



Postoperative recurrence of cystic hydatidosis: Management and outcome

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ABSTRACT

Surgical treatment is known as the basic treatment for hydatid cyst in all human body organs. The recurrence rate with all type of surgery appears to be high (4.6%–22.0%) within 5 years. The purpose of this study was to report our recurrence rate, management of recurrent hydatid cysts, evaluating the methods for diagnosis of recurrence, the site of recurrence (surgical site, next to the surgical site others organs), and therapeutic methods for the cases. We retrospectively reviewed the medical records of all patients who underwent surgery for hydatid cystic for all organs between 2006 and 2019. Generally 482 liver hydatid cysts, 289 pulmonary hydatid cysts, and 34 extra liver and pulmonary cysts underwent surgery between 2d and 19th years of our study; however, follow-ups were conducted entirely for 584 (72.5%) of cases. The recurrence of cysts were detected in 98 patients (16.7%). Among the recurrence cases in the liver 56 (11.6%) of them appeared next to the surgical site, while only 10 cases (2%) were found remote to the surgical site. Moreover, only one case was recurred on the surgical site. There were 14 (4.84%) cases of the recurrence in the same lobe and 15 (5%) cases of the recurrence in the other lobe between the recurrence cases of the lung, however, in 8 cases hydatid cysts were recurred in liver and lung simultaneously. Eleven cases were found in other organs. Eighty eight cases underwent the surgery while the others (n=10) were treated by oral Albendazole therapy. Removal of the cyst contents plus partial pericystectomy and local sterilization with external drainage plus chemotherapy is recommended for both primary and secondary operations with satisfactory long-term results.

Keywords: Hydatid cyst, hydatosis, hydatid cyst management, recurrence of hydatid cyst,

BACKGROUND

Hydatid disease (HD) is a prevalent zoonotic infection caused by *Echinococcus granulosus*, or less frequently, *E. multilocularis* (Manoucher Aghajanzadeh *et al.*, 2014; Manucher Aghajanzadeh, Safarpour, Amani, & Alavi, 2008). In addition, it has been considered as a serious public health problem in several countries. The disease is mostly endemic in central Asia, Northern and eastern of Africa, Australia, South America and the Mediterranean Basin (Sotiraki & Chaligiannis, 2010). In HD life cycle, dog is the definitive host while sheep is the intermediate one (Prousalidis *et al.*, 2012; Sotiraki & Chaligiannis, 2010). The adult worm lives in the intestine of the definitive host and discharges their eggs through their feces (Manucher Aghajanzadeh *et al.*, 2008; Prousalidis *et al.*, 2012). Then the intermediate host ingests the ovum while eating the contaminated vegetables and the embryo passes through the intestinal wall to enter the portal venous system and embedded in the liver organ, which is the most involved organ in this disease (Kilani *et al.*, 2001; Prousalidis *et al.*, 2012). When the intermediate host dies, their contaminated viscera are eaten by the definitive host (Prousalidis *et al.*, 2012). Afterward human could either get contaminated by direct contact with definitive host or by eating contaminated water or vegetables (Manucher Aghajanzadeh *et al.*, 2008; Kilani *et al.*, 2001). Hydatid disease could involve almost every organ of the human body; however, approximately 70% of the cysts infected the liver, followed by the lung (15%–47%), and 10% rest of body organs (Manoucher Aghajanzadeh *et al.*, 2014; Prousalidis *et al.*, 2012; Sotiraki & Chaligiannis, 2010). Accordingly, if a cyst is detected in each organ, liver and lung infection must be rolled out at the first place (Manucher Aghajanzadeh *et al.*, 2008; Kilani *et al.*, 2001; Sotiraki & Chaligiannis, 2010). The disease is less frequently found in the spleen, pancreas, heart, brain, kidney, bones, adrenal and muscles, soft tissue and rib (Manoucher Aghajanzadeh *et al.*, 2014; Manouchehr Aghajanzadeh, Glali, Palizkar, Jafari, & Ildari, 2018; Manucher Aghajanzadeh *et al.*, 2008; Delshad, Aghajanzadeh, Hemmati, Rimaz, & Shojaee, 2016; Kilani *et al.*, 2001; Prousalidis *et al.*, 2012). The clinical manifestations in human varies from being asymptomatic to fatal disease (Prousalidis *et al.*, 2012).

