Clinical and sonographic management of viable hydatid liver cysts

A. Giorgio*, G. de Stefano, A. Di Sarno, G. Liorre, U. Scognamiglio, S. Iaquinta, A. Mariniello, V. Giorgio, M. de Stefano, A. Perrotta

Infectious Diseases and Interventional Ultrasound Unit, D. Cotugno Hospital, Naples, Italy

KEYWORDS

Interventional ultrasound;
Hydatid liver cysts;
Percutaneous treatment;
Puncture–aspiration–injection and re-aspiration;
Double percutaneous aspiration and ethanol injection.

Abstract *Aim:* The aim of this study was to review our 18-year experience in the treatment of viable hydatid liver cysts (HLCs) with double percutaneous aspiration and ethanol injection (D-PAI) and to provide indications for the clinical management of HLCs.

Materials and methods: From January 1989 to December 2007, 127 patients (100 males; 13–80 years) with 184 viable HLCs (137 univesicular, 47 multivesicular; 2.8–20 cm) underwent D-PAI. *Results:* Ultrasonography (US) showed complete disappearance of 125/184 (68%) cysts; in the remaining 59 cases, an inactive solid (37 cases, 20%) or liquid pattern (22 cases, 12%) was observed with volume decreases of 50–80%. The final US pattern was unmodified during the follow-up in 96.8%. Local recurrences were observed in 5 patients (3.9%): 4 patients with 8 multivesicular cysts and 1 patient with a bilocular cyst (with a solid pattern on US) that ruptured into the biliary tree 2 years after the procedure and disappeared after endoscopic sphincterectomy. The mortality rate was 0.8%, and the overall morbidity was 8.6%. The mean hospital stay was 2.9 days. The time of healing for smaller cysts (<5 cm) was shorter than that of large cysts (≥5 cm) ($P < 0.001$).

Conclusion: Our long-term results confirm the high effectiveness of D-PAI in the treatment of HLCs. These results suggest that multilocular cysts require closer follow-up than unilocular cysts.

Sommario *Scopo:* Scopo di questo studio è stato quello di riportare i risultati a lungo termine del trattamento percutaneo delle cisti idatidiche epatiche con doppia puntura – aspirazione – e iniezione di etanolo (D-PAI).

Materiali e metodi: Centoventisette pazienti con 184 cisti idatidiche epatiche vitali (137 univescicolari, 47 multivescicolari) sono stati sottoposti a D-PAI.

Risultati: All'esame ecografico si osservava *restitutio ad integrum* del parenchima epatico in 125 (68%) delle 184 cisti trattate. Per le rimanenti 59, era visibile una riduzione volumetrica del 50–80%. L'aspetto ecografico risultava immutato per tutta la durata del follow-up nel 96,8% dei pazienti, fatta eccezione per 5 (3,9%) pazienti (4 con cisti multivescicolari, 1 con cisti biloculare) che presentavano recidive locali.

* Corresponding author. Infectious Diseases and Interventional Ultrasound Unit, D. Cotugno Hospital, via Quagliariello 54, 80131 Naples, Italy.

E-mail address: assanui1@virgilio.it (A. Giorgio).

Conclusioni: I nostri dati confermano l'elevata efficacia della D-PAI nel trattamento percutaneo delle cisti idatidiche epatiche e suggeriscono uno stretto follow-up nei pazienti con cisti multivescicolari.

© 2008 Elsevier Srl. All rights reserved.

Introduction

Cystic hydatid disease (CHD) is a parasitosis that generally targets the liver (50–70% of all cases) and less frequently the lung, spleen, kidney, bone, brain, heart, or other organs [1]. CHD is usually asymptomatic, and hydatid liver cysts (HLCs) often undergo spontaneous involution. HLCs rarely cause complications. However, in 3–17% of cases, the cyst ruptures, usually into the biliary tree or the abdominal or thoracic cavity, and these events can cause anaphylaxis and occasionally death [1,2]. Infection of the cyst can lead to the development of liver abscesses and local mass effects, such as compression of bile ducts and/or blood vessels, which may be associated with cholestasis, portal hypertension, or the Budd–Chiari syndrome [1–4]. Therefore, in spite of their benign nature, treatment must be considered mandatory in cases of symptomatic HLCs, and it is recommended for all viable cysts because of the risk of severe complications [5]. Chemotherapy alone is rarely curative, and it is associated with a high rate of side effects and recurrences [6]. For many years surgery was regarded as the treatment of choice for CHD [3,7], but percutaneous drainage with the PAIR procedure (puncture–aspiration–injection and re-aspiration) is now widely used. It produces excellent results, in terms of disappearance of the cyst, and is associated with very few side effects and low mortality [4,8–17]. In 1992, we presented a double puncture–aspiration–injection (D-PAI) technique that involves aspiration of the contents of the cyst and injection of ethanol without re-aspiration [10].

