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I. Kalaitzoglou
A. Drevelengas
A. Petridis
P. Palladas

Albendazole treatment of cerebral hydatid disease: evaluation of results with CT and MRI

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I. Kalaitzoglou · A. Drevelengas · A. Petridis · P. Palladas
Department of Radiology,
"G. Papanikolaou" General Hospital,
Thessaloniki, Greece

I. Kalaitzoglou (✉)
7 Agapinou street,
GR-54621 Thessaloniki, Greece
Tel. 0030 31 27 58 00;
fax 0030 31 28 18 28

Abstract We report a case of cerebral hydatid disease demonstrated by CT and MRI, treated with albendazole. Follow-up showed complete dissapearance of the cysts with residual focal calcification on CT and presumed gliosis on MRI.

Key words Echinococcosis, brain · Hydatid disease, brain · Albendazole · Computed tomography · Magnetic resonance imaging

Introduction

Cerebral hydatid disease (echinococcosis) is rare, occurying in 1 %–4 % of patients infected by *Echinococcus granulosus* [1–3]. Surgery, with its inherent risk of rupture and spillage of cyst contents, has been the traditional treatment. Response of abdominal hydatid disease to treatment with albendazole has been repeatedly reported [4–7]. We were able to find only three reports of successful application of this treatment to cerebral echinococcosis, in which remission was demonstrated by CT [8–10]. This is, we believe, the first report in which response to albendazole treatment has been documented with MRI.

Case report

A previously healthy 65-year-old man from a rural area presented with a right pyramidal syndrome of recent onset. A positive Babinski sign and diplopia was found on neurological examination. Routine blood and urine tests were normal. CT revealed 7 cystic lesions, one in the right cerebellar hemisphere, two in the right and one in the left frontal lobes, one in the right and two in the left parietal lobes (Fig. 1). They were at the grey-white matter junction, ranging from 5 to 15 mm in diameter, and had well-defined borders and contents of water density. No calcification or soft tissue nodules were seen, and they did not enhance with contrast medium. MRI confirmed the presence of unilocular cysts whose signal intensity was similar to that of cerebrospinal fluid on all pulse sequences. Their walls were not visualized, and one cyst in the left parietal lobe was surrounded by a small amount of edema.

Serological tests for echinococcosis were positive, both the indirect haemagglutination test (IHAT) and the enzyme-linked immunosorbent assay (ELISA). Chest and abdominal CT was normal. Since there was no evidence of hydatid disease elsewhere in the body, this was thought to represent a case of primary, multiple echinococcosis of the brain.

As the case was considered inoperable, the patient was put on albendazole 200 mg t. i. d. with meals. He tolerated the treatment well, without developing side-effects or laboratory test abnormalities. The symptoms resolved gradually and serological tests for echinococcosis returned to normal. CT at the end of the first month of treatment demonstrated complete dissappearance of the cysts. Four courses of treatment were administered. Liver enzymes were closely monitored and remained normal throughout. Regular outpatient follow-up was instituted with chest films, abdominal sonography, blood and urine tests at 6-month intervals.

CT 6 months after completion of the treatment demonstrated no evidence of cysts. Two years after initial presentation CT showed

that foci of calcification had developed at the site of the cysts in the right cerebellar hemisphere, right frontal lobe and left parietal lobe (Fig. 2). MRI at the same time demonstrated small areas of low signal intensity relative to grey matter on T1-weighted images, and high signal on T2-weighted images, at the same sites (Fig. 3). This appearance was interpreted as gliosis, more extensive than the punctate calcification seen on CT, which was not detected or MRI.

The patient's clinical condition remains stable 3 years after treatment. There are no changes in the imaging findings.

Discussion

The pathogenesis and life cycle of hydatid disease have been described in the literature [3, 11, 12].

Cerebral echinococcosis presents usually as a large cyst and much less often as disseminated cysts in the parenchyma [2, 11, 13]. Multiple cysts are believed to result from spontaneous, traumatic or surgical rupture of a solitary primary brain cyst, or from rupture of a cyst elsewhere and embolisation of hydatids to the brain. Isolated brain involvement is rare and occurs when the larvae succeed in passing through the hepatic and pulmonary filtering system to reach the brain. Brain hydatid disease is usually supratentorial, involving the middle cerebral artery territory, especially the parietal lobe [1, 11]. Involvement of the cerebellum is rare, representing only 2.5 % of intracranial echinococcosis [2]. Cysts are usually acquired in childhood and grow slowly but progressively [1]. Patients present with few neurological symptoms and signs apart from raised intracranial pressure, although seizures may occur [14].