The clinical management is almost complicated, in fact, the efficacy and effectiveness were reported poor while the recurrence rate and the costs are not low. Therefore, the current management of the HD is still mainly based on the experts opinion (Delshad *et al.*, 2016; Kilani *et al.*, 2001). In spite of existing surgical techniques and using the chemotherapy drugs, recurrence still remains as a major problem in the management of the HD (Symeonidis *et al.*, 2013). The recurrence rates has been reported to be highly variable (0-22%) and mostly has been detected between 3 months to 20 years after the first operation of the HD (Chautems *et al.*, 2005). Hydatid cyst recurrence mostly attributed to either the failure of the treatment or a newly contamination by HD (Pedrosa, Saíz, Arrazola, Ferreirós, & Pedrosa, 2000). The recurrence of the disease might be asymptomatic, or it might present with major complications such as pyogenic infection, intrabiliary rupture, anaphylaxis, and lung abscess. Thus long-term follow ups after the primary treatment of the disease has been recommended to detecting the asymptomatic ones (Manouchehr Aghajanzadeh, Glali, *et al.*, 2018; Pedrosa *et al.*, 2000). In this study we determine the frequency of HD recurrence, the clinical features, and the possible risk factors among the patients in our center.

METHOD

We retrospectively evaluated patients with HD, who were cured by primary surgery and were followed subsequently at Razi and Arya hospital of Rasht city in Iran between May1998 and December 2018. Patients who underwent surgery in another hospital for hydatid cyst and were referred to our hospital because of recurrence were also included in this study.

The data were collected about the clinical features, comorbidities, drug histories, diagnostic tools, surgical interventions and long-term results, postoperative complications, and hospital admission records of the patients. Recurrence is defined as the existence of an active cysts after therapy, either in the previous location or in a distant one. Follow-up program were carried out routinely for each patients after the surgical treatment. According to the protocols chest X-ray (CXR) and abdominal ultrasonography were conducted to detect pulmonary and abdominal cysts respectively about 4 months after the operation. Any

suspicion of recurrence based on the ultrasound was confirmed with computed tomography (CT). The minimum follow-up period for each patient was 5 years. In those who had recurrences factors including time, location, complications, and manifestations of the new cysts were collected precisely. We tabulated the data between the groups of patients who experienced recurrences and who had no recurrences based on their sex, age, type of the surgery, and cyst characteristics such as location, size, suppuration, calcification, multiplicity, multivesicularity, rupture. All the data were analyzed in SPSS software.

RESULTS

Generally 482 liver hydatid cysts, 289 pulmonary hydatid cysts, and 34 extra liver and pulmonary cysts underwent surgery between 2d and 19th years of our study; however, follow-ups were conducted entirely for 584 (72.5%) of cases (372 liver, 188 lung, and 20 in other organs). Among these cases 62% were males and 38% were females and the mean age of them was 45 years-old (10-68 years-old). Furthermore, 504 cases were treated primarily at our center while 80 cases were referred to our center after detecting the post-operative recurrence in another medical center. The initial site of the hydatid cysts in those with recurrence and the type of their operation were indicated in Table.1 in details.

Totally, recurrence were observed in 98 cases (16.7%) during the follow-ups sessions. These recurrence occurred asymptomatic in 15% of the cases; as a result, the incidental findings make to the diagnosis.

The remains presented mostly with cough (21%), pain (12%), mass (21%), fever (13%), and dyspnea (15%). The majority of these recurrences were detected between 2 to 5 years after their operation (Mean Time= 3 years).

The chosen diagnostic tool mainly was attributed to the site of the cyst, for instance ultrasonography and CXR were chosen for detecting the cysts in abdomen and lung respectively. The second choice for detecting the recurrence rate was CT while the Magnetic Resonance Imaging (MRI) was considered for some extra liver and pulmonary cysts.

Liver recurrences occurred in 56 patients. In 20 (28.5%) cases the cysts developed at the previous site of the primary hydatid cysts and in 26 cases the recurrence appeared remote to the primary surgical site, for instance one cyst recurred on the laparotomy surgical site, three cases in the peritoneal cavity, and two cases in the spleen.

Lung recurrences developed in 29 patients. Among these cases, 12 cases (5%) recurred in the same lobe, 12 cases (5%) in the other lobes, 3 cases in contralateral lung, one case in peritoneal cavity, one case on the thoracotomy site on the chest wall

Simultaneous recurrence in liver and lung happened in 8 patients. Furthermore, three cases were developed at the initial site of the surgery while 5 cases reappeared remote to the initial site (fig.1). The location of the recurrences were all depicted in Table.2 in details.