In this paper we analyze the long-term efficacy of D-PAI in the percutaneous treatment of HLCs in a series of patients followed for up to 18 years.

Patients and methods

Patients

From January 1989 to December 2007, we performed D-PAI on 127 patients (100 males, 27 females, aged 13–80 years; mean 45 years) with 184 viable HLCs (diameters ranging from 2.8 to 20 cm; mean 4.8 cm). Most of the cysts (137/184) were univesicular (World Health Organization types CL/CE1/CE3); the 47 multivesicular cysts were type CE2 [18]. The patients have been followed for up to 18 years (range 14–215 months; mean 51 months). Five of the 127 patients (3.9%) with 5 (2.7%) viable unilocular HLCs had been operated on, and surgery was followed by recurrence of the cyst in another segment of the liver. These five were among the 28 patients (all with type CL, CE1 and CE2 HLCs) [18] whose cysts were associated with symptoms (e.g., right upper quadrant pain associated with a palpable mass, jaundice, and mild dilatation of intra-hepatic bile ducts). None of the patients had extra-hepatic disease.

Methods

The double puncture–aspiration–injection technique

D-PAI was carried out as previously described [10,15,17]. The cyst was punctured under ultrasound (US) guidance using a 22-, 20- or 18-gauge needle (Ecojekt, Tokyo, Japan), depending on the volume of the cyst. Up to 90% of the fluid content was aspirated, and 95% sterile ethanol was then injected into the cyst and left in situ. The volume of ethanol injected was equal to 50–60% of the volume of fluid drained from the cyst (Figs. 1–3). When possible, at least 1 cm of liver parenchyma was generally interposed between the wall of the cyst and the surface of the liver. The needle was inserted directly into subcapsular cysts. Freshly aspirated cyst fluid was subjected to direct microscopy and staining with 0.1% neutral red to detect the presence of viable scolices. To exclude the presence of a biliary fistula, the bilirubin level in the aspirate was assessed with a semiquantitative method (Combur-Test; Roche Diagnostics, Indianapolis, IN) a few seconds before the alcohol injection. Multiple cysts were treated during the same session. Three days after the initial puncture–injection, treatment was repeated in all cases. Mebendazole (3 g/days in the first 10 cases) or albendazole (800 mg/days in the remaining cases) was administered for 3 days before and for 3 weeks after D-PAI in all but 2 patients (one who was pregnant and one with chronic liver disease). All procedures were performed with an anesthesiologist present. General anesthesia without endotracheal intubation (intravenous [IV] atropine, 0.5 mg; induction with propofol, 1.0–1.5 mg/kg IV; maintenance with IV propofol, 9.0–12 mg kg⁻¹ h⁻¹ and fentanyl citrate, 50 mg) was used routinely after July 2000 following the death of 1 patient due to anaphylactic shock (see [complication](#) section). Use of the procedure was approved by the institutional review board of the D. Cotugno Hospital, where patients were treated. All patients gave their informed written consent.

Fig. 1 Type CE3 hydatid liver cyst before treatment.

Fig. 2 The needle is inserted into the cyst.

Follow-up

The median overall follow-up was 54 months (range 14–215 months). Thirty-two patients (25.2%) were followed from 1 to 4 years, 59 (46.4%) were followed from 5 to 8 years, and 36 (28.3%) were followed from 9 to 18 years. These data are summarized in Table 1.

After the procedure, clinical, laboratory, and US assessments were made every month for the first 3 months and every 6 months thereafter. Indirect hemagglutination assays (IHA) or enzyme-linked immunosorbent assays of titers were performed monthly during the first 6 months and then twice a year. Chest radiography was scheduled every 6 months, and total body computed tomography was scheduled every 2 years.

Statistical analysis

Statistical analysis was based on the Student's *t*-test.

