Short Report: Primary Super-Infection of Hydatid Cyst—Clinical Setting and Microbiology in 37 Cases

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Abstract. The clinical and microbiological characteristics of super-infected hydatid cysts are described. In our cohort, 7.3% of 503 patients had a super-infected cyst. Four patients developed severe sepsis, and two of them died. *Escherichia coli*, viridans group streptococci, and *Enterococcus* species in liver cysts and *Aspergillus fumigatus* in lung cysts were the microorganisms most frequent involved.

INTRODUCTION

Human hydatidosis caused by *Echinococcus granulosus* is a zoonotic infection. There are areas where this infection is highly endemic, such as South America, China, Africa, and European Mediterranean countries.¹ In a recent survey in our area, the incidence in humans was 12 per 100,000 inhabitants per year in the 1996–2003 period.² Seroprevalence in the same region was above 2%.³

Cystic echinococcosis is usually asymptomatic. However, it can clinically manifest as a complicated cyst. The most frequent complication is compression or rupture of pericystic structures.^{4–6} Another important complication is a hypersensitivity reaction caused by circulating immune complexes or by the activation of an alternative complement pathway, which give rise to glomerulonephritis or an anaphylactoid reaction, respectively.^{7–9} Finally, the cyst can become super-infected by other microorganisms. Bacterial and fungal infections have been described in case reports or in small series with a limited number of patients.^{10,11} This article's aim is to describe the frequency, clinical setting, and microbiology of super-infected hydatid cysts.

MATERIALS AND METHODS

The design was an observational retrospective study. We reviewed the medical records of all patients with a diagnosis of echinococcosis from January 1996 to December 2007 in the University Hospital of Salamanca, a tertiary care hospital for a population of about 350,000 in western Spain.

Definitive diagnosis was considered in the following circumstances: (i) positive culture of bacterial or fungal pathogens from drainage samples, or (ii) surgical or percutaneous drainage of purulent material from the cyst and growth of the organism in blood cultures. Probable diagnosis was defined by surgical or percutaneous drainage of purulent material and one of the following: (i) clinical data of systemic inflammatory response, or (ii) radiological settings suggestive of hydatid cyst infection.¹² Patients with previous percutaneous or surgical intervention were excluded.

The BACTEC 9240 blood-culture system (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD) with a standard aerobic and anaerobic medium was used in all blood samples. Surgical samples were processed for both aerobic and anaerobic cultures. In the histochemical study, Grocott's methenamine silver or periodic acid Schiff was only used when the tissue biopsy was suspected of having *Aspergillus* co-infection.

Statistical tests were carried out using the SPSS Statistical Package (SPSS Inc., Chicago, IL). The results are expressed as means, SDs, and percentages. Fisher's exact test was used for evaluation of the association between microbial diagnosis and localization of complicated hydatid cyst.

RESULTS

Five hundred and three patients were newly diagnosed of hydatidosis between 1996 and 2007. Of these patients, 37 (7.3%) had a primary super-infection of a hydatid cyst (Table 1) that was hepatic in 24 (64.9%) cases, thoracic in 11 (29.7%) cases, and in other localizations (vertebral, muscle, and pleuro-costal) in 2 (5.4%) cases. In eight patients (21.6%), other hydatid cysts were found besides the infected one. The mean age was 55.4 ± 18.1 years, and 62.2% were male.

The most frequent symptoms and signs in these 37 patients were fever (75.7%) and localized pain (64.9%). Only one (2.7%) patient presented as an anaphylactoid reaction with angioedema. Four patients (10.8%) developed severe sepsis, and two (5.4%) died. In three cases, infection was documented after programmed surgery in an asymptomatic patient. It is noteworthy that two (66.6%) of these patients had thoracic hydatid disease, and *Aspergillus fumigatus* was the responsible microorganism. Leukocytosis ($> 12 \times 10^3/\mu\text{L}$) and eosinophilia ($> 450/\mu\text{L}$) were detected in 37.8% and 30.6% of patients, respectively.

Only five (13.5%) patients had classic risk factors for infection: three were diabetic, one received steroids, and one had a hepatocellular carcinoma.

Diagnostic image findings suggested the diagnosis in 31 of 37 (83.8%) patients. Average size of the super-infected cysts was 10.0 ± 5.8 cm. In the patients with ultrasonographic testing (US), the most frequently detected type (International Classification; Ultrasonographic Testing of World Health Organization [US WHO]) was CE2 (15 patients; 55.5%) followed by CE5 (6 patients; 22.2%) and CE3 and CE4 (3 patients each; 11.1%). Patients were treated with cyst drainage and

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TABLE 1

Demographic and clinical data with super-infection hydatid cyst patients

Variable	
Patients (n)	37.0
Age (mean $\pm$ SD; years)	55.4 $\pm$ 18.1
Male (%)	62.2
Clinical setting (%)	
Fever	75.7
Pain	64.9
General syndrome	27.0
Leukocytes count (mean $\pm$ SD; cells/mL)	1,2167.0 $\pm$ 9010.0
Eosinophil count (mean $\pm$ SD; cells/mL)	400.7 $\pm$ 565.9
Eosinophilia (%)	30.6
Positive serological echinococcus (%)	75.6
Location of cyst echinococcus super-infected (%)	
Liver	64.9
Lung	29.7
Other	5.4
Average size (mean $\pm$ SD; cm)	10 $\pm$ 5.8
WHO classification (%)*	
I	–
II	55.5
III	11.1
IV	11.1
V	22.2

*WHO International classification of ultrasound images in cystic echinococcosis.¹⁵

antimicrobial therapy. Drainage was done by surgery in most patients (36; 97.2%). Only one patient was treated by percutaneous aspiration (2.8%).

