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A retrospective study on the coexistence of hydatid cyst and aspergillosis

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KEYWORDS

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Summary

Objectives: Hydatid cyst is a zoonotic disease with an endemic regional distribution, and *Aspergillus* is a saprophytic fungus that may cause allergic pulmonary aspergillosis, aspergilloma, and semi-invasive and invasive aspergillosis. The coexistence of a saprophytic fungus and hydatid cyst is extremely rare. The aim of this retrospective study was to evaluate the coexistence of aspergillosis and echinococcosis in archival materials and to discuss its probable clinical significance.

Methods: Hematoxylin–eosin (HE)-stained sections of 100 archival cases with the diagnosis of hydatid cyst were reevaluated by four pathologists independently. Grocott's methenamine-silver (GMS) and periodic acid-Schiff (PAS) were applied to the slides that were suspected of having co-infection with *Aspergillus* to confirm the diagnosis.

Results: Two cases of aspergillosis and hydatid cyst coexistence were found out of the 100 reevaluated archival cases with a diagnosis of hydatid cyst. Both of the cases were located in the lung, in immunocompetent patients.

Conclusions: Aspergillosis and hydatid cyst coexistence may be important in patients with immune deficiency and in cases with pre- or perioperatively ruptured cysts. There are no reliable data on the specificity and sensitivity of radiological imaging techniques in detecting the existence of *Aspergillus* in hydatid cysts. Histopathological evaluation is essential for diagnosis and for the planning of management.

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Introduction

Hydatid cyst is a zoonotic disease most commonly caused by *Echinococcus granulosus*, while *Echinococcus multilocularis* is the most common type that causes pulmonary infection.

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Humans act as intermediate hosts and acquire the disease by ingesting the parasite eggs that are distributed into the environment via the feces of infected carnivores. Two of the major blood filtering organs, the liver and lungs, are most commonly involved, but infection may occur in any organ of the body.¹ Turkey is in one of the endemic regions for echinococcosis, and the disease is particularly common in the southeast of Turkey, which is the locality of our institution.

Aspergillosis is a saprophytic fungal infection. There are more than 100 species of *Aspergillus*, and of these only approximately 20 are pathogenic; *Aspergillus fumigatus* is the most common cause of aspergillosis in humans.² *Aspergillus* may cause allergic pulmonary aspergillosis, aspergilloma, and semi-invasive and invasive aspergillosis.² Immune suppression and structural pulmonary defects may predispose to this infection.

There are only a few case reports in the English literature on the coexistence of aspergillosis and echinococcosis.^{3–5} This retrospective study was designed to evaluate the coexistence of aspergillosis and any other mycosis in hydatid cysts in this endemic area, and to discuss the probable clinical significance of this coexistence.

Materials and methods

The archives of the Department of Pathology, Gaziantep University Medical School, were searched for cases that were diagnosed as hydatid cyst between the years 1999 and 2004. One hundred cases were included in the study, and all hematoxylin–eosin (HE)-stained slides of these cases were retrospectively reevaluated under light microscopy by four pathologists independently. The medical records of the selected patients were checked; age and sex of the patients, localizations of hydatid cysts, and radiological findings were noted. Histochemically, Grocott's methenamine-silver (GMS) and periodic acid-Schiff (PAS) were applied to the samples that were suspected to have *Aspergillus* co-infection, to confirm the diagnosis.

Results

Fifty-eight patients were female and 42 patients were male. Their ages ranged from 3 to 76 years, with a mean age of 34.6 years. The liver was the most common localization of the hydatid cyst (45%), followed by the lungs (42%), brain (6%), spleen (2%), gall bladder (2%), and soft tissue (2%). One case had multiple involvement, with one hydatid cyst in the liver and another in the spleen.

Aspergillus invading the hydatid cyst was found in two cases out of 100 and both of them were located in the lung (Figures 1–4). There was no co-infection with any other fungus in the remaining cases. None of the cases, including the two co-infected ones, were serologically evaluated for the presence of *Aspergillus* before or after the operations.

