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Continuous albendazole therapy in alveolar echinococcosis: long-term follow-up observation of 20 cases

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Summary Twenty patients with primary hepatic alveolar echinococcosis were treated with continuous long-term albendazole at a dose of 20 mg/kg/d for an average of 5.7 years (1.5—13.5 years) and were followed up for an average of 12.7 years (4.1—13.5 years). The therapeutic effects were evaluated by clinical, laboratory (haemogram, liver function tests), ultrasonography and computed tomography (CT) examinations. The CT pattern of hepatic lesions was classified into three types: solid form (5 cases), pseudocystic form (6 cases) and 'geographic map' (mixed) form (9 cases). Short-term results were encouraging. Jaundice and haemoptysis disappeared within 1 month of starting treatment, and hemiparesis in a patient with cerebral metastases also gradually improved. Treatment was less effective in two patients with advanced disease. On long-term follow-up, three patients were apparently cured, and the remaining 17 patients showed a good initial response, but recurrence occurred in 13 patients (65%). Therapeutic outcome was favourable with the solid form, but poor with the pseudocystic form. The mixed form was a transitional phase and slowly progressive. Involvement of the porta hepatis was the cause of various complications with high morbidity and mortality. Five patients (25%) died during the period of observation, the 10-year survival rate being, therefore, 75%.

1. Introduction

Alveolar echinococcosis (AE) is one of the most serious parasitic zoonoses, caused by the metacestode of *Echinococcus multilocularis*. It has a wide but discontinuous distribution in the northern hemisphere, with wild dogs and foxes being the principal definitive hosts. Humans are accidentally infected through ingestion of eggs. In contrast to

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cystic echinococcosis, caused by *E. granulosus*, the metacestode spreads aggressively in the liver, producing large irregular masses. In addition, it may disseminate to other organs such as the lungs and brain, with resulting high mortality.

AE occurs in several provinces of China (Xinjaing, Qinghai, Tibet, Sichuan, Ningxa and Inner Mongolia) and is a major public health problem in rural communities.[1] Until 30 years ago, surgery was the only treatment. The introduction of the benzimidazole carbamate anthelminthics, mebendazole and albendazole, has led to a significant change in therapeutic approach. These drugs act by inhibiting tubulin polymerase, disrupting microtubules and leading to death of the metacestode through disruption of a number of metabolic pathways.[2] Unlike mebendazole, albendazole is metabolized in the gut wall and liver to another active compound, albendazole sulphoxide, and this has been shown to be effective in in-vitro and animal models.[3] Intermittent albendazole chemotherapy, 10—12 mg/kg/d, in 28 d cycles, with a 14 d drug-free interval between cycles, was originally recommended. However, the results were rather disappointing.[4–7]

To achieve adequate drug levels on a continuous basis and penetration into the parasite mass requires long-term treatment without the reduction in blood levels produced by intermittent treatment. In the present study we have used continuous long-term albendazole therapy at higher doses to evaluate the therapeutic effect and monitor the adverse event profile in AE. In earlier reports of AE treatment, follow-up has been of limited duration: the current report covers very long periods of follow-up in order to define therapeutic outcome more clearly.

2. Materials and methods

2.1. Patient population

From June 1984 to March 1999, 20 patients were enrolled, treated and followed up at Chongqing University Hospital. All patients came from distant endemic areas, with symptoms of active infection, and most had advanced late-stage disease. There were 18 males and 2 females, aged between 25 and 71 years. Hepatic lesions were present in all patients, with pulmonary metastases in 5 patients and cerebral metastases in 1. The duration of symptomatic illness at diagnosis was <1 year in 6 cases, 1—2 years in 6 cases, 2—3 years in 1 case, 3—4 years in 1 case and >5 years in 6 cases, with a mean age at onset of symptoms of 45 years. The diagnosis of each patient was based on a positive Casoni test (intradermal injection of whole parasite extract), serum ELISA using whole metacestode extract, Western blot using Em2 and Em16 antigens,[8] ultrasonography (US) and computed tomography (CT). Eight patients had already undergone exploratory laparotomy and diagnosis had been confirmed by histopathological examination of biopsy material.

US and CT scans were performed before and after treatment in every patient (average 3.7 times per patient). The CT pattern was classified into three forms:[9] solid mass (CT images showing a homogenous hypodense lesion without any visible liquid component); pseudocystic [CT images showing predominantly a large cystic lesion with the density of water (+5 to +10 Hounsfield Units) with a ragged necrotic wall]; mixed (geographic map) (CT images showing heterogeneous lesions with both solid and liquid components in varying proportions appearing like a geographical map) (see Table 1).

Table 1 Results of CT scans of hepatic lesions showing distribution, number, size and type of lesions in the 20 patients at initial diagnosis

Location[a]	Right lobe only	14
	Left lobe only	1
	Both lobes	5
No. of lesions[b]	1	13
	2	8
	3	1
Size of lesion (cm)[b]	<5.0	8
	5.1—10.0	14
	10.1—15.0	5
CT pattern	Solid	5
	Pseudocystic	9
	Mixed (geographic)	6

[a] Liver hilum invaded in five cases.
[b] Numbers exceed number of patients due to multiple lesions.

Albendazole was supplied by Smith Kline and French Laboratories, Tianjin, People's Republic of China, and was given postprandially at a dose of 20 mg/kg/d divided into two or three equal doses. Treatment was continuous, without interruption, with a maximum daily dose of 1.2 g (400 mg three times a day). Albendazole was given for a mean of 5.7 years (Tables 2, 3 and 4).

As our patients came from distant endemic areas, all were admitted to hospital during each follow-up visit for observation, investigation of clinical symptoms and side effects, haematology, liver function tests, ultrasonography and CT scanning. The mean duration from first admission to last follow-up was 12.7 years (Tables 2, 3 and 4).

Therapeutic response was assessed both in the short term and throughout the period of follow-up as follows. (1) Apparently cured: disappearance of clinical symptoms; CT scans showing that hepatic lesions had disappeared or almost completely calcified and had remained unchanged for at least 10 years. (2) Improved: disappearance of clinical symptoms; CT scans showing reduction in size of hepatic lesions with markedly increased calcification. (3) Ineffective: clinical symptoms not improved; CT scans showing extension of hepatic lesions or appearance of new lesions or metastasis.

3. Results

3.1. Short-term results

The short-term results were encouraging. Treatment was effective in all but two patients with late-stage disease. Symptoms were alleviated within 1—2 months in five patients with obstructive jaundice due to hepatic hilar lesions, and two patients with haemoptysis due to pulmonary metastasis.[10] One patient with cerebral metastasis had a right-side paresis, which gradually resolved.[11] The