

PULMONARY ECHINOCOCCAL CYST WITH A FILAMENTOUS FUNGUS CO-INFECTION

P. PANDEY¹, A.K. DIXIT², A. TANWAR¹ and N. C MAHAJAN¹

Departments of Pathology¹ and Pharmacology², Maharishi Markandeshwar Institute of Medical Sciences and Research, M M University, Mullana, Ambala, Haryana, India

Corresponding Author: Dr. Pinki Pandey

E mail: pnkdxt@yahoo.co.in

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SUMMARY

Fungal infections are known to colonize the pre-existing lung cavities formed as a result of diseases like tuberculosis, sarcoidosis, bronchiectasis and cavitary neoplasia, mostly encountered in immunocompromised patients. Pulmonary echinococcal cysts have been reported coexistent with cryptococcosis and other saprophytic mycosis, but the coexistence of aspergillosis and echinococcal cyst is extremely rare and occasionally been reported in English literature. Active invasion and proliferation of the fungi in the laminated ectocyst of the echinococcal cyst is very unusual. We report a case of 60 years old immunocompetent female, presented with cough, chest pain and shortness of breath. The chest X-ray showed a large thick walled cavity in the lower and mid zone of right lung with positive water lily sign. Surgical enucleation of the echinococcal cyst revealed aspergilloma involving the cavity with massive invasion of laminated ectocyst by filamentous fungus, morphologically resembling an *Aspergillus* species and was further treated with Itraconazole for 3 months. This unique coexistence of active pulmonary echinococcosis and aspergillosis is being reported because of its rarity and clinical importance for its management.

Keywords: Aspergillosis, echinococcosis, echinococcal cyst, pulmonary, mycosis.

INTRODUCTION

Isolated pulmonary aspergilloma as well as cystic echinococcosis is known to occur in lungs. Fungal infections are known to colonize pre-existing lung cavities formed as a result of diseases such as tuberculosis, sarcoidosis, bronchiectasis, lung abscess and cavitary neoplasia, mostly encountered in immunocompromised patients. The co-existence of aspergillosis and echinococcal cyst is extremely rare, with a handful of case reports in English literature.¹⁻⁹

Active invasion and proliferation of the fungi in the laminated ectocyst of echinococcal cyst is very unusual. We report such a unique coexistence of aspergilloma involving the cavity of echinococcal cyst as well as

massive invasion of the laminated ectocyst with filamentous fungus, morphologically resembling an *Aspergillus* species in a 60 years old immunocompetent patient. Echinococcosis is a cosmopolitan zoonotic problem of man caused by the larval stage of the cestode of the genus *Echinococcus*. Three of the four echinococcus species are of medical importance in the human beings, including *E. granulosus* responsible for cystic echinococcosis, *E. multilocularis* that causes alveolar echinococcosis and *E. vogeli*, a rare form reported mainly in the southern parts of South America.

Infection of the intermediate host, caused by ingestion of the eggs of *E. granulosus* leads to the development of cystic echinococcosis characterized by the appearance of echinococcal cysts. Normally *Echinococcus* completes its lifecycle involving dogs (definitive host) and sheep and goats (intermediate host). Man is an incidental or accidental intermediate host. This can happen only when man consumes vegetables contaminated by the excreta of infected stray dogs. Echinococcal cysts may develop anywhere from the toe to the crown of the head. The endemic areas are the Mediterranean countries, the Middle East, the southern part of South America, Iceland, Australia, New Zealand, and southern parts of Africa; the latter five are intense endemic areas.

The incidence of cystic echinococcosis in endemic areas ranges from 1-220 cases per 100,000 inhabitants, while the incidence of alveolar echinococcosis ranges from 0.03-1.2 cases per 100,000 inhabitants, making it a much more rare form of echinococcosis.¹⁰ In India, cystic echinococcosis is more commonly seen in the Kurnool district of Andhra Pradesh, Madurai district of Tamil Nadu and Punjab.¹¹

Aspergillus is a saprophytic fungus. Although around 200 species of *Aspergillus* have been identified, very few cause human disease, *Aspergillus fumigatus* being the most common type.⁶ *Aspergillus* may cause chronic pulmonary aspergillosis, allergic pulmonary aspergillo-sis, semi invasive and invasive aspergillosis.³

Chronic pulmonary aspergillosis includes two major clinical entities; aspergilloma which depicts a single pulmonary cavity, containing a fungal ball, which changes little over months or years of observation, and may spontaneously regress, and chronic cavitary pulmonary aspergillosis (CCPA) which depicts single large empty or multiple pulmonary cavities not necessarily with an aspergilloma, symptoms (usually weight loss, cough, hemoptysis and breathlessness) for at least 3 months and serology, cultures, or molecular detection implicating *Aspergillus* species.

