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Case report

An unexpected guest: Pulmonary echinococcosis diagnosed by intraoperative frozen section examination. A case report and literature review

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ABSTRACT

Echinococcosis is caused by tapeworms belonging to the Echinococcus genus. The most common site of infection is the liver although it may involve almost any organ. Symptoms of pulmonary echinococcosis vary depending on the location and structure of the cyst. While uncomplicated cysts usually appear at imaging as well-defined homogeneous lesions with fluid content and smooth walls of variable thickness, complicated lesions may have a more heterogeneous content with higher density making more difficult the distinction from malignancies or other infections. Hereby we describe the case of a 61-year-old Northern African male admitted to our tertiary center for left upper chest pain who then underwent a chest computed tomography (CT) scan which demonstrated a large hypodense lesion, with smooth and thick walls, in the upper left lobe. The following magnetic resonance confirmed the homogeneous fluid content, and the 18 F- fluorodeoxyglucose-positron emission tomography/CT demonstrated a mild uptake of the walls. According to these findings, the main differential diagnoses at imaging included bronchogenic cyst, synovial sarcoma, and pulmonary hematoma although the patient denied any recent trauma. Given the large size and clinical symptoms he underwent surgery. Intraoperative frozen section, supported by imprint cytology, excluded the presence of malignancy while suggested an echinococcal laminar exocyst. The final pathological examination confirmed the diagnosis of echinococcosis (i.e., Echinococcus Granulosus protoscolex). After surgery he was treated with albendazole and at the six-month follow-up he was in good clinical conditions. Our case highlights the importance of considering rare infections, particularly in individuals from endemic areas. Frozen tissue analyses can be a diagnostic challenge and often require ancillary tools such as imprint cytology and serial sections for more sensitive and accurate diagnosis.

1. Introduction

Echinococcosis, also known as hydatid disease, is caused by tapeworm larvae belonging to the Echinococcus genus. The most common cause of human infections is E. granulosus, which causes cystic echinococcosis (CE), although other species such as E. multilocularis, E. vogeli, and E. oligarthrus may also occur [1]. CE is listed by the World Health Organization as one of seven Neglected Zoonotic Diseases [2,3]. Humans are accidental hosts, typically contracting the disease from infected dogs. In Italy, CE is relatively uncommon, particularly in urban Northern regions where sheep breeding, the most important risk factor, is less prevalent than in rural areas of Central and Southern Italy [4,5].

The most common sites of infection include the liver, lungs, and spleen, with the liver being the most commonly affected organ in cases of multiple visceral involvement [6]. Single pleuropulmonary involvement accounts for 10–30% of cases and can cause various respiratory symptoms such as chest pain, dyspnea, dry coughing, and hemoptysis due to the cyst compressing surrounding structures [1]. Cyst rupture is

Abbreviations: CE, cystic echinococcosis; CT, Computed tomography (CT); 18 F-FDG/PET, [^{18}F] Fluorodeoxyglucose positron emission tomography; MR, magnetic resonance.

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the most common complication and can cause acute-onset chest pain, cough, hemoptysis with membrane expectoration, and anaphylactic reactions [7,8]. The degeneration of cyst membranes is responsible for rupture, and it depends on several factors, such as the age of the cyst, chemical reactions, defense mechanisms of the host, and drug administration [8]. Although the radiological features of liver CE are well-established, imaging of other less common sites such as thoracic CE is less frequently described and can be challenging [9].

Thus, to highlight the importance of considering this diagnosis even in non-endemic areas we report a rare case of pulmonary CE and include the findings of a brief literature search on the topic.

2. Search strategy and case selection for the review

Medline-indexed research was performed on the topic using PubMed as the main database, with different search strings on 11th October 2022. The aim of our review was to encompass cases where ancillary studies, such as frozen sections and imprint cytology, were employed to assist or directly establish the final diagnosis. Including such cases can be valuable as it highlights the role and impact of these diagnostic modalities in improving diagnostic accuracy and patient outcomes.