Table1- Operative procedure and site of initial cysts in patients with recurrence

Operative procedure	Site of initial cyst; no.						
	Hepatic	Lung	Peritoneal	Spleen	Hepatic and peritoneal	Hepatic and lung	
Cystopericystectomy	3	3	2	—	—	2	3
Lobectomy	—	2	—	—	—	—	1
Splenectomy	-	—	-	—	2	—	—
Partial pericystectomy, drainage	12	3	2	—	—	3	2
Partial pericystectomy, capitonage	5	4	1	-	-	—	2
Partial pericystectomy, omentoplasty	4	—	1	—	—	2	—

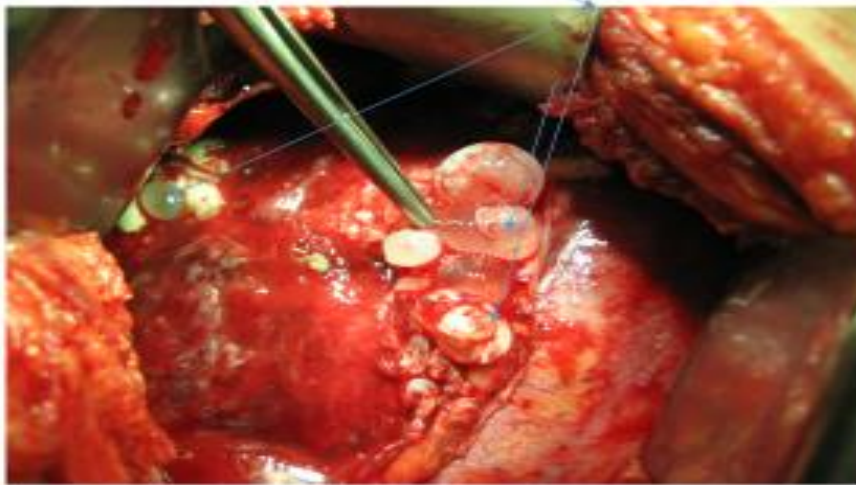


Figure1: Daughter hydatid cysts in the pleural cavity due to the liver cysts perforation after the thoracotomy

Table.2 -Postoperative recurrence in patients with previously operated hydatid cysts

Site of recurrence	patients	Site of initial cysts (no.) - remote site (no)- other organs
Liver	56	16) 21 peritoneum (3), spleen (2), AW (2)*
Lung	29	12 12 other Lung (3), peritoneum, SP(1), CW(1)**
Liver, lung	8	3 5 - -
Total	98 (16.7%)	

*Abdominal wall

**Spleen, Chest wall

Our operative strategy included sterilization the cyst with either povidone idone 20% or hypertonic saline solution and total removing of the cyst via either evacuating the total contents or pericystectomy. Then in pulmonary cysts the bronchial opening bases were closed and in liver cysts the cavities were obliterated with either omentum or capitonnage technique, although in case of intrabiliary rupture obliteration was conducted with external drainage. In addition, when the cysts were infected or huge, lobectomy or wedge resection were considered for pulmonary and liver cysts respectively.

Among these recurrent cases, 42 cases of liver cyst and 19 cases of the lung cysts underwent surgery while 10 cases of the liver and spleen cysts and 14 cases of the lung and peritoneal cysts were treated via Albendazole therapy. Moreover, among the patient with the simultaneous recurrence in liver and lung 5 cases were required surgery while 3 cases was on Albendazole therapy.

The most prevalent complications of the surgery were chronic bill leakage, atelectasia, air leakage, hemorrhage, and wound infection. Among our patients, 10 patients experienced morbidities related to their prolonged hospital admission because of long-lasting bile leakage or surgical site infection. Also 4 patients experienced common respiratory or circulatory complications. Atelectasia of the lung was detected in 4 patients and air leaks happened in 3 of them which all improved with physiotherapy.

The median length of staying in the hospital was 12 (range 6–22) days in these patients. . Mortality was negative in these patients and the recurrence rate was zero in the first 2 years after the surgery.

Among our patients, there were various factors which could increase the possibility of the recurrence. For instance, intraperitoneal spillage presented with pain, allergic reactions, and bill peritonitis were detected in 8 patients before the initial surgery (fig.2). In two other patients signs of intra-abdominal contamination due to the leakage of the cyst content were observed during the surgery.

