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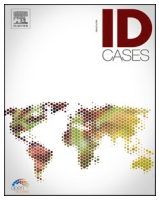

Case report

Pulmonary cystic echinococcosis acquired during a short-term tourist travel

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ABSTRACT

Background: Cystic echinococcosis is non-endemic in Denmark and primarily diagnosed in migrants from endemic areas. Here, we report a case of pulmonary cystic echinococcosis in a Danish woman with no history of longer-term stays abroad, only holiday travelling to tourist destinations. This is the first case reported in international literature from Denmark where the causative parasite was identified to species and genotype level.
Case: A 27-year-old pregnant Danish woman was admitted for examination because of haemoptysis for three months.
Chest X-ray and computed tomography revealed a cystic structure in the left lung and a left-sided thoracotomy was performed to remove the cyst. Postoperative histopathological examination revealed a hyaline membrane and protoscoleces. Subsequently, infection with *Echinococcus granulosus* was confirmed by molecular methods. The causative agent was further characterised as *E. granulosus sensu stricto* G1, which is not known to have an established life cycle in Denmark. It was concluded that the infection was most likely acquired during a tourist travel to an endemic country. The patient was treated with albendazole for four weeks.
Conclusion: This case of pulmonary cystic echinococcosis in a person who had lived in Denmark and had history of only short-term tourist travelling abroad highlights that the disease may be acquired during tourist travelling. Thus, a diagnosis of cystic echinococcosis should be considered not only in migrants from endemic countries but also in travellers upon incidental findings of a lung or liver cysts. The case also exemplifies the importance of reaching a diagnosis at species and genotype level.

Introduction

Echinococcosis is a zoonotic disease caused by tapeworms belonging to the genus *Echinococcus*. Humans can be incidental intermediate hosts and acquire the infection by ingesting eggs of the parasite with *e.g.* contaminated food [1]. There are multiple different species, and species-level diagnosis is important: *E. granulosus sensu lato* and *E. multilocularis* cause very different diseases in humans, cystic echinococcosis (CE) and alveolar echinococcosis (AE), respectively [2,3]. Denmark is a non-endemic country for *E. granulosus sensu lato*; CE cases are rarely seen and almost exclusively in migrants from endemic areas.

The adult *Echinococcus granulosus* parasites live in the intestine of their definitive hosts, such as dogs and other canids. Eggs are released in faeces to the environment and ingested by an intermediate host. In the intermediate host, the parasites develop into echinococcal cysts. In humans, the cysts are frequently located in the liver and lungs [2,3].

The clinical presentation of CE depends on the organ(s) involved. Infection may be asymptomatic and subclinical for several years, and symptoms often only occur when the cyst is large enough to cause a mass effect within the organ, or if the cyst ruptures [4]. When the lungs are affected, common symptoms include cough, chest pain and haemoptysis [3,4].

CE is generally diagnosed using imaging technologies like ultrasound, X-ray, computed tomography (CT) and magnetic resonance imaging (MRI) [5]. Immunodiagnostic tests can be used to support the diagnosis, but the cysts may isolate their contents from the immune

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system, leading to a minimal antigen release and a lack of antibody production [2]. Thus, negative serology cannot rule out CE [5].

Here, we present a case of CE diagnosed postoperatively in a young Danish woman who had only travelled abroad for ordinary tourist holidays.

Case description

A 27-year-old Danish woman with no previous medical record was admitted to Department of Respiratory Diseases at Aarhus University Hospital in Denmark in September 2021 with monosymptomatic haemoptysis lasting for three months. On the day of admission, she had acute progression to multiple daily episodes of haemoptysis. At that time, the woman was pregnant in week 13 with no pregnancy-related discomforts, except for nausea. She was afebrile, all vital signs were stable, and blood samples showed slightly elevated leukocyte levels (12.9 ×10^9 cells/L). Other parameters were normal, including a lactate dehydrogenase level of 116 U/L (upper limit 205 U/L). Levels of alpha fetoprotein and human chorionic gonadotropin were both elevated with values of 35 ng/mL and 66,619 mIU/mL respectively, which are levels corresponding to a week 13 pregnancy.

A fibreoptic nasopharyngoscopy and bronchoscopy did not reveal any source of the bleeding. A chest X-ray revealed a perihilar solid structure in the left pulmonary hilus, and a subsequent CT scan revealed a cystic unilocular structure with the size of 6.1 × 3.2 × 4.1 cm (Fig. 1). Gynaecological examination and an abdominal ultrasound did not reveal any molar or other abnormalities. Whole-body MRI confirmed a cystic structure in the left lung. A bronchogenic cyst was primarily suspected, and CE was not considered a differential diagnosis at that point. Due to the patient's history of pronounced haemoptysis, it was not possible to make a core-needle biopsy of the cyst, and it was decided to perform a left-sided thoracotomy and remove the cyst *in toto* (Fig. 2).