A search for "frozen section" + "echinococcus" yielded 6 results. Of these, 3 [10–12] out of 6 were considered significant and included in the final count. Two were duplicated results, and one was duplicated and non-adherent. A search for "hydatid cyst" + "frozen" yielded 14 results. Of these, 6 [13–18] were included, and 8 were discarded for various reasons. A search for "frozen" + "echinococcus" in PubMed on October 11, 2022, yielded 30 results. Of these, one [19] was considered relevant, and the remaining 21 were either duplicates from the previous searches or not relevant to the aim of this article. A search for "imprint cytology + (hydatid cyst and/or echinococcus)" yielded two results, one [20] of which was considered relevant for this research.

We were made aware of another paper [21] through a colleague, which is not indexed in MEDLINE. It is worth noting that a different diagnosis was reached despite following the same diagnostic path, as reported in another article [22].".

The final 12 papers list the importance of ancillary techniques, either as an aid or even the primary means of correctly addressing the diagnosis. These techniques are summarized in the Table 1.

3. Case presentation

We present a case study of a 61-year-old Northern African male who worked as a carpet merchant and had been living in Italy for almost 20 years, with frequent travel to his home country. In July 2021, the patient referred to our tertiary center for left upper chest pain without any additional symptoms. The patient was overweight, but his medical history was otherwise unremarkable.

A computed tomography (CT) scan was then performed, and it revealed a 10 cm large hypodense cyst with smooth and thick walls in the left upper lobe (Fig. 1A, B). The patient underwent a magnetic resonance (MR) scan which confirmed the fluid content of the lesion (Fig. 1C, D) and a 18 F- fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT scan which demonstrated a moderate uptake (maximum standardized uptake value, SUVmax from 3.7 to 7) of the walls as well as a mild uptake of a few left hilar lymph nodes (SUVmax 2.5).

Given these imaging findings, the main differential diagnoses included bronchogenic cyst, synovial sarcoma, and pulmonary hematoma although the patient denied any recent trauma.

First-line laboratory tests, including a broad screening of microbiological and blood analyses, were normal, except for a slight increase in C-reactive protein (16 mg/L). Respiratory function tests and blood gas analysis were also within the normal range. Given the radiological features, the size and the symptoms, the patient underwent surgical resection via open lateral thoracotomy. Intraoperative analysis was promptly requested to rule out malignancy. Frozen sections revealed a thick, dense, fibrous, and acellular material. Concurrent imprint cytology showed only a delicate amorphous background with rare, scattered leukocytes. (Fig. 2). The provisional diagnosis was negative for

Table 1
Results of the review of the literature.

Author	Patient		Organ involved	Dimensions (via imaging and/or pathology)	Symptoms	Clinical suspect	Imprint cytology	Frozen section	Endemic area
	Age (years)	Sex							
Delbecque[19] (2002)	76	F	Liver	70 mm	None reported	Liver metastasis	Not performed	Performed-Not useful	No
Toker[18] (2004)	8	F	Lung	20 × 20 mm	Hemoptysis	Mass without suggestions	Not performed	Performed-Confirmed E.	Yes
Zulfikaroglu [17] (2008)	50	F	Thyroid/ Neck	25 × 23 mm	Painless neck/thyroid mass	Thyroid neoplasm	Not performed	Performed-Confirmed E.	Yes
Moghimi[16] (2009)	35	F	Thyroid/ Neck	78,5 × 73,8 mm	Enlarging neck mass	Hydatid cyst or cold thyroid nodule	Not performed	Performed-Confirmed E.	Yes
Sharma[20] (2012)	30	F	Pelvis	60 × 40 mm	Abdominal distension and pain in lower abdomen	Ovarian malignancy	Performed-Confirmed E.	Not performed	Yes
Abdullah[15] (2016)	22	F	Uterine adnexa	170 × 120 mm	Urinary retention, haematuria, constipation with dull abdominal pain	Ovarian malignancy	Not performed	Performed-Confirmed E.	Yes
Koç[13] (2017)	25	F	Uterus	100 × 100 mm	Lower abdominal pain and tenesmus	Uterine leiomyoma with cystic degeneration	Not performed	Performed-Confirmed E.	Yes
Tas[12] (2018)	44	F	Uterine adnexal mass	218 × 107 mm	Abdominal distension; weight loss	Ovarian malignancy	Not performed	Performed-Confirmed E.	Yes
Jafari[21] (2019)	15	F	Thyroid/ Neck	55 × 50 × 40 mm	Enlarging asymptomatic cervical mass	Cyst	Not performed	Performed-Confirmed E.	Yes
Bartels[11] (2020)	65	F	Liver	109 × 76 mm	None reported	Primary liver malignancy	Not performed	Performed-Confirmed E.	No
Asnani[14] (2021)	79	F	Pouch of Douglas	120 × 120×80 mm	Abdominal pain and increased micturition	Ovarian malignancy (cystadenocarcinoma)	Not performed	Performed-Confirmed E.	Yes
Greimelmaier [10] (2021)	25	M	Lung	90 mm	Back and Thoracic pain; Hemoptysis; Weight loss	Echinococcosis or tuberculosis	Performed-Confirmed E.	Performed-Confirmed E.	Yes