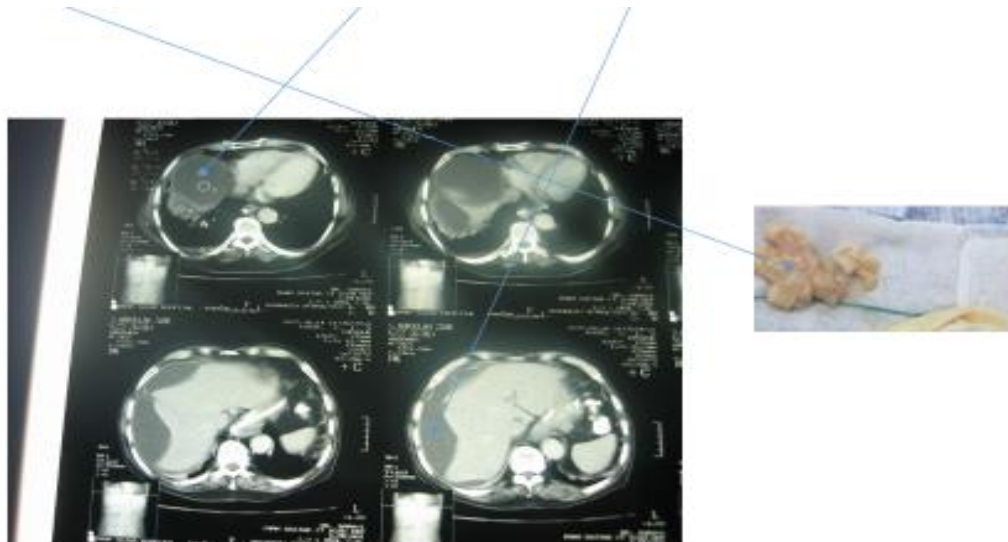


Figure2: A: The liver hydatid cyst perforated into the peritoneal cavity before the surgery. The CT scan showed the liquid in the peritoneal cavity.

B: Liver hydatid cysts elements which were extracted by laparotomy.

Moreover, development of new cysts at remote locations in these patients have been considered as the disseminated disease. In this regard, there were 8 patients who had the history of spillage during their first surgery. Among those, 4 patients had extrahepatic intra-abdominal cysts, 5 had incomplete excision of huge multivesicular cysts with exophytic small cystic growth at inaccessible or difficult locations.

In 7 patients, the initial cysts were localized in the posterior segment of the right hepatic lobe, resulting in incomplete evacuation and pericystectomy. On the other hand, it was impossible to kill or evacuate all of the living cysts and protoscolices during the first operation in 9 patients due to their small size or difficult locations.

The benefit of local scolicidal agents is still controversial; however, we routinely performed intracystic injection of hypertonic normal saline and in order to avoid the complications, the usual concentration ranged from 6% to 10%.

The total oral dose of albendazole varied between 600 mg and 800 mg (10mg/kg), often for 7 days preoperatively and three cycles of 28 days followed by 14 drug-free days postoperatively. This drug had been prescribed in all patients especially with multiple cysts in an organs or multiple organs or difficult location of cyst.

DISCUSSION

The goals in standard surgical management of the hydatid cysts includes eliminating the local disease, spillage avoidance, preserving the lung and liver parenchyma as much as possible without allowing intra operative spillage, and minimizing the complications, recurrence, morbidity, and mortality (Manucher Aghajanzadeh *et al.*, 2008; Kilani *et al.*, 2001; Pedrosa *et al.*, 2000).

In this study we tried to use conservative surgical procedures such as: aspiration, cystostomy, evacuation and external drainage; however, cysts size and location, the possible complications, and surgeons experience also influenced our operation approach. In this regard, our approach for the cysts of posterior segment of liver was posterolateral thoracotomy, which was a simple way to access to those cysts (Manoucher Aghajanzadeh *et al.*, 2014; Manucher Aghajanzadeh *et al.*, 2008; Symeonidis *et al.*, 2013). However, according to the recent studies total pericystectomy and liver resections for the complicated types of the liver Cysts are mostly preferred due to its lower recurrence rates (Chautems *et al.*, 2005). In this study we preferred the open surgery method for the complicated ones, and we did not use radical surgery because of its higher mortality and morbidity than conservative surgical procedures (Manouchehr Aghajanzadeh, Glali, *et al.*, 2018;

Manucher Aghajanzadeh *et al.*, 2008; Chautems *et al.*, 2005; Symeonidis *et al.*, 2013).