The CT appearance of cerebral hydatids is well documented [1–3, 15, 16], and MRI descriptions have also been published [12–14, 16, 18]. Unilocular hydatid is seen on CT as a large, round, well-defined, smooth-walled cyst, with no surrounding oedema and little, if any, rim enhancement. The density of the contents is identical to that of cerebrospinal fluid or water. The cyst membranes cannot be seen, unless calcified. Calcification of the cyst wall may help differentiate it from other cystic intracranial lesions, but is seen in few cases [1]. The observation of daughter cysts is considered pathognomonic but has been very rarely reported [1]. The characteristic "water-lily" sign may occur in cerebral hydatid cysts which have ruptured [15]. Rarely the cysts are multilocular or multiple.

On MRI, superior soft tissue contrast shows features which cannot be appreciated clearly with CT, in particular multilocularity, multiplicity, perifocal oedema, and the presence of adhesions to neighbouring intracranial structures. The layers of the wall of the intact cyst cannot be separated but a smooth, low-signal rim on T2-weighted images is considered strong evidence for a hydatid. The contents have a signal intensity identical to that of cerebrospinal fluid on all pulse sequences. MRI may demonstrate cyst contents, such as daughter cysts and aggregated scolices ("hydatid sand").

The aim of surgical treatment is total removal of the intact cyst, without spillage of contents, because this can result in an immediate allergic reaction to echinococcal antigens and, more importantly, in recurrence and spread of disease [3, 9].

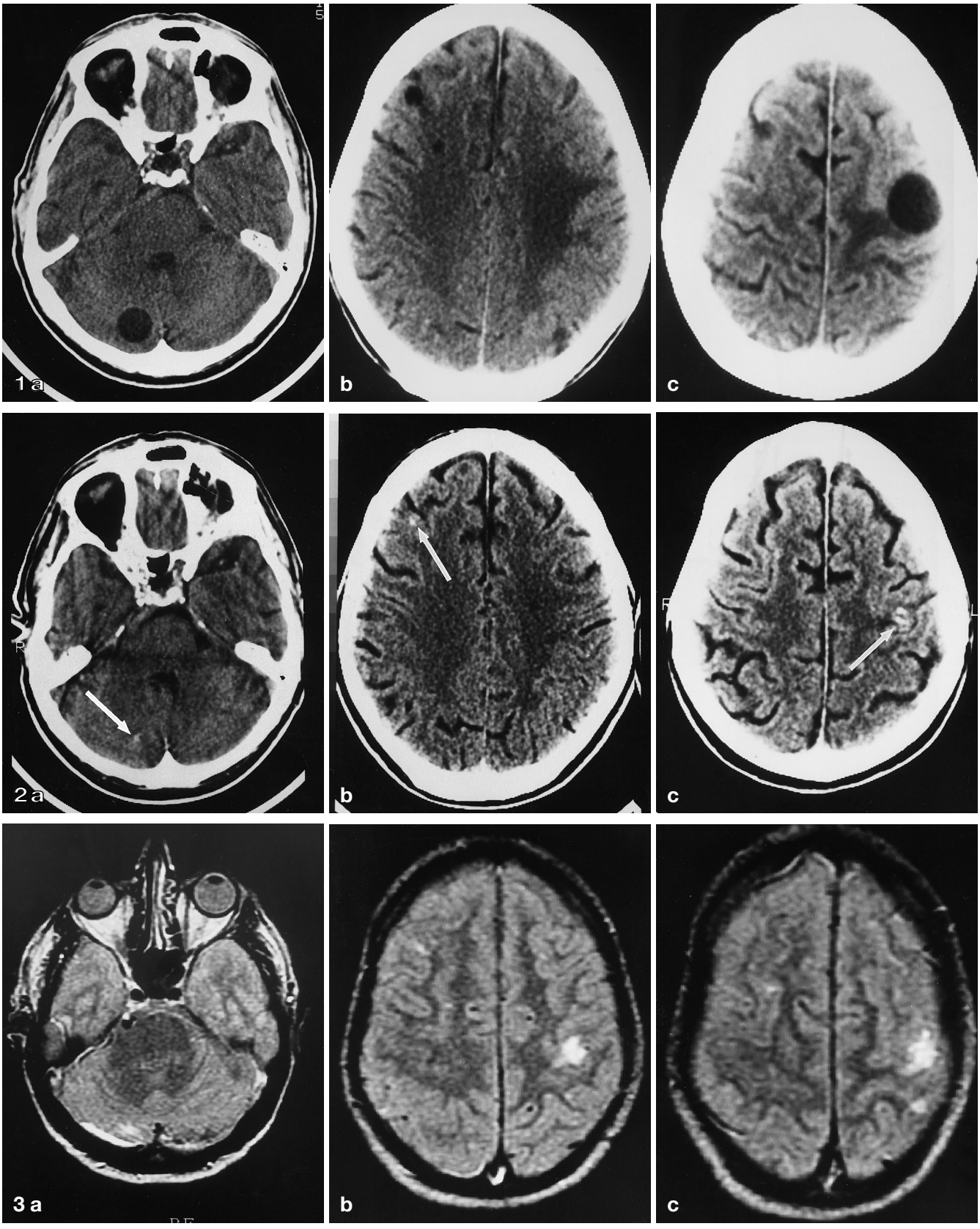
The benzimidazole compounds albendazole and mebendazole were first used in hydatidosis in 1983 [1, 9], the former being more successful [4, 10]. Albendazole acts as a parasiticidal agent by blocking glucose uptake by susceptible larvae and adult parasites. Their glycogen stores are depleted and adenosine triphosphate formation is blocked. The parasite is thus immobilised and killed. Later, the membrane shrinks and calcification marks the completion of the curative process [8, 9].

