

## Liver cystic echinococcosis in humans – a study of 30 cases

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### Summary

The aim of this study is to demonstrate the clinical manifestations and diagnostic approach to liver hydatid disease and suggest its treatment. The prospective study was carried out on 30 patients with liver hydatidosis. Hepatologic examinations were based on: medical history, physical examination, biochemical and serological tests, ultrasonography and computed tomography scanning. Twenty-five (83.3 %) patients underwent radical cyst resection, while in 5 (16.7 %) cases liver resection with left lobectomy was also performed. Hydatid cyst was histopathologically verified in all the patients. Our results showed that the patients with multiple cysts had impaired functional liver tests significantly more often than patients with unilocular cyst. In addition, ultrasonography and computed tomography scans are the valid imaging procedures in diagnosis. Radical, surgical resection of hepatic hydatid cysts is the goal of treatment.

**Key words:** *Echinococcus granulosus*; liver; humans; diagnostic; treatment

### Introduction

*Echinococcus granulosus* and *Echinococcus multilocularis* are important zoonotic pathogens that cause serious diseases in humans and animals. Infections with *Echinococcus vogeli* (jaguar tapeworm) and *Echinococcus oligarthrus* (puma tapeworm) are rare and occur only in South America (Kammerer *et al.*, 1994). Additionally, molecular studies have revealed a number of diverse genetic strains of *E. granulosus*. Until now, eight distinct genotypes (G1 – G8) have been identified (Bowels & McManus, 1993; Thompson & McManus, 2002).

The adult tapeworms, a few millimetres in length, live in the small intestine of their final host, which are mainly dogs for *E. granulosus*, and foxes for *E. multilocularis*.

Embryonated eggs of the parasites are shed into the environment in the faeces of the final host and represent the infective stage for intermediate hosts, which commonly are numerous ungulates and ruminants for *E. granulosus* and rodents for *E. multilocularis*. These eggs contain an oncosphere that is activated during its passage through the stomach and intestine, and penetrates the intestinal wall to reach the lymphatic and blood vessels. They are preferentially targeted to the liver, where they transform into the metacestode (or cystic) stage. Metacestodes are fluid-filled vesiculated larval parasites, delineated by the parasite tissue (germinal layer), and completely surrounded by an acellular laminated layer of variable thickness. Both species of genus *Echinococcus* can develop this way in humans, that can act as hosts, by a differentiation process taking place within the germinal layer of these parasites, numerous protoscolices are formed, which, when ingested by the final host, again give rise to the adult worms (Thompson & Lymbery, 1995).

The aim of this study was to demonstrate the clinical manifestations and diagnostic approaches to liver hydatid disease and to suggest treatments.

### Material and Methods

The prospective study was carried out on 30 patients with liver *E. granulosus*, examined and treated during January – November 2006 at the Institute of Digestive Diseases, Clinical Center of Serbia, Belgrade.

Hepatologic examinations were based on: medical history, physical examination, laboratory and serological tests. Laboratory tests included: hepatocyte integrity (levels of aminotransferases), cholestasis (levels of bilirubin, alkaline phosphatase and serum gamma-glutamyl transpeptidase) and synthetic liver function (serum albumin and prothrombin time). Laboratory parameters were tested on VITROS

350 analyzer, Ortho-Clinical, using standard procedure: bilirubin (Jandrasik-Groff), aminotransferases (IFCC/SFBC), alkaline phosphatase (p-NPP, AMP (2-amino-2-methyl-1-propranol buffer) gamma-glutamyl transpeptidase (gamaglutamil-4-nitroanilidin).

Enzyme-linked immunosorbent assay (ELISA) was used for diagnosis of *E. granulosus*. The assay was done manually. IgG antibody in serum was detected with anti-human IgG-alkaline phosphatase conjugate. After incubation and washing, the absorbance was read on an Elisa reader, Behring.

Morphological studies included real-time and duplex Doppler ultrasonography on Toshiba Core Vision SSA-350A with 3.75 MHz sector duplex probe. The computed tomography scanning (CT scans) was performed as the next step after ultrasound diagnosis had been made. The following morphological parameters were analyzed: number, segmental location and diameters of the cyst. Using the prolate ellipse volume calculation (height x length x width x Pi/6) ultrasonography cyst volume was determined (Park *et al.*, 2000).

Chest x-ray radiography, was performed in all patients.

After establishing diagnosis, radical surgical resection of hepatic hydatid cyst/s was performed, including liver resection, pericystectomy or cystectomy.