Distinguishing chronic invasive aspergillosis from genuine aspergillomas is important because the former require systemic antifungal therapy. Co-existence of aspergillosis and echinococcosis is extremely rare. Here we describe this rare entity of aspergilloma in a pulmonary echinococcal cyst with invasion into the ectocyst layer as well.

CASE REPORT

A 60 years old female, from rural areas of Punjab belonging to shepherd community, presented with history of cough, chest pain and shortness of breath for the last six months. Following a febrile illness she developed a persistent cough productive of about 150ml of foul mucoid purulent sputum daily. There was neither past or family history of diabetes mellitus, hypertension or tuberculosis nor history of abuse of steroids. Systemic examination revealed evidence of hydropneumothorax for which a chest tube was inserted.

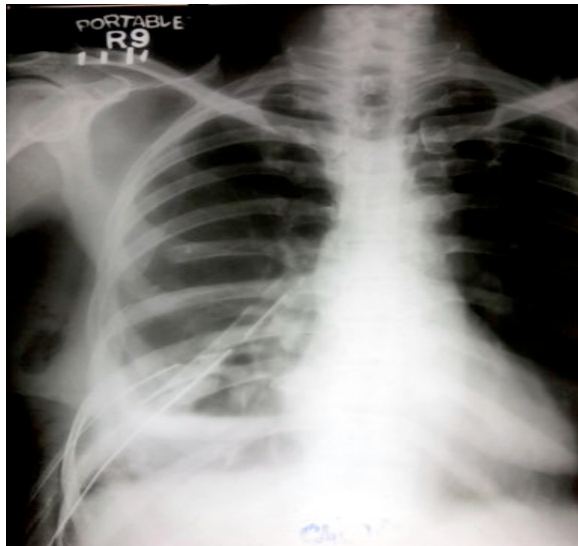


Figure 1 Chest X-ray shows ruptured solitary echinococcal cyst in the lower and mid zone of right lung with irregular wavy fluid level (water lily sign or sign of the camalote)

The chest X-ray showed a large thick walled cavity in the lower and mid zone of right lung with positive water lily sign (Figure 1) giving an impression of pulmonary echinococcosis with bronchopleural fistula.

Results of laboratory investigations such as haemogram, routine urine and stool examination did not reveal any abnormality. Repeated sputum smears were negative for acid-fast bacilli. She was non-reactive for Human Immunodeficiency Virus (HIV). The patient was treated surgically with enucleation of the cyst along with two daughter cysts and sent for histopathological examination.

Grossly two pearly white cystic masses resembling the albumin of boiled egg of size 18x10x5cm and 7x3x2cm were received. The cyst wall was acellular laminated membrane with uniform thickness and showed blackish area on the surface (Figure 2).



Figure 2 Gross photograph showing pearly white hydatid cyst wall resembling the albumin of a boiled egg, and showing black areas on the surface (black arrows).

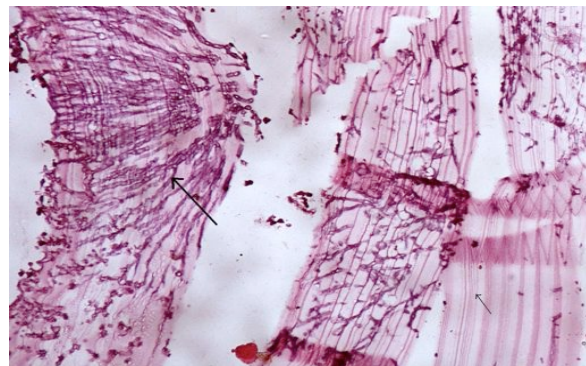


Figure 3 Photomicrograph showing acellular laminated membrane (ectocyst) of the hydatid cyst (thin arrow) diffusely infiltrated by uniform septate, dichotomously branched fungal hyphae (thick arrow) (Hematoxylin and Eosin; X 200)

On cutting, the cavity of the cyst contained fungal necrotic material. Microscopic examination of the cyst wall revealed the acellular laminated membrane (ectocyst) of an echinococcal cyst colonized by fungal hyphae. These fungal hyphae were uniform, tubular, regularly septate, branching dichotomously at acute angles morphologically resembled those of *Aspergillus* (Figure 3), surrounded by mixed inflammatory cells.