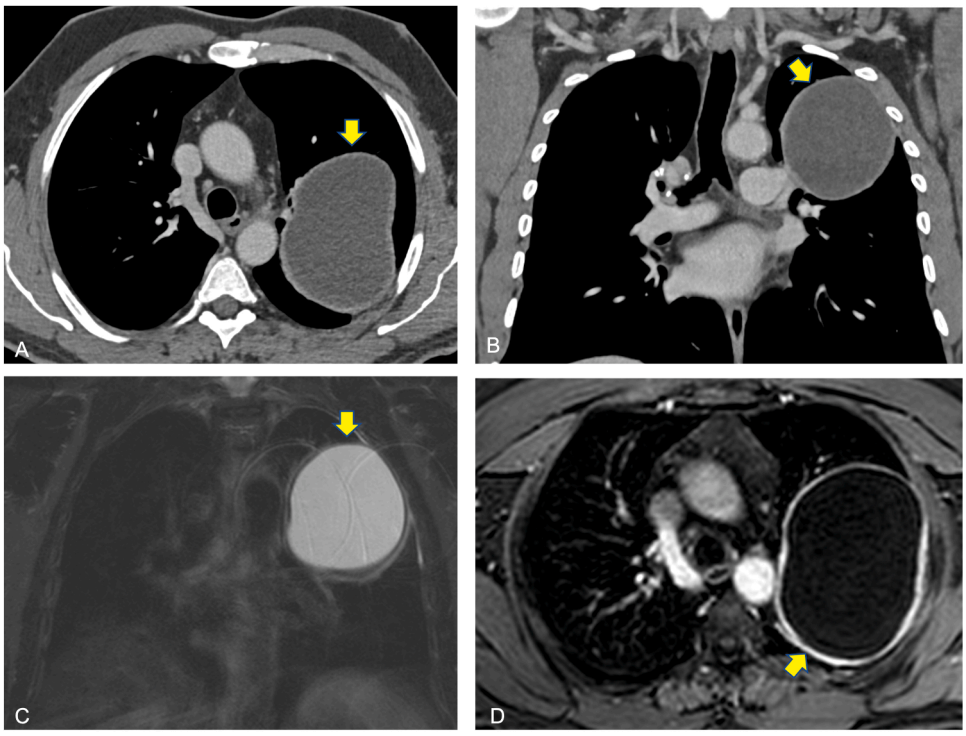

Fig. 1. Axial and coronal contrast enhanced computed tomography images (**A** and **B**, respectively) well demonstrating the large hypodense lesion in the upper left lobe (yellow arrows) with a smooth and thick wall. The subsequent magnetic resonance (yellow arrows on the corona T2 weighted fat-sat and axial T1weighted fat-sat axial image after contrast injection in **C** and **D**, respectively) confirmed the fluid content of the lesion and nicely showed the contrast enhancement of the walls.