Intraperitoneal perforation of the liver cysts, which occurred in 4 patients in our study, is one of the most dangerous complications. In addition, abdominal traumas have been considered as a predisposing factor particularly for the large and superficial cysts of the inferior part of the liver (Manouchehr Aghajanzadeh, Glali, *et al.*, 2018). The most frequent clinical manifestations are acute abdomen, skin rash, and anaphylactic shock, although some patients would not experience any symptoms, which may lead them to dissemination and secondary abdominal echinococcosis (Manouchehr Aghajanzadeh, Glali, *et al.*, 2018; Chautems *et al.*, 2005; Symeonidis *et al.*, 2013). In this way, our approach to prevent the recurrence included laparotomy and removal of the whole cysts plus profuse peritoneal irrigation with scolicidal agents such as povidone iodine 10%; however, hypertonic sodium chloride has been used in a few studies (Symeonidis *et al.*, 2013).

Another reported complication is intrabiliary perforation of the liver cysts with an incidence rate of 1% to 25% (Agayev & Agayev, 2008; Manouchehr Aghajanzadeh, Glali, *et al.*, 2018; Chautems *et al.*, 2005; Dadoukis, Gamvros, & Aletras, 1984; Erzurumlu *et al.*, 2005; Karydakos *et al.*, 1994; Pedrosa *et al.*, 2000). Cystobiliary could cause infection subsequently (Agayev & Agayev, 2008; Kabiri, El Maslout, & Benosman, 2001; Vakhidov, Il'khamov, Strusskiĭ, & Azat'ian, 1998) and the clinical presentation of this infection includes fever, chills, sepsis, and growing pain (Symeonidis *et al.*, 2013). The diagnosis could be made either preoperatively or intraoperatively through bile staining the cyst contents (Agayev & Agayev, 2008; Manouchehr Aghajanzadeh *et al.*, 2021; Manouchehr Aghajanzadeh, Glali, *et al.*, 2018; Chautems *et al.*, 2005; Pedrosa *et al.*, 2000; Symeonidis *et al.*, 2013). Patients with cystobiliary communication could be classified in two groups of symptomatic and asymptomatic (Manouchehr Aghajanzadeh *et al.*, 2021; Dadoukis *et al.*, 1984; Erzurumlu *et al.*, 2005; Murtaza *et al.*, 2008). In our study, 52 cases were symptomatic while only 9 cases were asymptomatic. In this study, most of the silent cases were the ones who had intrabiliary rupture in small bile ducts similar to the previous studies. On the other hand, perforations which involved the larger ducts may result in obstructing the biliary tree and jaundice consequently

(Manouchehr Aghajanzadeh *et al.*, 2021; Delshad *et al.*, 2016; Murtaza *et al.*, 2008; Symeonidis *et al.*, 2013). We detected 4 patients presented with obstructive jaundice in our study. Various methods such as: radical surgical resections, operative conservative interventions, medical therapy with anti-helminthic agents, and drainage after sterilization visualized ultrasonography have been recommended in this regard (Manucher Aghajanzadeh *et al.*, 2008; Sotiraki & Chaligiannis, 2010; Symeonidis *et al.*, 2013).

In spite of various available therapies recurrence still remains as one of the major problems in the management of HD, which has been reported 4.6% to 22.0% in different series (Agayev & Agayev, 2008; Manucher Aghajanzadeh *et al.*, 2008; Sotiraki & Chaligiannis, 2010; Symeonidis *et al.*, 2013). In our study the rate of recurrence was 16%, regardless of the type of intervention. The main reasons for recurrence appeared to be microscopic spillage of live parasites, failure to remove all viable cysts at inaccessible or difficult locations, or leaving a residual cyst wall at the initial operation. The latter was especially true among the patients with long-standing active cysts, where there may have been penetration through the original pericyst.

Recurrence detected during the early postoperative period is indicative of inadequately treated cysts in the first operation (Manouchehr Aghajanzadeh *et al.*, 2021; Chautems *et al.*, 2005; Kapan, Kapan, Goksoy, Perek, & Kol, 2006; Pawłowski *et al.*, 2001). However, recurrence has never been found following the complete resection of an intact cyst with radical surgical interventions when feasible (Manouchehr Aghajanzadeh *et al.*, 2021; Mottaghian & Saidi, 1978; Murtaza *et al.*, 2008; Pawłowski *et al.*, 2001). Our results are in line with these reports, since statistical analysis indicated that the most important determinants for recurrence of hydatid cysts were rupture and minute spillage of the hydatid cyst, missing the cysts pre- or intraoperatively and incomplete pericystectomy.