Fig. 3 The ethanol injected into the cyst appears as a hyperechoic cloud.

Table 1 Length of follow-up of 127 patients with hydatid liver cysts treated with D-PAI

	No. of patients	Follow-up	
		%	Range (years)
	32	25.2	1–4
	59	46.4	5–8
	36	28.3	9–18
Total no. of HLCs	184	—	—

Results

D-PAI procedures

A total of 297 US-guided needle punctures were performed. In all cases viable scolices were found in the aspirates. The amounts of ethanol injected per session ranged from 12 to 250 mL. One hundred and twenty-three patients (96.8%) had one course of D-PAI. In the remaining 4 (3.2%) cases (all involving multivesicular cysts), 3 (3 patients) or 4 (1 patient) courses of D-PAI were administered. The procedure was completed in all but 2 patients: in 1 case, the treatment had to be terminated because of intracystic bleeding during aspiration of the cyst contents, and the second case was complicated by fatal anaphylactic shock after the aspiration of 10 mL of cyst fluid. The procedures themselves lasted from 15 to 45 min, and the mean hospital stay was 2.9 days (range 2–7 days). In symptomatic patients, reduction of the intracystic pressure caused immediate disappearance of abdominal mass, and jaundice disappeared within 17 days.

US follow-up findings

During the follow-up, 125 (68%) of the 184 cysts (size range 2.8–16 cm; mean 5.3 cm) disappeared, and complete reconstitution of the liver parenchyma was observed; in 37 (20%) others, US revealed a solid pattern, and in the remaining 22 (12%) a minimal fluid component persisted. These latter cysts were subjected to a third aspiration, but no viable scolices were found in the aspirated fluid. Both solid and liquid cysts exhibited post-treatment volume reductions of 50–80%, compared with the initial volume.

The interval between treatment and appearance of the final US pattern was directly proportional to cyst size. In fact, there was a statistically significant difference between the healing times observed with the smaller (<5 cm) and larger (≥5 cm) cysts (up to 70 days for the former, up to 2 years for the latter; $P < 0.01$) (Table 2).

None of the patients had US or CT evidence of new intra- or extra-hepatic cysts. Local recurrences, i.e., reappearance of a small liquid component with a hyperechoic wall in a treated cyst that had previously appeared solid, were observed in 5% of the cases, all involving multilocular cysts. Only 1 patient with a unilocular cyst experienced recurrence. D-PAI had resulted in the appearance of a solid hyperechoic pattern, but 5 years later a liquid component was noted, and the cyst was treated with another course of D-PAI. One other patient with a bilocular cyst presented a solid hyperechoic pattern after D-PAI which remained

Table 2 Final US pattern observed at last follow-up examination of 184 HLCs treated with D-PAI

Total no. of viable HLCs	Interval between D-PAI and appearance of final US pattern	US pattern	No. cysts	%
184	Smaller cysts (<5 cm)	Healed	125	68
	15–70 days			
	Largest cysts (>5 cm) up to 2 years	Solid	37	20.1
		Liquid	22	12

stable for 2 years. The patient then developed fever and jaundice, and dilatation of the bile ducts was evident on US. A diagnosis of cyst rupture into the biliary tract was made, and the patient was treated with endoscopic retrograde cholangiopancreatography. No viable scolices were found in the aspirate, and 2 months later an US scan revealed full reconstitution of liver parenchyma.

Complications

The overall morbidity rate was 8.6%, and 1 patient died (mortality 0.8%). Major complications were recorded in 2.5% of the cases. Hepatic abscesses developed at the site of 2 treated cysts (2 patients) 15 and 60 days after D-PAI. In both cases, the abscesses were drained percutaneously, and 1 month later, reconstitution of liver parenchyma was observed on the US exam. A biliary fistula was diagnosed in 1 case in which bile-stained fluid was collected during the second aspiration. Since the patient's condition was stable, no other diagnostic or therapeutic procedures were carried out, and the second treatment was postponed until the fistula had closed spontaneously (6 months later). Minor side effects included nausea and vomiting (1 case) and abdominal pain lasting 15 min (2 cases).

Discussion

In the recent past, conservative or radical surgery was the approach recommended for treatment of viable HLCs [19]. The introduction of chemotherapeutic agents with significant activity against *Echinococcus granulosus* made it possible to perform US-guided percutaneous transhepatic drainage of these cysts, a procedure known by the acronym PAIR [19]. Chemotherapy alone is less effective, even for uncomplicated active HLCs. Maximum size reductions have been observed in cysts treated with percutaneous drainage plus albendazole [6,20].