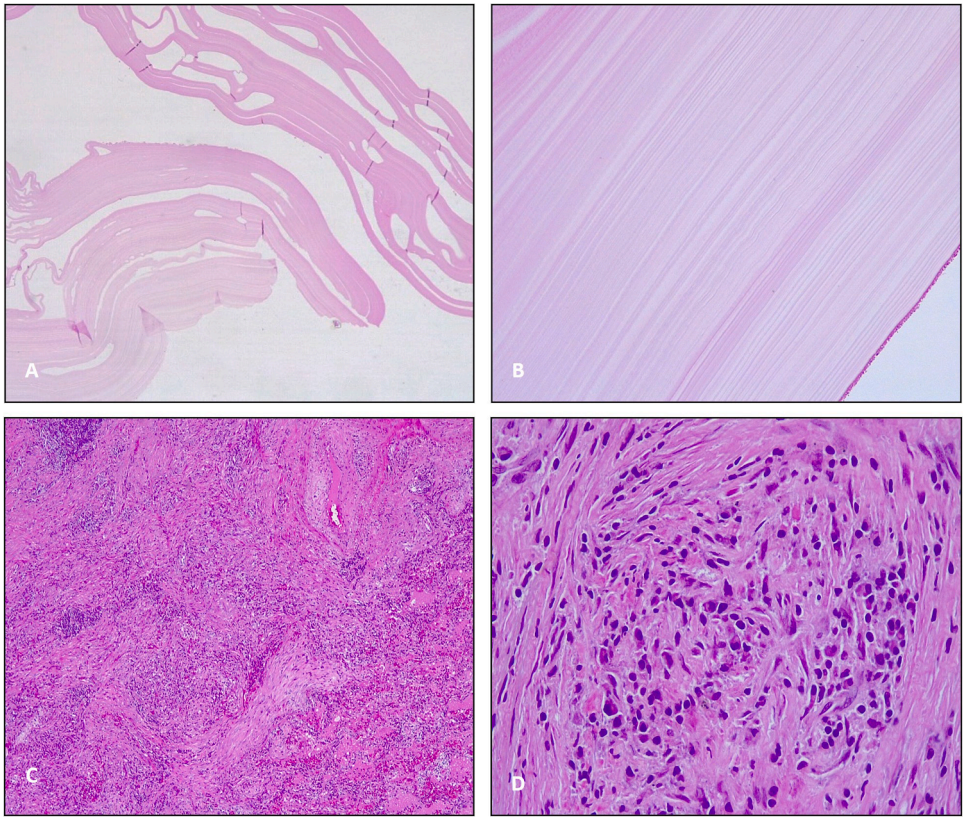

Fig. 2. Representative histological images of the intraoperative slides. A, B) The cystic wall was composed of acellular fibrous-lamellar structures (A, hematoxylin and eosin stain, 25X original magnification; B, hematoxylin and eosin stain, 20X original magnification). C, D) The perilesional lung parenchyma showed inflammatory and reactive alterations (C, hematoxylin and eosin stain, 5X original magnification; D, hematoxylin and eosin stain, 10X original magnifiction).

neoplasia and highly suggestive of a hydatid cyst. The definitive examination included the evaluation of the entire whitish fibrous capsule (three samples) and perilesional tissue (four samples). A complementary cytoblock of the cyst liquid was also performed. Microscopic routine hematoxylin-eosin sections revealed an acellular fibrous lamellar structure (PAS staining-positive) with an inner, brighter eosinophilic germinative coating, with only a single organism morphologically consistent with Echinococcus granulosus protoscolex, identified after several consecutive serial sections. The surrounding pulmonary parenchyma was characterized by areas of atelectasis, diffuse inflammatory cell infiltration mainly of lymphocytes and macrophages sometimes aggregated in a follicular pattern. Rare eosinophils and foci of organizing pneumonia were also observed. The cytoblock demonstrated the same findings as the imprint cytology (Fig. 3).

After the pathological diagnosis, a specific serologic test (Echinococcus IgG ELISA) was performed, but it was negative. The patient recovered well from the surgical procedure and was treated with oral albendazole. At the last follow-up, six months later, he was in good clinical conditions.

4. Discussion

Our case demonstrates a typical presentation of a widely paucisymptomatic pulmonary cyst. It is hard to diagnose at imaging hydatid cysts in unusual sites, especially in patients from non-endemic regions, since they may resemble other benign and even malignant lesions. As in our case, several differentials could have been taken into account such as bronchogenic cysts or synovial sarcoma. In the literature, especially in case of more inhomogeneous features, mature cystic teratoma, and thymomas with cystic degeneration, have been described as mimickers of pulmonary echinococcosis [9]. By a radiological point of view, pulmonary EC are usually classified as uncomplicated (i.e., cystic lesions with smooth walls rarely associated with calcifications and daughter cysts) or complicated (i.e, completely ruptured or partially ruptured or infected) [23]. The latter are characterized by higher HU values due to mucus, infection, or hemorrhagic content.