The intracavitary necrotic fungal material showed conglomeration of intertwined degenerated fungal hyphae assuming bizarre shapes with globose varicosities and inconspicuous septa suggestive of aspergilloma (Figure 4). Periodic-acid Schiff (PAS) stain was done which stained the acellular laminated membrane of echinococcal cyst strongly positive and better demonstrated the hyphal morphology (Figure 4 inset).

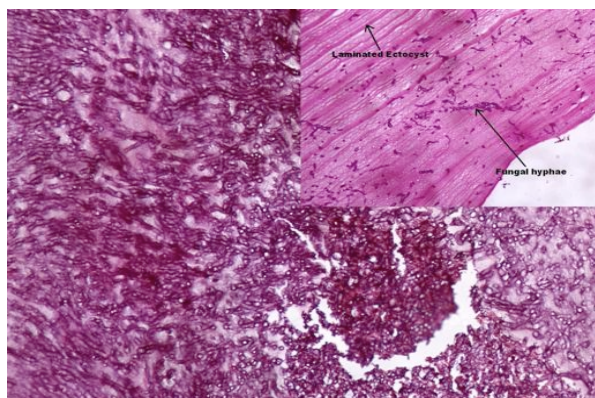


Figure 4 Photomicrograph showing conglomeration of intertwined degenerated fungal hyphae assuming bizarre shapes with globose varicosities and inconspicuous septa. Inset: PAS positive laminated ectocyst with septate fungal hyphae (Hematoxylin and Eosin; X 200, Inset: Periodic acid Schiff stain X 200).

The fungal culture was not done in the present case. She had an uneventful recovery and was given Itraconazole 100mg/day for 3 months.

DISCUSSION

Pulmonary aspergilloma frequently complicates an existing cavity, tuberculosis remain the most frequent underlying disease. Conversely, aspergilloma can develop in any type of pulmonary cavity, akin to cavities due to bronchial cysts and bullae, removal of a hydatid cyst, neoplasms and pulmonary infarction.⁴ Aspergilloma was reported in residual cavities left after a cystectomy with or without capitonnage.^{1,4,5,6,7} Development of aspergilloma in echinococcal cyst cavities is very rare and we could identify only a single reported case as per the literature published worldwide.⁷ Our case demonstrates aspergilloma involving the cavity as well as massive invasion of the echinococcal laminated

ectocyst, by a filamentous fungus seen as hyphae branching dichotomously at acute angles morphologically resembling those of an *Aspergillus* species.

The clinical presentation of pulmonary echinococcosis depends on the size and site of the cyst and whether the cyst is intact or ruptured. Intact cysts are incidental findings or present with cough, dyspnoea, pleuritic chest pain. Furthermore, patients with a complicated cyst may present with expectoration of cystic contents and/or repetitive hemoptysis, fever or anaphylactic shock. It has been reported that approximately 60% of pulmonary echinococcosis affects the right lung and 50% to 60% involves the lower lobes, which is consistent with the findings in our patient.⁷ The great majority of patients with aspergilloma are asymptomatic with clinical picture ranging from incidental radiologic findings to life threatening hemoptysis. Hemoptysis is an important complication which may range from minor blood streaking to massive life-threatening haemorrhage and this may be due to direct invasion of blood vessels by *Aspergillus* or, reaction of killed hyphae of *Aspergillus fumigatus* with vascular endothelium.^{3,12}