Additionally, each specimen of the resected liver and cyst was histopathologically analyzed after staining by H&E. Statistical analyses were performed using (Basic Statistic Software)  $\chi^2$  (Yates corrected) -test.

## Results

The study included 18 (60 %) female and 12 (40 %) male patients. A total of 17 (56 %) patients came from the rural areas while 13 (44 %) were from the urban ones. The patients were aged 47 years on average (min = 19; max = 75; SD  $\pm$  16).

The most frequent symptom, nonspecific right upper abdominal pain, was present in 18 (60 %) patients, followed by right upper abdominal pain with vomiting in 3 (10 %) patients. Occasional episodes of urticaria were evidenced in 3 (10 %) patients, accompanied by asthma-like symptoms. Nine patients (30 %) were symptomless, and the disease was detected incidentally by abdominal ultrasound examination.

Functional liver tests indicated mildly increased levels of alkaline phosphatase and serum gamma-glutamyl transpeptidase in 8 (26.6 %) patients, associated with mild increase of aminotransferases in two cases. The levels of bilirubin and liver synthetic function were all normal. Additionally, the patients with multiple cysts had impaired functional liver tests significantly more often than patients with unilocular cyst ( $\chi^2$  (Yates corrected) test = 4.66;  $p < 0.05$ ).

The ELISA test was positive in only 19 (63.3 %) patients. In this group 6 patients had multiple cysts and 13 patients unilocular cysts. In the group with negative serology 7 patients had a unilocular cyst and 4 patients had multiple cysts. Statistically no significant difference was found bet-

Table 1. Characteristics of patients with liver echinococcosis

Characteristics	Patients N = 30
Gender	
Male	12 (40 %)
Female	18 (60 %)
Age	47 $\pm$ 16
ELISA	
Positive	19 (63.3 %)
Negative	11 (26.7 %)
Liver cysts location	
V segment	27.7 %
VII segment	27.7 %
VIII segment	22 %
Left lobe	13.8 %
Cyst volume	49.03 $\pm$ 023 ccm <sup>3</sup>
Surgery	
Cyst resection	25 (83.3 %)
Left lobectomy	5 (16.7 %)

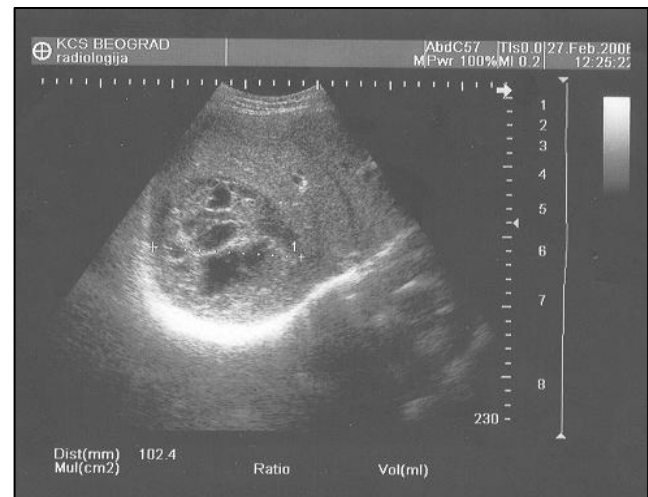


Fig. 1. Ultrasonography showed in the projection of the right liver lobe heteroechoic hydatid cyst

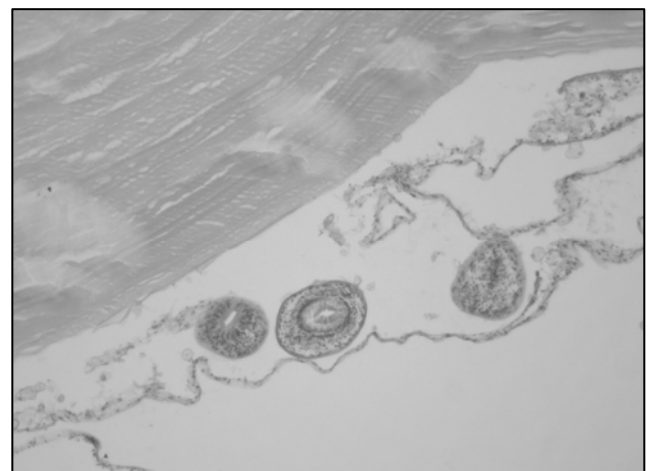


Fig. 2. Histopathological analysis of echinococcus cyst showed the germinative membrane with scolices (H&E, magnification 112x)

ween group with positive and negative ELISA tests with regard to their number of cysts ( $\chi^2 = 2.92$ ,  $p = 0.0877$ ).

