in posterior part of L4, L5 vertebral body with spreading of the cysts into the spinal canal on CT	Cysts excision with L4–L5 laminectomy 3 years earlier
6	52/M	Back pain, weakness of legs movements	Paraparesis, sensory loss below L1	Multiple extradural cyst in the canal at Th12–L1 levels on CT	Cysts excision via a posterior approach at the same levels 2,5 years earlier
7	54/M	Urinary retention, back pain	Sensory loss below Th10	Multiple extradural cyst in the canal at Th8–Th9 levels on CT	Cysts excision via a posterior approach at the same levels 2,5 years earlier
8	10/F	Urinary incontinence, low back pain, weight loss	Gastrocnemius atrophy in the right, bilateral loss of achil reflex	Presacrally located mass lesion with septation on sagittal MRI. Axial images shows invagination through the both S2–S3 neural foramina to the extradural space	
9	22/M	Weakness of legs	Bilateral foot drop, cauda equina syndrome	Lytic lesions at sacrum, multiple cyst in the canal at L3–S2 levels, invading soft tissue at this levels on CT	Cysts excision via L4–L5 laminectomy 4 years earlier

Abbreviations: M = male; F = female.

The youngest patient was a 4-year-old male child with the radiological findings of a posterior fossa cyst. He had macrocrania and ataxia. In the remaining cranial cases, the presenting symptoms were usually due to increased intracranial pressure and in the spinal cases were pain, sensory and motor deficits related to spinal cord compression. The presenting complaints, neurological and radiological findings are summarized in Table I. CT showed hypodense cystic lesions in all cranial cases. In case 2, a posterior fossa cyst causing hydrocephalus resembled all other

cystic lesions of the posterior fossa apart from hydatid disease (Fig. 1). In Case number 8, CT and MRI showed an anterior sacral cystic mass with septations (Fig. 2). Myelography showed no connection of the lesion with the dural sac. At first we thought it might be an anterior sacral meningocele, but positive serology identified it as a hydatid cyst. In the remaining spinal cases, CT findings were of multiple cystic lesions with septation, causing destruction in vertebral bone tissue, invading the canal and compressing the dural sac (Fig. 3).

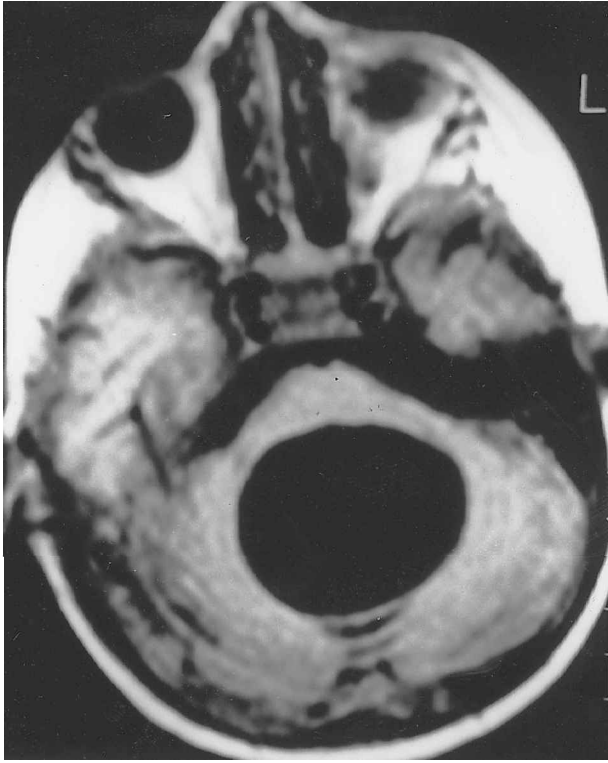


FIG. 1. Unenhanced T1-weighted axial magnetic resonance imaging scan of case 2 show a large hypointense posterior fossa cystic lesion. The brain stem and fourth ventricle were compressed.

The operative techniques, complications and results of follow-up are summarized in Table II. In all cranial cases, resection of the cysts was carried out by the Dowling technique.⁹ In case 2, a ventriculo-peritoneal shunt was performed, succeeded by a posterior fossa craniectomy approach to deliver the cyst at another session. Four of five spinal cases had had a previous operation for hydatid disease. We approached the pathology in two of these patients transabdominally and in another patient, we combined posterior and anterior approaches. In all cases, the diagnosis were confirmed histopathologically.