These findings show radical excision may be the best treatment for hydatid disease. However, there is a trade-off between a low recurrence rate and increased mortality associated with the procedure (Agayev & Agayev, 2008; Kapan *et al.*, 2006; Murtaza *et al.*, 2008; Pawłowski *et al.*, 2001; Prousalidis *et al.*, 2012). In our clinic, we do not usually perform radical excisions,

which entail increased mortality, for such nonmalignant disease. On the other hand, when performing conservative surgery, we emphasize avoiding spillage and removing all cyst contents.

The confirmation of therapeutic efficacy is difficult since recurrences may develop many years later, the onset is frequently asymptomatic and clinical evaluation, even supplemented by serum liver tests and serologic tests, may not be diagnostic (Pedrosa *et al.*, 2000; Vakhidov *et al.*, 1998). Thus, the postoperative follow-up period should be at least 4 years and continued as long as possible (Chautems *et al.*, 2005; Pedrosa *et al.*, 2000; Prousalidis *et al.*, 2012). In our series, follow-up of at least 4 years was considered to be complete in 8 years.

Blood titers did not return to normal values soon after the operation, therefore positive serologic tests were not significant for the diagnosis of the recurrence, which had to be confirmed by ultrasonography or CT. Differentiation of remaining cavities of effectively treated cysts from locally recurrent disease was difficult, therefore we relied on the accepted imaging marker of the increase in size of the cyst on serial examination, which has been proved to be effective (Agayev & Agayev, 2008; Manouchehr Aghajanzadeh *et al.*, 2021; Pawłowski *et al.*, 2001; Prousalidis *et al.*, 2012).

We routinely used CT for the patients in whom a second operation was planned to reveal the nature of the cyst, association with the biliary system, vascular structures and related organs as well as to demonstrate the extent of compensatory hyperplasia (Agayev & Agayev, 2008; Manouchehr Aghajanzadeh *et al.*, 2021; Prousalidis *et al.*, 2012). The choice of operation (radical or conservative) was based on cyst location, size, morphology, complications (infection or biliary obstruction), prior treatment and presence of technical difficulties owing to adhesions. The fact that appropriate primary treatment had failed owing to "vitality" of the parasite suggested that more radical treatment might be indicated. In patients with recurrence after evacuation of cyst contents, complete cyst resection could appear to be reasonable, so long as it would be done safely. However, these radical operations are technically more difficult, and reoperations have higher morbidity and mortality rates (Manouchehr Aghajanzadeh, RasoulHerfatkar, FarzadGhotbi, Mohtasham, & Mosafaiee, 2018; Pawłowski *et al.*, 2001; Prousalidis *et al.*, 2012).

Recurrence itself appeared to increase technical difficulties due to adhesions in the secondary operations. This finding is in line with other reported mortality rates of 10% (Kapan *et al.*, 2006; Mottaghian & Saidi, 1978; Pawłowski *et al.*, 2001). Therefore, in most recurrent cases, we preferred conservative treatment (repeat evacuation with or without partial cystectomy).

Satisfactory pulmonary long-term palliation was attained and was preferable to the likelihood of mortality subsequent to excessively enthusiastic attempts at a complete cure with radical excisions. Complications, such as infection or biliary obstruction, were treated first. Moreover, unlike recurrent malignant disease, recurrent hydatid disease progresses slowly and is rarely life-threatening, therefore not all patients have to be treated (Manouchehr Aghajanzadeh, RasoulHerfatkar, *et al.*, 2018; Kapan *et al.*, 2006; Pawłowski *et al.*, 2001; Prousalidis *et al.*, 2012). In our series, 1 patient of advanced age with local recurrence and serious comorbid diseases and 1 asymptomatic patient with intrahepatic recurrence in a difficult location were followed expectantly and would be treated only for complications.

CONCLUSION

The management of patients with recurrent hydatid disease is difficult and should be carried out in centers familiar with hepatic and pulmonary hydatid cyst surgery. To diffract remnant cavity of the first surgery from the recurrence, is very difficult, Thus, CT-scan and ultra-sonography can help for diagnosis. For prevention of recurrences chemoprophylaxis, avoiding intraoperative spillage and total removal of hydatid cyst element from difficult location is recommended. Puncture, Aspiration, Injection, and Re-aspiration (PAIR) inactivation plus chemotherapy as well as treatment by laparoscopic thoracoscopic approach and use of intraoperative ultra-sonography seem reasonable to apply in patients with recurrent hydatid disease. We did not make use of these modern methods in our cases.

Conflicts of Interest: The authors declare no conflict of interest.

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