Ultrasonography (Fig. 1) and CT examinations confirmed that the majority of the patients (67 %) had one cyst, while the remaining 10 (33 %) had two and/or more cysts, up to maximum number of seven evidenced in one patient. The hydatid cysts were most frequently located in the V (27.7 %), VII (27.7 %) and VIII (22 %) segments of the right lobe, while the left liver lobe was affected in 13.8 %. The average cyst volume was 49.03 ccm<sup>3</sup> (min = 6.28; max = 150.72; SD  $\pm$  0.23). Chest x-ray radiography, confirmed hydatid cysts in lungs in 3 (10 %) patients.

Twenty-five (83.3 %) patients underwent radical cyst resection, pericystectomy or cystectomy, while in 5 (16.7 %) cases liver resection with left lobectomy was also performed (Basic characteristics of patients are showed in table 1). Hydatid cyst was histopathologically verified in all of the patients (Fig. 2).

## Discussion

In humans, the liver is the organ most frequently affected by *E. granulosus* (55 % to 93 % of patients) (Amr *et al.*, 1994; Canda *et al.*, 2003). Another common site of *Echinococcus* cysts localization includes the lungs (5 % to 16 %) and the liver together with the lungs can be affected simultaneously in about 5 – 13 % of cases. However, cysts may also affect other locations, including the brain, the spleen, soft tissues, bones and the spinal extra-dural space (Gómez *et al.*, 1995; Anthi *et al.*, 2004; Kir *et al.*, 1995).

In our study, simultaneous occurrence in the liver and lungs was confirmed in 3 (10 %) patients.

Hepatic cysts may exist as long as 20 years before becoming large enough to be visible or cause pressure-related problems such as pain, nausea, cirrhosis, and other manifestations of liver disease. The most frequent symptoms are the following: increasing intra-abdominal pressure and increasing abdominal volume (Kumar *et al.*, 2003).

Many patients with *Echinococcus* infections are asymptomatic, especially in the early stages. Additionally, right upper abdominal pain due to the mass effect of the enlarging cyst, is the most characteristic symptom. Pain may be intermittent or continuous, gradually increasing over a long period of time. Malaise, anorexia and abdominal distension are the accompanying symptoms.

The most frequent symptoms evidenced in our study included nonspecific right upper abdominal pain, right upper abdominal pain with vomiting were less frequently. Nine patients were symptomless, and they were diagnosed incidentally after abdominal ultrasound examination.

Anaphylactic shock due to spontaneous or traumatic cyst rupture or during surgery is a rare and severe complication. The patients may die when diagnosis is not recognized, appropriate treatment is not immediately at hand or anaphylaxis is refractory to treatment (Yahya *et al.*, 1997; Mooraki *et al.*, 1996). In addition, urticaria, asthma-like symptoms, fever, and itching may occur as a response to the *Echinococcus* antigen in cyst fluid (Losanoff *et al.*, 2002).

In our study, occasional episodes of urticaria were evidenced in 3 (10 %) patients, out of whom one had skin changes accompanied by asthma-like symptoms.

Seeding of cyst content into the peritoneal cavity is a serious secondary complication of cyst rupture. Viable protozoa may develop in the new hydatid cysts causing substantial morbidity in the future (King, 2000).

Cysts may become infected following bacteremia or via communicating bile ducts, especially when endoscopic retrograde cholangiopancreatography has been performed. These patients present with high fever, sepsis syndrome and a tender liver (King, 2000).

Rupture into the biliary tree typically occurs with larger cysts containing multiple daughter cysts. Association of hepatic hydatid cyst with bile duct obstruction is not a common occurrence. In the countries where the hydatid disease is common, the reported incidence of intrabiliary rupture varies from 5 – 17 % of the cases with hepatic involvement (Kattan, 1977; Barros, 1978). Because these symptoms mimic those characteristic for obstructing bile stones, the diagnosis of intrabiliary rupture is easily overlooked (Mathur *et al.*, 1983).

In our series, communication of the hydatid cyst with the biliary tree was surgically verified in two patients, however, neither biliary obstruction nor cyst infection developed.

Less threatening complications are related to the mass effect of the cyst, and include compression of the bile ducts and portal or hepatic veins. This may result in obstructive jaundice, post obstructive cholangitis, and impaired blood flow in the portal and hepatic veins (Perišić *et al.*, 1997; Magistrelli *et al.*, 1991).