All nine cases received 10–20 mg/kg/day (three times a day) mebendazole treatment after the operative removal and this continued over 12 months, with 1 month discontinuation of drug after each 3-month period. No side-effects were seen.

All cases are stable clinically or radiologically except one at the end of a mean 27-month follow-up period. Case number 2 showed normal psychomotor development although he has severe enlargement of the 4th ventricle and hydrocephalus. Case number 8 is asymptomatic without any complaints at the end of 4 years, still being followed-up. Neurological findings are still present and there is radiological evidence of recurrence in patient 9, 3 years after the second operation. However, in the remaining cases

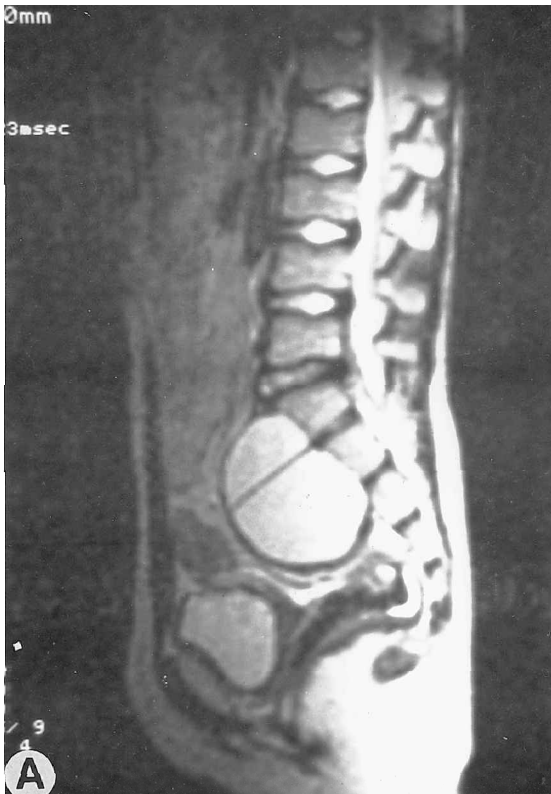


FIG. 2. Unenhanced sagittal and coronal magnetic resonance imaging scans show a presacrally located cystic lesion (case 8). The lesion appeared hypointense on (A) T1-weighted and on (B) T2-weighted images.

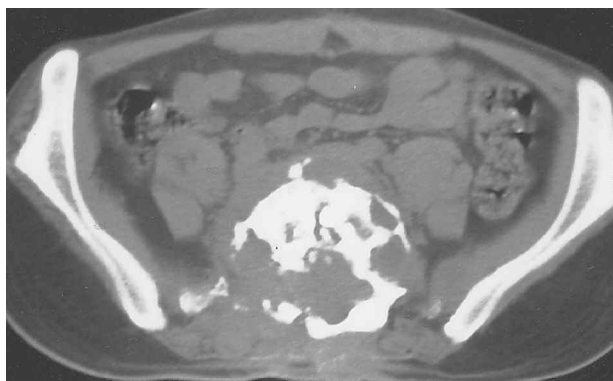


FIG. 3. Axial CT scan at the S1 level showing hydatid disease of bone causing destruction vertebral bone, invading the canal and compressing the dural sac (case 9).

there were no prominent radiological changes or findings indicating recurrence of the disease. Follow-up results are summarized in Table II.

Discussion

Cerebral and spinal involvement in hydatid disease is rare, 0.5–2%.^{10–13} Although definite treatment consists of surgical excision, recurrence is common.

The recurrence rate reported in the literature is between 20 and 30%.^{12, 14, 15} There are also several methods such as irrigating the cavity with formaldehyde, 5% silver nitrate or hypertonic saline solutions to prevent recurrence.^{9, 16}

During recent years, there have been several reports of benzoimidazole carbamate derivatives (mebendazole and albendazole) in the treatment protocol of hydatid disease combined with surgery and without it.^{7, 17} The use of mebendazole in the treatment of echinococcosis started in 1970s.¹⁸ Even though the mechanism of action is not known exactly, it probably prevents the glucose uptake of the parasite and therefore production of ATP. On the other hand, by attacking the parasite's germinal layer, it causes degeneration of the layer which leads to a disturbance of homeostasis.^{19, 20} When compared with albendazole, mebendazole has a decreased uptake in the intestines, which means that mebendazole treatment is required for longer with higher doses.^{19–21} In our cases, we used mebendazole 10–20 mg/kg/day with alternating 3-month periods.