Percutaneous injection of scolicidal agents (absolute alcohol and hypertonic saline solution) has produced excellent results in terms of disappearance of the cysts. It is also associated with very few side effects and a low mortality rate [4,8–16]. In previous studies [10,15,17] we evaluated the effectiveness of a modified version of PAIR for the treatment of active HLCs. During this procedure, which is known as D-PAI, the injected ethanol is not re-aspirated but left inside the cyst. The procedure is then repeated 3 days later to maximize the contact between the alcohol and scolices and enhance the scolicidal effects.

We also performed a second puncture in order to verify the scolicidal effect of the procedure.

This report describes the results of our 18-year experience with D-PAI as first-line treatment for a large series of viable HLCs. The data collected during this period have clinical implications for the management of these patients. Our results show that in patients with viable HLCs, D-PAI is highly effective in shrinking the HLCs and inducing reconstitution of the liver parenchyma. In fact, 68% of the treated cysts were no longer visible on US, and the remaining cysts showed a solid (20%) or liquid (12%) pattern, volume decreases of 50–80%, and no evidence of viable scolices in the cyst fluid (Figs. 4 and 5). Therefore, parasitological cures can be achieved with D-PAI in 100% of cases. These results are not surprising. The injected ethanol induces a very strong inflammatory reaction that leads to the destruction of the inner membrane of the cyst. Moreover, the ethanol is left inside the cyst to prolong its contact with the scolices and maximize the scolicidal effect. Repetition of the treatment 3 days later further increases the likelihood that all scolices and protoscolices will be killed.

Multivesicular cysts are an exception. Five patients with multivesicular cysts (3.9% of the total series) [10,15,17] experienced intracystic relapses. Therefore, in patients with multivesicular cysts, we suggest closer follow-up to ensure early recognition of relapse.

In other reported series involving long-term experience, such as those of Ustunsoz et al. and Etlik et al. [13,21], cyst elimination rates were significantly lower than the ones reported herein.

From the very outset of our experience with D-PAI [10,15], we noted considerable variation in the time that elapsed before the final US pattern was observed. In fact, smaller cysts healed within 70 days of the treatment whereas the largest cysts took up to 2 years. After this point, no changes in the US pattern (solid or liquid) are observed.

Fig. 4 Large multilocular cyst before treatment.

Fig. 5 Nine years after D-PAI treatment, the same cyst shown in Fig. 4 exhibits a decreased volume and a solid inactive pattern on US.

In our series, 1 patient died. In the literature, only one other death has been reported following D-PAI [14]. However, it should be stressed that the complication rate in our series was very low and not significantly different from rates reported in other series of HLCs treated with percutaneous approaches [4,5,14,22].

Fig. 6 Flow-chart of percutaneous approach in the treatment of hydatid liver cysts.

Based on the analysis of our results, some proposals can be made for the clinical management of viable HLCs:

- After percutaneous treatment and during the follow-up, US should be performed every 12–18 months in most cases.
- The exception is the subset of patients with multivesicular cysts. In these cases closer follow-up (every 6–12 months) is mandatory for prompt detection of relapses. However, in our opinion, surgery is the treatment of choice for patients with multivesicular cysts, especially those with a high number of daughter cysts.
- In patients with large, active cysts treated with D-PAI, up to 2 years may pass before US evidence of hepatic parenchymal reconstitution of liver parenchyma is observed. Consequently, the follow-up in these cases should be prolonged.
- Finally, in patients with a local relapse (single or multiple) we suggest a second course of D-PAI (see the flow-chart in Fig. 6).

In conclusion, our 18-year experience with D-PAI confirms that this approach is effective and safe for treatment of viable HLCs. In our opinion, it should be considered the first-line treatment for univesicular viable HLCs. This approach is especially useful in developing countries, where the percutaneous approach is often the only therapeutic option for HLCs because it is so much less expensive than either surgery or medical therapy.

Conflict of interest

The authors have no conflict of interest.