The diagnosis is based on: history and geography, imaging, and serology. If the ultrasonography and CT scans shows a cyst regardless of confirmation by serology the diagnosis should be made.

Ultrasonography is the preferred diagnostic tool for hepatic hydatid cysts. It is easily available, cost-effective, and used to classify cysts and assess their viability (Gharbi *et al.*, 1981). CT is usually the next step after an ultrasound diagnosis has been made. The main purpose of CT is to visualize the relation between the hydatid cyst and the surrounding liver tissue, bile ducts, and portal and hepatic veins, and to identify its segmental location.

Several serological tests are specific to hydatidosis and are used to confirm the diagnosis. Enzyme-linked immunoelectrotransfer blot, where available, is the test of choice. In some studies, it has greater than 95 percent sensitivity and specificity (Hunter & Strickland, 2000; Garcia & Bruckner, 2001). In addition, ELISA has up to 84 percent sensitivity (Mandell *et al.*, 2000). It has been reported that the detection of specific IgG1 and IgG4 serum antibodies to echinococcosis can enhance the specificity of ELISA (Shambesh *et al.*, 1997; Mandell *et al.*, 2000).

As opposed to previous reports, in our series the ELISA test, showed low sensitivity. Probably, due to manual ELISA performance, the procedure required more incubation and washing levels.

Complete surgical resection of hepatic hydatid disease should be attempted whenever possible. The ultimate goal of treatment is to eliminate the germinal layer, although the hydatid cyst itself and its mass effect on the surrounding liver tissue assume prominence. The core principles of hydatid surgery are firstly, total removing all infectious parts of a cyst; and secondly, avoiding of intra-abdominal spillage of the cyst contents. Additionally, radical surgical resection (liver resection, pericystectomy, and cystectomy) is the best way of preventing intra-abdominal spillage (Chautems *et al.*, 2003; Waghlikar & Skiora, 2001).

All the patients from our series underwent radical cyst resection, pericystectomy or cystectomy, however, in 5 cases, liver resection, left lobectomy, was also performed. In two cases, liver surgery was preceded by surgery of the hydatid lung cyst.

The recurrence rate of this disease is still relatively high, being approximately 10 %. The risk of recurrence seems to be increased after incomplete resection when compared to complete removal. Recurrence will become symptomatic 3 – 4 years after surgery (Kune & Morris, 1989).

Surgical re-intervention was performed in one patient from our series, due to the recurrence of hydatid liver cyst, which developed after 16 years.