Discussion

Hydatid cyst is endemic in the Mediterranean countries, the Middle East, South America, the southern parts of Africa, Iceland, New Zealand, and Australia.¹ Turkey is amongst these countries. The most common localization is the liver

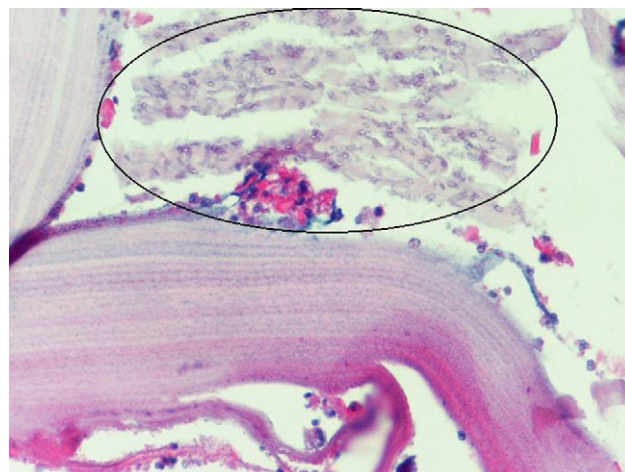


Figure 1 Photomicrograph revealing *Aspergillus* filaments (encircled) in hydatid cyst (HE $\times 200$).

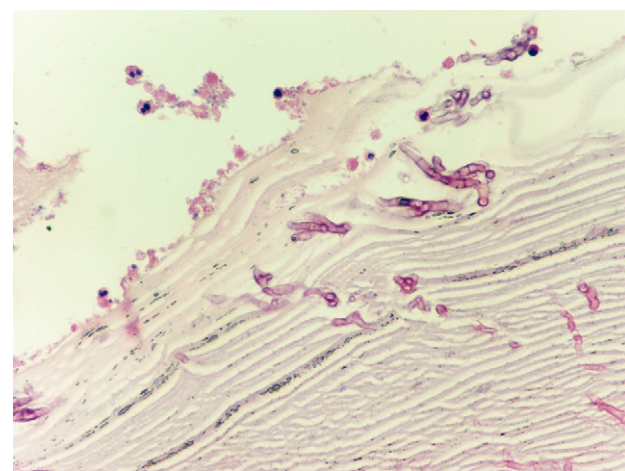


Figure 2 *Aspergillus* hyphae located in hydatid cyst accompanied by hooklets and a few eosinophils (HE $\times 400$).

(50–70% of all cases), and the lungs are the second most common site of involvement (20–30%).¹ In our study, 45% of the cases were located in the liver, while 42% were located in the lungs. Gender predilection and age distribution may vary

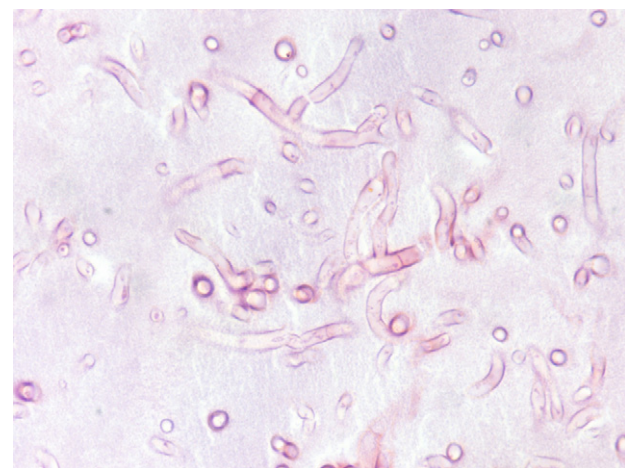


Figure 3 Septate filaments and conidia of *Aspergillus* (HE $\times 1000$).

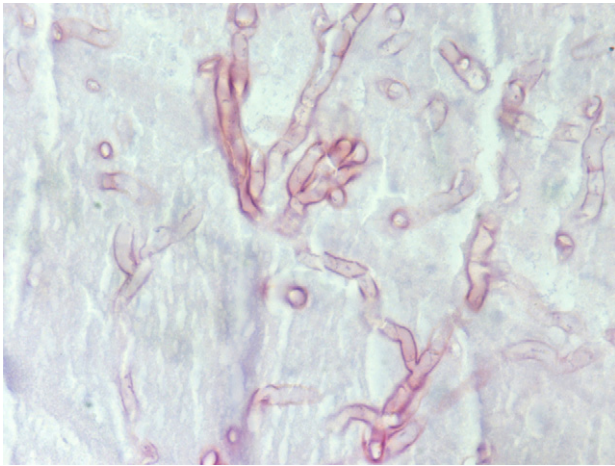


Figure 4 Aspergillus filaments branching with narrow angles (HE $\times 1000$).

from country to country due to lifestyle and habits. Fifty-eight of our cases were female, and the mean age of all cases was 34.6 years.