References

- [1] Ammann RW, Eckert J. Cestodes. *Echinococcus*. Gastroenterol Clin North Am 1996;25:655–89.
- [2] Becker K, Fieling T, Saleh A, Haussinger D. Resolution of hydatid liver cyst by spontaneous rupture into the biliary tract. *J Hepatol* 1997;26:1408–12.
- [3] Yaghan R, Heis H, Bani-Hani K, et al. Is fear of anaphylactic shock discouraging surgeons from more widely adopting percutaneous and laparoscopic techniques in the treatment of liver hydatid cyst? *Am J Surg* 2004;187:533–7.
- [4] Khuroo MS, Wani NA, Javid G, et al. Percutaneous drainage compared with surgery for hepatic hydatid cysts. *N Engl J Med* 1997;337:881–7.
- [5] Rozanes I, Güven K, Acunaş B, Emre A. Cystic echinococcal liver disease: new insights into an old disease and an algorithm for therapy planning. *Cardiovasc Intervent Radiol* 2007 Nov–Dec;30(6):1112–6 [Epub 2007 May 29. Review].
- [6] Khuroo MS, Dar MY, Yattoo GN, et al. Percutaneous drainage versus albendazole therapy in hepatic hydatidosis: a prospective, randomized study. *Gastroenterology* 1993;104:1452–9.
- [7] Morris DL, Richards KS. Hydatid disease: current medical and surgical management. 1st ed. London, England: Butterworth-Heinemann; 1992. p. 1–24.
- [8] Ben Amor N, Gargouri M, Gharbi HA, Golvan YJ, Ayachi K, Kchouk H. Trial therapy of inoperable abdominal hydatid cysts by puncture. *Ann Parasitol Hum Comp* 1986;61:689–92.
- [9] Gargouri M, Ben Amor N, Ben Chechida F, et al. Percutaneous treatment of hydatid cysts (*Echinococcus granulosus*). *Cardiovasc Intervent Radiol* 1990;13:169–73.

- [10] Giorgio A, Tarantino L, Francica G, et al. Unilocular hydatid liver cysts: treatment with US-guided, double percutaneous aspiration and alcohol injection. *Radiology* 1992;182: 705–10.
- [11] Bastid C, Azar C, Doyer M, Sahel J. Percutaneous treatment of hydatid cysts under sonographic guidance. *Dig Dis Sci* 1994;39: 1576–80.
- [12] Akhan O, Ozmen MN, Dincer A, et al. Liver hydatid disease: long-term results of percutaneous treatment. *Radiology* 1996;198:259–64.
- [13] Ustunsoz B, Akhan O, Kamiloglu MA, et al. Percutaneous treatment of hydatid cysts of the liver: long-term results. *Am J Roentgenol* 1999;172:91–6.
- [14] Men S, Hekimoglu B, Yucesoy C, et al. Percutaneous treatment of hepatic hydatid cysts: an alternative to surgery. *Am J Roentgenol* 1999;172:83–9.
- [15] Giorgio A, Tarantino L, de Stefano G, et al. Hydatid liver cyst. An 11-year experience of treatment with percutaneous aspiration and ethanol injection. *J Ultrasound Med* 2001;20:729–38.
- [16] Yagci G, Ustunsoz B, Kaymakcioglu N, et al. Results of surgical, laparoscopic and percutaneous treatment for hydatid disease of the liver: 10 years experience with 355 patients. *World J Surg* 2005;29:1670–9.
- [17] Giorgio A, de Stefano G, Esposito V, et al. Long term results of percutaneous treatment of hydatid liver cysts: a single centre 17 years experience. *Infection* 2008;36(3):256–61.
- [18] Eckert J, Gemmel MA, Meslin F-X, et al, editor. WHO/OIE Manual of echinococcosis in humans and animals. Paris; 2001.
- [19] Smego Jr RA, Sebanego P. Treatment options for hepatic cystic echinococcosis. *Int J Infect Dis* 2005;9(2):69–76.
- [20] Dziri C, Haouet K, Fingerhut A. Treatment of hydatid cyst of the liver: where is the evidence? *World J Surg* 2004;28:731–6.
- [21] Etlik O, Arsalin H, Bay A, et al. Abdominal hydatid disease long-term results of percutaneous treatment. *Acta Radiol* 2004; 45(4):383–9.
- [22] Langer JC, Rose DB, Keystone JS, et al. Diagnosis and management of hydatid disease of the liver: a 15-year North American experience. *Ann Surg* 1984;199:412–7.