Microbiological diagnosis was achieved in 14 (58.3%) hepatic cysts versus 4 (36.4%) of those localized in the lungs (Odds ratio [OR] = 2.45; 95% CI = 0.5–10.6; P = 0.28). Table 2 shows the organisms identified and their distribution according to location of cyst echinococcus. We detected a higher frequency of bacterial infection in complicated hepatic cysts (14 patients; 58.3%) compared with those in other localizations (1 patient; 9.1%; OR = 14; 95% CI = 1.5–127.6; P = 0.028).

The most frequently identified microorganisms were *Escherichia coli* (4 cases), viridans group streptococci (3 cases), *Enterococcus* spp. (3 cases), and *Staphylococcus aureus* (2 cases). Polimicrobial infection was detected in three (8%) patients. *A. fumigatus* was isolated in three patients with a diagnosis of super-infected thoracic cysts.

DISCUSSION

In this work, we reviewed the medical records of patients diagnosed with cystic echinococcosis in our hospital during a 12-year period. As we have previously shown, there is still

TABLE 2

Organisms identified and their distribution according to the location of cyst echinococcus

Organism	Hepatic CE (n)	Thoracic CE (n)
<i>Escherichia coli</i>	4	–
<i>Acinetobacter baumannii</i>	1	–
<i>Aeromonas hydrophila</i>	1	–
<i>Klebsiella oxytoca</i>	1	–
<i>Pseudomonas aeruginosa</i>	1	–
Viridans group streptococci	3	1
<i>Enterococcus</i> species	3	–
<i>Staphylococcus aureus</i>	2	–
<i>Aspergillus fumigatus</i>	–	3
Definitive/all	16	4

CE = cyst echinococcus.

a high incidence of hydatidosis in western Spain,² and 503 patients had this diagnosis.

Previous reports have shown a rate of super-infection in cystic hydatidosis of 1–8% in recently diagnosed cases. None of them was specifically designed to study this complication, and inclusion criteria were not well-defined.^{12,13} In our work, we only included patients with definitive culture of bacterial or fungal pathogens or percutaneous drainage of purulent material from the cyst. Using these diagnostic criteria, we found cyst super-infection in 37 (7.3%) of the patients with a new diagnosis of hydatidosis. There is a selection bias in our cohort, because only hospital cases were included. Because outpatients were not considered, this 7.3% figure is probably an overestimate of the real incidence of cyst super-infection. Nevertheless, we can conclude that the super-infection is a frequent form of hydatid cyst presentation.

The super-infection probably occurs from sites next to the hydatid cyst (e.g., biliary or bronchial tree) or as a complication of bacteremia of any cause. Thus, a small rupture on the cyst's wall could induce infection of a thoracic hydatid cyst by the *Aspergillus* species. There is also evidence that abnormalities in the biliary tree are associated to pyogenic liver abscess. However, in our study, only one patient with a hepatic hydatid cyst had previous biliary disease. Therefore, it is probably the cyst itself that promotes the super-infection by the compression and distortion of the biliary tree. Bacteremia arising from a variety of sites is another possible origin of hydatid cyst super-infection. Classic risk factors for bacteremia, such as cirrhosis, cancer, diabetes mellitus, and steroid use, were found in five patients.

The different types of microorganisms involved according to the localization of the cyst and their clinical manifestations were another point of interest in our cohort. We found that patients with pulmonary cysts infected by *Aspergillus* spp. were asymptomatic at the diagnosis. Recently, Kocer and others,¹⁰ in a retrospective study, found that 2 of 100 patients with thoracic hydatidosis had super-infection caused by *Aspergillus* spp. Unlike our patients, who were asymptomatic, these two patients presented cough, hemoptysis, chest pain, and fever.

However, patients with bacterial super-infection had systemic inflammatory response. Four patients had severe sepsis, and two of them died of multiple organ dysfunction. This stresses the fact that hydatid cyst super-infection can be a main cause of mortality in cystic hydatidosis. The bacteria most frequently detected were Gram-positive cocci and Gram-negative bacilli, which is also the case in other pyogenic liver abscesses.

Non-complicated hydatidosis does not present with eosinophilia.¹⁴ High eosinophil levels in hydatid disease have been associated with cyst rupture and anaphylactoid reactions. The finding in our series that 30.6% of patients had eosinophilia above 450/ μ L suggests that cystic rupture accompanies cystic super-infection. Whether or not this rupture precedes and facilitates super-infection and whether or not this is a consequence cannot be concluded from our data.

Finally, 55.5% of super-infected cysts were type cystic echinococcosis 2 (CE WHO ultrasonographic classification).¹⁵ This result supports the theory that larval viability does not preclude cystic super-infection.

The high morbidity associated with hydatidosis caused by *E. granulosus* should be considered by public health authorities as a serious warning to implement adequate measures to eradicate canine teniasis.

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