Despite the characteristics at imaging, overall, the diagnosis of such an uncommon condition relies upon histological examination. In fact, also additional laboratory tests are not useful for diagnostic practice. The recorded sensitivity of serological methods for testing patients varies from 60% to 90% [24]. The low sensitivity of serological tests for echinococcosis is due to the encystment of the pathogen, which prevents the stimulation of antibody-producing cells, inducing false-negative results. Thus, negative results from blood samples, particularly when testing for anti-Echinococcus IgG, are not uncommon, as was the case in our patient.

In terms of treatment, surgery is the mainstay of management of pulmonary hydatidosis, and pharmacological therapy can be sought in patients with surgical contraindication, in case of single, mall, uncomplicated cyst, and for disseminated diseases [25]. Albendazole chemotherapy is considered to be the main pharmacological treatment for managing CE. However, combining albendazole with praziquantel has shown to be more effective in terms of scolicidal and anti-cyst activity, and has a higher chance of leading to a cure or improvement compared to using albendazole alone [26].

Due to the high risk of intraoperative fluid spillage potentially causing anaphylactic shock, frozen section examination and imprint cytology are not routine practices, although they have been variably reported.

Intraoperative pathological diagnosis, including imprint cytology and frozen section analysis, plays a crucial role in enhancing patient care by facilitating immediate decision-making, guiding surgical procedures, and optimizing treatment outcomes [27]. These techniques provide timely feedback to surgeons and pathologists, enabling them to make critical decisions during surgery, such as determining the extent of surgical resection, identifying involved margins, and assessing the need for additional interventions. This reduces the risk of incomplete excisions and ensures timely and appropriate treatment. Additionally, imprint cytology and frozen section analysis enable rapid evaluation of cellular or tissue morphology, aiding in distinguishing between benign and malignant lesions and identifying specific pathological features. Moreover, these techniques serve as valuable educational tools, offering real-time learning experiences for trainees to understand intraoperative decision-making and develop proficiency in interpreting rapid pathological assessments.

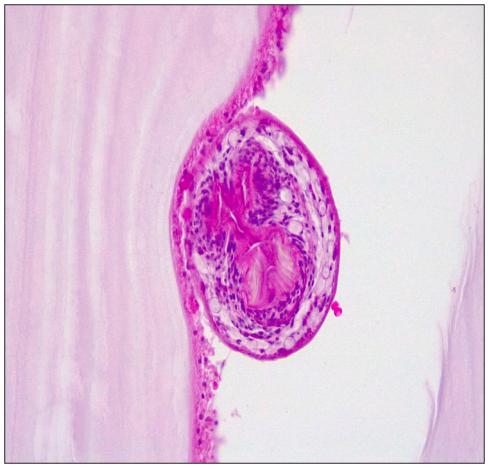

Fig. 3. Representative histological images of the routine slides. Histological examination of the whole cyst revealed the presence of a germinative coating in the cystic wall, along with a single protoscolex that was morphologically consistent with Echinococcus (hematoxylin and eosin stain, 40X original magnification).

In the context of Echinococcal infection, frozen section, if performed correctly, is an invaluable tool for directing the correct diagnosis and determining the appropriate surgical approach to lesions, particularly in anatomically complex areas such as the pelvis or neck, where echinococcal disease is rare or anecdotal. After formalin fixation and paraffin embedding, the morphological diagnosis is usually clear due to the lesion's distinctive morphological characteristics. Serial sections are mandatory for the discovery of the scolex.

5. Conclusions

All medical specialists should be aware of pulmonary echinococcosis. This case serves as a reminder to never underestimate a patient's occupational and travel history, and to always consider uncommon causes of disease, especially when radiological findings are not univocal. Ancillary techniques, such as imprint cytology and frozen section examination, along with careful sampling of cyst wall specimens and examination of multiple microscopic slides, are always the best methods for approaching difficult or peculiar cases. Otherwise, as in this case, the correct diagnosis could easily be missed.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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