The echinococcal cyst consists of 2 layers: an outer, thick, non-nucleated, carbohydrate-rich acellular laminated layer (ectocyst) and an inner, nucleated, germinal layer (endocyst) from which brood capsules develop. There is also an adventitial layer or pericyst which is formed by the host reaction. Cyst contains deposits of brood capsules and scolices at the bottom of the cyst, known as hydatid sand. Daughter cysts are formed when these brood capsules are attached to the germinal layer of the mother cyst by a pedicle. True daughter cysts are rare in the lung, because they usually develop only if a cyst becomes traumatized or infected, and an echinococcal cyst in the lung is relatively protected from trauma.¹³

Typical hyphae of the *Aspergillus* have a characteristic appearance in tissue section. The hyphae are uniform, regularly septate, branched dichotomously and tend to arise at acute angles from parent hyphae. But degenerated hyphae encountered in pulmonary aspergilloma (fungus ball) assume bizarre shapes with globose varicosities and inconspicuous septa, as was noted in the intracavitary necrotic material. Similar to the present report, in a majority of reported cases had clinical symptoms. Serology was not done in any of the cases whereas culture was done in 3 of the cases.^{5,7,9} In five of the studies aspergilloma was formed in a residual cavity left after a cystectomy with or without capitonnage,^{1,4,5,6,7} whereas half of the studies showed active invasion and proliferation of fungi in laminated pulmonary echinococcal ectocyst similar to our case.^{2,3,8,9}

Although patients with immune deficiencies are prone to aspergillosis, the coexistence with echinococcosis has been reported in immunocompromised as well as immunocompetent patients.^{2, 3, 8} In our case, the patient had a normal immune status. Pulmonary echinococcal cysts have been reported coexistent with cryptococcosis and other saprophytic mycosis on histopathological examination of the affected lung tissue. Pulmonary echinococcosis leads to higher susceptibility to saprophytic fungal coinfection than echinococcosis located in other sites of the body,³ probably because it is in communication with external environment.

As demonstrated in our patient and in other series,^{4,5,6,10} pulmonary echinococcosis is picked up on routine radiography. Unless the cyst ruptures, it appears as uniform density on the plain chest X-ray. When a cyst ruptures, the endocyst membranes may collapse inwards and become visible as a folded membrane on the chest X-ray. The fragmented endocyst membrane may float on the top of the remaining fluid to produce an irregular fluid level, described as the 'water lily' sign or sign of the camalote because of its resemblance to water lilies found floating upon the Amazon river. This water lily sign or sign of the camalote is pathognomonic of an echinococcal cyst.¹³

The presence of radiological opacity with the air crescent sign is of specific importance in the diagnosis of aspergilloma. The aspergilloma usually moves when the patient changes position. Although radiological imaging techniques are highly accurate both in echinococcosis and aspergillosis,³ the sensitivity and specificity of imaging procedures in detecting the *Aspergillus* colonies entrapped in an echinococcal cyst is not clear. In our case there was no clinical suspicion of aspergillosis and therefore serological tests were not performed preoperatively. Our patient was diagnosed as pulmonary echinococcal cyst but not suspected of having pulmonary aspergilloma radiographically.

The presence of *Aspergillus* therefore came as a surprise. Immunesuppression and structural pulmonary defects may predispose to this infection. In our case, the echinococcal cyst probably communicating with the bronchus could have been the source of *Aspergillus* infection. The Postoperative histopathological examination revealed pulmonary aspergilloma involving the cavity of echinococcal cyst and also colonizing the laminated ectocyst membrane.

The determination of the clinical significance of this coexistence is important for adequate management. Treatment of echinococcosis is essentially surgical, although its role is diminishing because of the success of chemotherapy along with PAIR (puncture-

aspiration-injection-reaspiration).¹³ Medical cysticidal therapy alone for one year duration, has recently been reported to have favorable outcome in 41.10% to 57.70% of the patient with pulmonary echinococcosis and is considered as a supplement to surgical excision.¹⁴ 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. Although rare, this coexistence may be life threatening, especially in immunocompromised patients and close follow up and prophylactic chemotherapy for aspergillosis may be useful to prevent further complications.

In essence, isolated pulmonary aspergilloma and echinococcal cysts are known to occur in lungs; however the coexistence of both has occasionally been described. This unique coexistence of active pulmonary echinococcosis and aspergillosis is being reported because of its rarity and clinical importance for its management

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