## References

- AMR, S. S., AMR, Z. S., JITAWI, S., ANNAB, H. (1994): Hydatidosis in Jordan: an epidemiological study of 306 cases. *Ann. Trop. Med. Parasitol.*, 88: 623 – 627
- ANTHI, A., KATSEKOS, C., GEROGOPOULOU, S., MANDRAGOS, K. (2004): Massive rupture of a hepatic hydatid cyst associated with mechanical ventilation. *Anesth. Analg.*, 98: 796 – 797
- BARROS, J. L. (1978): Hydatid disease of the liver. *A. J. Surg.*, 135: 597 – 600
- BOWELS, J., MCMANUS, D. P. (1993): NADH dehydrogenase 1 gene sequences compared for species and strains of the genus *Echinococcus*. *Int. J. Parasitol.*, 23: 969 – 972
- CANDA, S., GÜRAY, M., CANDA, T., ASTRACIOGLU, H. (2003): The pathology of echinococcus and the current *Echinococcus* problem in western Turkey - A report of pathologic features in 80 cases. *Turk. J. Med. Sci.*, 33: 369 – 374
- CHAUTEMS, R., BUHLER, L., GOLD, B., CHILCOTT, M., MOREL, P., MENTHA, G. (2003): Long term results after complete or incomplete surgical resection of liver hydatid disease. *Swiss. Med. Wkly.*, 133: 258 – 262
- GARCIA, L. S., BRUCKNER, D. A. (2001): Tissue cestodes: larval forms. In WASHINGTON, D. C (4<sup>th</sup> Ed): *Diagnostic medical parasitology*. ASM Press, 387 – 403
- GHARBI, H. A., HASSINE, W., BRAUNER, M. W., DUPUCH, K. (1981): Ultrasound examination of the hydatid liver. *Radiol.*, 139: 459 – 463
- GÓMEZ, R., MORENO, E., LOINAZ, C., DE LA CALLE, A., CASTELLON, C., MANZANERA, M., HERRERA, V., GARCIA, A., HIDALGO, M. (1995): Diaphragmatic or transdiaphragmatic thoracic involvement in hepatic hydatid disease: surgical trends and classification. *World. J. Surg.*, 19: 714 – 719
- HUNTER, G. W., STRICKLAND, G. T. (2000): *Hunter's Tropical medicine and emerging infectious diseases*. 8<sup>th</sup> Ed. Philadelphia: Saunders, 866 – 876
- KAMMERER, W. S., SCHANTZ, P. M. (1994): Echinococcal disease. *Inf. Dis. North. Am.*, 7: 605 – 618
- KATTAN, Y. B. (1977): Intrabiliary rupture of hydatid cyst of liver. *Ann. Roy. Coll. Surg. Eng.*, 59: 108 – 114
- KING, C. (2000): *Cestodes (tapeworms)*. In MANDELL, G., BENNETT, J. and DOLIN, R. (Eds.): *Principles and practices of infectious diseases* (5<sup>th</sup> Ed.). New York: Churchill Livingstone
- KIR, A., BARAN, E. (1995): Simultaneous operation for hydatid cyst of right lung and liver. *Thorac. Cardiovasc. Surgeon.*, 43: 62 – 64
- KUMAR, M. J., TOE, K., BANERJEE, R. D. (2003): Hydatid cyst of liver. *Postg. Med. J.*, 79: 113 – 114
- KUNE, G. A., MORRIS, D. I. (1989): *Hydatid disease*. In: Schwasyz & Ellis, eds. *Maingot's Abdominal Operations*, 9<sup>th</sup> Edn. Appleton & Lange
- LOSANOFF, J. E., JONES, J. W., RICHMAN, B. W. (2002): Percutaneous drainage for liver hydatid cyst. *Can. J. Surg.*, 45: 69 – 70
- MAGISTRELLI, P., MASETTI, R., COPPOLA, R., MESSIA, A., NUZZO, G., PICIOCCHI, A. (1991): Surgical treatment of hydatid disease of the liver a 20-year experience. *Arch. Surg.*, 126: 518 – 522
- MANDELL, G. L., DOUGLAS, R. G., BENNETT, J. E., DOLIN, R. (2000): In MANDELL, DOUGLAS and BENNETT'S (5<sup>th</sup> Ed.): *Principles and practice of infectious diseases*. Philadelphia: Churchill Livingstone, 2956 – 2965
- MATHUR, S. K., SHAH, R. R., SAMSI, A. B., KELKAR, M. D. (1983): Hydatid cyst as a cause of common bile duct obstruction (a case report). *J. Postgrad. Med.*, 29: 262 – 266
- MOORAKI, A., RAHBAR, M. H., BASTANI, B. (1996): Spontaneous systemic anaphylaxis as an unusual presentation of hydatid cyst: report of two cases. *Am. J. Trop. Med. Hyg.*, 55: 302 – 303
- PARK, S. B., KIM, J. K., CHOI, S. H., NOH, H. N., JI, E. K., CHO, K. S. (2000): Prostate volume measurement by TRUS using heights obtained by transaxial and midsagittal scanning: comparison with specimen volume following radical prostatectomy. *Kor. J. Radiol.*, 5: 110–113.
- PERIŠIĆ, M., ČULAFIĆ, DJ., SAGIĆ, D., STOJKOVIĆ, M., ČOLOVIĆ, R. (1997): Syndroma inferior caval vein and portal hypertension caused by large liver echinococcus cyst. *Arch. Gastroenterohepatol.*, 16: 47 – 51
- SHAMBESH, M. K., CRAIG, P. S., WEN, H., ROGAN, M. T., PAOLILLO, E. (1997): IgG1 and IgG4 serum antibody response in asymptomatic and clinically expressed cystic echinococcosis patients. *Acta. Trop.*, 64: 53 – 63
- THOMPSON, R. C. A., MCMANUS, D. P. (2002): Towards a taxonomic revision of the genus *Echinococcus*. *Trends. Parasitol.*, 18: 452 – 457
- THOMPSON, R. C. A., LYMBERY, A. J. (1995): *Echinococcus and Hydatid Disease*. Wallingford, Oxon, UK, CAB International

WAGHOLIKAR, G. D., SIKORA, S. S. (2001): Surgical management of liver hydatid. *Trop. Gastroenterol.*, 22: 159 – 162  
YAHYA, A. I., PRZYBYLSKI, J., FOUAD, A. (1997): Anaphylactic shock in a patient with ruptured hydatid liver cyst owing to trivial abdominal trauma. *J. R. Coll. Surg. Edinb.*, 42: 423 – 424

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