Mebendazole is not used routinely for intracranial hydatid disease in our department. In three of the

TABLE II. Surgical procedures, complications and results of follow-up

Case no.	Surgery	Complications	Follow-up
1	Craniotomy and cyst extirpation with Dowling technique	Peroperative rupture, subduro-peritoneal shunt because of large subdural effusion	Asymptomatic with antiepileptic treatment. Follow-up period 1,5 year
2	Ventriculo-peritoneal shunt, posterior fossa craniectomy and cyst extirpation	Large 4th. ventricle causing moderate ataxia	Normal psychomotor development 2 years after operation
3	Craniotomy and cyst extirpation with Dowling technique	Peroperative rupture	Normal at the end of 2 years
4	Craniotomy and cyst extirpation with Dowling technique	Peroperative rupture, persistent asymptomatic subdural effusion	Normal at the end of 1.5 years
5	2-stage operation. First, L4, L5 vertebrectomy, iliac bone fusion, second posterior approach and multiple epidural cyst excision	Wound infection, CSF fistula stopping with success if lumbar puncture	Paraparesis, bilateral foot drop, walk with a cane. No evidence of hydatid disease on CT 3 years after
6	Multiple epidural cyst excision via a posterior approach		Urinary incontinence, difficulty in walking. No evidence of hydatid disease recurrence on CT at the end of 3 years
7	Multiple epidural cyst excision via a posterior approach		Normal at the end of 2 years
8	Transabdominal, retroperitoneal hydatid cyst en bloc excision		No recurrence detected on MRI 4 years after operation
9	L4, L5 vertebrectomy and iliac bone fusion, radical epidural and paraspinial multiple hydatid cysts excision. Posterior stabilization with Harrington bars	Neurogenic bladder, urinary incontinence necessitating intermittent catheterisation	Bilateral foot drops. Evidence of cyst recurrence at the same levels on CT 3 years after operation

four cranial patients who received mebendazole treatment, the cysts ruptured during surgical removal. We started to give mebendazole for patient number 2 who had an atypically located cyst, for prophylaxis after VP shunt placement. Spinal cases received mebendazole because of evidence of recurrence in four cases and for prophylaxis of retroperitoneal spreading in case 8.

In the literature, the efficacy of mebendazole is debated.^{15,22} For the treatment of 337 cases with systemic involvement, the efficacy of mebendazole or albendazole was found to be 70%.¹⁷ Cardona *et al.*¹⁹ published successful treatment of two spinal hydatid cysts with surgery and mebendazole. He used mebendazole 50 mg/kg/day with alternating 1 month periods. Erşahin *et al.*²² used mebendazole in children with intracranial hydatid cysts in situations when recurrence occurred, or if there were hydatid cysts in other organs like liver and lungs or if rupture of the cyst occurred during surgical removal. He reported that he did not see any recurrence in five of seven cases. Therefore, he suggested including mebendazole in the treatment if there is systemic involvement, if the cyst ruptures during the operation or if there is recurrence verified.²²

Charles *et al.*²³ used mebendazole in amounts of 300 mg/day for 3 months in four spinal cases, following surgery and reported successful results. According to him, the prognosis of spinal hydatid disease is not as ominous as previously thought if an anterior spinal operative approach is combined with mebendazole.²³

In our nine spinal and intracranial patients who underwent operative cyst removal and also given mebendazole, we did not find any clinical or radiological evidence of recurrent disease except in one at the end of a mean 27-month follow-up period. Four of the five spinal cases had an attempt of surgical treatment previously but had shown recurrence.

Conclusion

We emphasize that mebendazole treatment in complicated cranial and spinal cases of hydatid disease may prevent possible recurrences or at least postpone them although the follow-up periods were not long enough to make a definitive statement on this matter.

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