Albendazole treatment of cerebral echinococcosis is indicated in inoperable cases of multifocal disease, or involving vital brain structures [8, 10]. It is also advised as a presurgical treatment to reduce the size of a big cyst considerably and prevent the spread of daughter cysts, and finally, in cases with intraoperative rupture of cysts or recurrence [8]. The suggested dose is 10 mg/kg/day in four 1-month courses, separated by 15 day intervals [4, 5, 7, 9]. The drug is tolerated well. Side-effects reported include fever, gastrointestinal pain, anaphylactic reaction and hepatic toxicity [5, 8]. The last seems to be the most important and can lead to irreversible liver damage. Enzyme abnormalities are reversible and should be closely monitored in order to discontinue the drug in case of pathological elevation.

Cyst size and age seem the most important factors determining the response to treatment. Smaller and younger cysts respond better, the penetration of the drug depending on the thickness of the cyst wall and the presence of calcification, which usually characterizes older cysts outside the neuraxis [4, 5]. Multiple cysts respond equally well, provided they are small. The aforementioned factors presumably apply to cerebral as well as systematic hydatid cysts with the exception of bone cysts, which respond poorly [4].

Objective evidence of response is obtained by sonography, CT or MRI depending on the location of the cyst. Smaller cysts disappear, while big cysts are reduced in size and appear deformed or collapsed [4, 8]. Disappearance of daughter cysts has also been reported [5]. Small foci of calcification have been seen on CT in the site of prior cysts, 12–18 months after completion of treatment [9, 10].

Focal areas of encephalomalacia, occasionaly with punctate calcification or mineralisation, can be demonstrated on MRI after medical treatment of toxoplasma encephalitis [17]. This appearance corresponds to the findings in our case, and suggests that parasitic brain infections heal by the same mechanism after pharmacological treatment.


1 a
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◀ **Fig. 1** CT at time of diagnosis. Cysts in the periphery of the right cerebellar hemisphere (**a**) and right frontal (**b**), and left parietal lobes (**c**) have well-defined borders and contents of uniform water density. A small amount of oedema is seen in the left parietal white matter

Fig. 2 CT after albendazole treatment, at same levels as Fig. 1. The cysts have disappeared and small dense foci of calcification have developed at their sites *(arrows)*

Fig. 3 Proton density-weighted MRI obtained at the same time as Fig. 2, with slightly different orientation. High-signal foci are seen at the sites of calcification on CT. The left parietal lobe focus is most extensive and appears on two consecutive slices (**b, c**)

The success rate of albendazole treatment of echinococcosis has been reported to be from 64 % to 100 % [5, 6, 10]. In cases of partial success or failure, retreatment is recommended [6]. The World Health Organisation suggests that follow-up for evaluation of the efficacy of treatment should be at least 12 months [8].

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