Leading article – Tropical infection of the gastrointestinal tract and liver series

Echinococcus of the liver

There are two forms of echinococcus that affect the liver of humans, *E granulosus* and *E multilocularis*. The second is comparatively rare and geographically isolated. Differentiation between the two is important and easy using specific serological tests. Treatment and prognosis differ considerably; *E granulosus* is comparatively simple to treat and death is exceptional, whereas *E multilocularis* is often inoperable and death has until recently been common in all but early disease – although chemotherapy is now changing the outcome. The clinical presentations of both forms of hydatid disease are comparatively non-specific. The past 10 years have seen considerable changes in the treatment of hydatid disease. The introduction of mebendazole, albendazole, and praziquantel¹⁻³ has improved treatment. What now are the relative places of surgery and chemotherapy? Patients with genuinely inoperable disease and those who are unfit for surgery should clearly receive medical treatment while the young and fit with symptomatic, easily removable cysts should have surgery but adjuvant chemotherapy may reduce the risks of recurrence.^{4,5} The treatment of asymptomatic cysts is less clear. For large cysts, surgery should be favoured but many patients can now be successfully treated medically. The treatment of patients who do not fall into these extremes is less clear. Most patients probably remain best served by an operation but with both pre and postoperative chemotherapy.

What are the contraindications to chemotherapy?

Pregnancy is a contraindication to the medical treatment of hydatid disease. Embryotoxicity and teratogenicity are seen with benzimidazole carbamates (mebendazole and albendazole). Adequate medical knowledge must be available and the ability to monitor haematology and liver function tests⁶ is mandatory.

While acute presentation of hydatid with sepsis is not a contraindication to treatment, chemotherapy will seldom if ever contribute to the short term well being of a patient because the acute presentation with sepsis, rupture, embolism or compression of vital structures simply is not altered by anti-parasitic chemotherapy. The acute treatment of these complications should include chemotherapy but this is principally aimed at longterm control/eradication of their disease and does not replace the role of appropriate surgery, antibiotics, and anti-allergy treatment for the complicated cyst.

The causes of jaundice in the patient with hydatid cyst include intra-duct cyst debris, compression, and complications of treatment including sclerosing cholangitis from scolicides and hepatocellular injury from chemotherapy.

Which drug(s)?

Our own experience is almost exclusively with albendazole. The in vitro and animal model superiority of

albendazole over mebendazole, however, and our encouraging clinical results now seem to have been vindicated by others and most recently by comparative clinical studies.^{8,9} There has been one recent very negative report from India reporting no improvement in 10 patients with pulmonary hydatid disease treated with albendazole.¹⁰

Praziquantel seems to be a very effective scolicide³ but has limited activity on the germinal layer¹¹ so it may be useful in prophylaxis around the time of surgery or other time of spillage. There is little clinical work with praziquantel to date. We have experimental data suggesting that albendazole and praziquantel may be better than either alone.^{12,13}

Chemotherapy: how much, how long?

Our recommendation for primary treatment of liver cysts from *E granulosus* is three months continuous albendazole at approximately 10 mg/kg/day in two divided daily doses.

Some situations deserve longer treatment – bone hydatid should probably be treated for longer – perhaps a year. There really is little information on duration of treatment for *E multilocularis* – perhaps for life and at least five years, with careful radiological and serological review thereafter. The length of 'prophylactic' or adjuvant treatment also deserves consideration. Preoperative albendazole treatment designed to sterilise cysts should be for at least one month. The length of postoperative treatment should be at least one month and probably two, while protoscoleces will almost always be killed by one month's treatment, if there is any remaining germinal layer – for example, a tiny adjacent cyst in the pericyst layer that has been missed – then length of treatment will be more important. The adequate length of praziquantel treatment is unestablished, although in the laboratory very short exposure times are needed.¹⁴ Fifty mg/kg/day in divided dosage should be used.

Safety of chemotherapy

Chemotherapy with albendazole is generally safe except that hepatocellular toxicity is common and significant abnormality necessitates drug withdrawals.⁶ More minor abnormalities should be carefully monitored. Cautious re-challenge at a lower dose may be attempted but an alternative drug treatment is more appropriate. Bone marrow depression can occur with both mebendazole and albendazole and necessitates prompt drug withdrawal.

New drugs

There have been two positive reports of different types of compound with positive laboratory results – isoprinosine, an immune stimulant, significantly reduced growth

of *E. multilocularis*¹⁵ and trans 2-phenoxy cyclohexanol ethers produced both in vitro and in vivo inhibition of growth of *E. multilocularis*.¹⁶ New compounds and combinations^{12 13} of old established ones should provide improved treatment.

Surgery

While hepatic hydatid cyst is usually a simple disease to treat and the risks of surgery are small, the results in experienced hands are better. The choice of operation is important. Except for the experienced hepatic surgeon, this should be a simple cystectomy. This operation is the safest procedure and, while many advocate pericystectomy, this is a non-anatomical liver resection through a distorted, compressed, non-anatomical liver. The advocates of this procedure claim a lower recurrence rate; this is not yet well established. There are no controlled studies. Our ability to detect residual cysts in the cyst margin has been considerably improved by intra-operative ultrasound and peri-operative chemotherapy will also probably reduce recurrence rates. Cholangiography is necessary during surgery to exclude intra-duct debris; its ability to detect cyst/biliary communication is limited. If there is cyst/biliary communication, scolical agents must not be injected into the cyst because the potentially fatal complication of sclerosing cholangitis may occur. The choice of scolicides is covered elsewhere.¹⁷ There is also a risk of cyst debris entering the biliary tree and causing obstruction, with secondary sepsis. Bile leaks from cyst/biliary communication will probably not close if intra-duct debris has been overlooked.

Liver resection can seldom be justified for *E. granulosus* but is the preferred treatment – indeed, currently the only chance of cure – in *E. multilocularis*.

Laparoscopic surgery has been used for *E. granulosus*. Laparoscopic puncture of a large, tense cyst full of material where spillage may be fatal, should be viewed with caution. Even if adequate packing with scolical soaked swabs is used devices such as the suction curette are useful^{18 19} to minimise blockage.

Percutaneous aspiration

The risks of fluid leakage are high and anaphylaxis has been well reported.²⁰

In conclusion, the treatment of hydatid disease requires both medical and surgical treatment. It is usually a simple benign disease that is most rewarding to treat.

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