Aspergillus is a saprophytic fungus. Immune deficiencies and structural deformities of the lung are predisposing conditions for aspergillosis. Aspergillus is recognized in histologic sections with its septate filaments branching at 40° angles.² Aspergillus tends to invade the blood vessels, therefore the most common symptom in pulmonary aspergillosis is hemoptysis.⁶ However, killed hyphae of *Aspergillus fumigatus* have been shown to react with vascular endothelium resulting in vascular injury, so the presence of hemoptysis may not be an indicator of direct vascular invasion by the fungus.⁷ Also, a relationship between pulmonary aspergillosis and serum vascular endothelial growth factor (VEGF) levels has been shown.⁸

In our study, both of the patients who had aspergillosis co-infection with echinococcosis were admitted to the hospital with symptoms of cough, chest pain, hemoptysis, and fever. In the first patient, hemorrhagic foci in the right upper lobe were observed on bronchoscopic examination and Serratia was cultivated from the bronchial lavage. Hemoptysis persisted despite antibiotic treatment, and computed tomography (CT) revealed a lesion compatible with an 'infected hydatid cyst'. In the second patient, magnetic resonance imaging (MRI) revealed a lesion compatible with a 'complicated hydatid cyst'. The cyst was resistant to treatment with albendazole. Cystectomy and capitonnage were performed in both cases.

Although patients with immune deficiencies are prone to aspergillosis, the coexistence of Aspergillus and hydatid cyst has been reported in both immunocompromised and immunocompetent patients.^{3–5} Both of our patients were immunocompetent and no structural deformities of the lungs that may predispose to aspergillosis were found. Cryptococcosis is also reported to coexist with echinococcosis.⁹ We found neither Cryptococcus nor any other fungus except Aspergillus in this study. We also found no saprophytic mycoses, including Aspergillus, coexisting with hydatid cysts located in organs other than the lungs.

Both the number of cases reported in the literature and the results of this study verify the fact that the coexistence of Aspergillus and echinococcosis is rare, and also that

pulmonary echinococcosis leads to higher susceptibility to saprophytic fungal co-infection than echinococcosis located in other sites of the body.

The determination of the clinical significance of this coexistence is important for adequately managing these patients. Although radiological imaging procedures are highly accurate both in echinococcosis and aspergillosis,^{10,11} the sensitivity and specificity of imaging procedures in detecting the Aspergillus colonies entrapped in a hydatid cyst is not clear. One of our cases was reported as having an 'infected hydatid cyst' by CT and the other was reported as having a 'complicated hydatid cyst' by MRI.

A correlation between serum VEGF levels and aspergillosis has been shown in a study, as mentioned above, but high VEGF levels may be seen in any inflammatory condition.⁸ Detection of Aspergillus galactomannan antigen (AGA) is valuable in invasive aspergillosis.¹² This test is performed only if a suspicion exists, and AGA levels may not be helpful in non-invasive cases. Both of our cases were non-invasive and there was no clinical suspicion of aspergillosis; no serological tests were performed before the operation or after the diagnoses. Cytopathologic examination of cyst aspirate may be effective where there is no contraindication for aspiration.⁵ As a result of the limited chance of detecting the coexistence of these two entities before histopathologic examination of the resected materials, preplanned adequate management may not be possible before operation.

Light microscopic evaluation of the excised hydatid cysts is 'dull' work for the pathologists working in endemic areas, and in sending the specimen to the laboratory, the surgeons undertaking this routine procedure 'already know' what will be written in the pathology report. But these specimens may contain potential threats to the patients, and traps for the physicians. Adequate sampling of the excised specimen and careful evaluation of the HE-stained sections is essential.

Since reports appearing in the literature are very few in number and are only sporadic case reports, there are no reliable data on the optimum management of these patients. Our patients were immunocompetent and no post-operative complication or dissemination of either infection occurred. Both of the cysts were intact before surgery and the surgical resections were carried out successfully without rupturing the hydatid cysts. So we can claim that aspergillosis was limited to the cysts, and surgical resection was curative both for hydatid cysts and aspergillosis. However, in cases with ruptured cysts, especially in immunocompromised patients, the patient may be at risk of further Aspergillus infection, which may even advance to the invasive form.⁴ It is known that invasive aspergillosis is one of the major causes of death in bone marrow transplantation and leukemia patients.⁷ Although it is rare, this coexistence may be life-threatening, particularly in patients with immune suppressing diseases, and close follow-up and prophylactic chemotherapy for aspergillosis may be useful to prevent further complications.

Conflict of interest: No conflict of interest to declare.

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