Surprisingly, pathological examination described the structure as a cyst composed of a hyaline membrane and protoscoleces (Fig. 3) – CE. Therefore, the patient was referred to Department of Infectious Diseases for further evaluation and treatment. She was prescribed albendazole 400 mg twice daily with outpatient follow up during four weeks of treatment. Treatment was initiated to avoid spread of the infection after removal. Additional blood tests did not reveal any eosinophilia; her serum immunoglobulin E was within the normal range, and serology for *Echinococcus* was negative. Both conventional PCR followed by Sanger sequencing and a metabarcoding assay targeting nuclear ribosomal genes were used to detect parasite-specific DNA from paraffin-embedded tissue samples. Both analyses identified *E. granulosus sensu lato* from the parasitic cyst structure. Cytochrome c oxidase subunit 1 gene analysis allowed to further characterise the causative agent as *E. granulosus sensu stricto* G1.

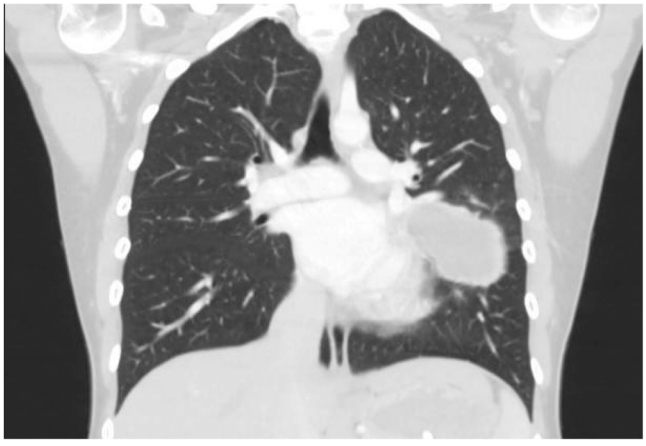

Fig. 1. Computed tomography of the lungs of the patient showing the structure in the left lung that was later diagnosed as cystic echinococcosis.

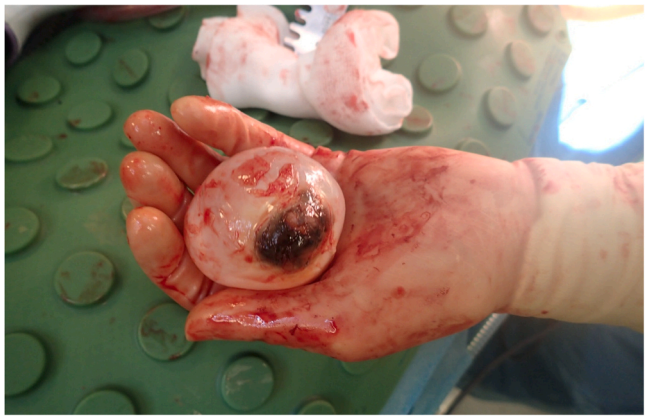

Fig. 2. Removed echinococcal cyst.

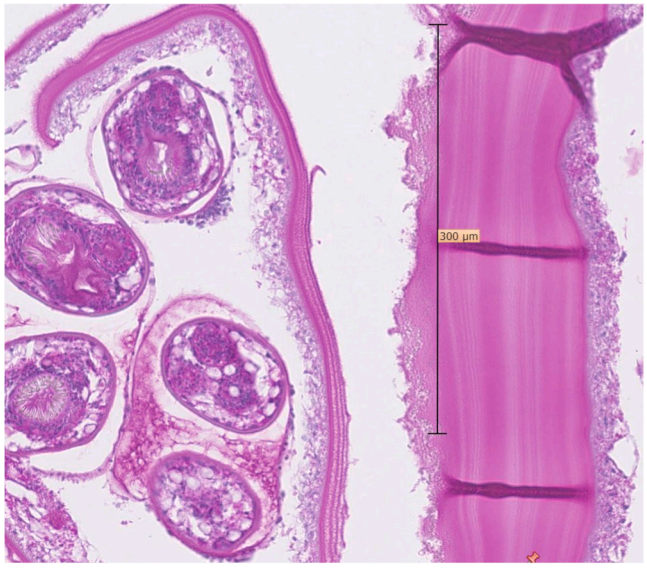

Fig. 3. Histopathology of the echinococcal cyst, H&E staining. Protoscoleces (left) and hyaline membrane (right).

The patient did not have any adverse effects from the treatment and had an uneventful recovery. Later she delivered a healthy baby girl. She did not seroconvert postoperatively, and was seronegative at later follow up, eight months after the operation. A control chest X-ray one month after the operation and a control chest CT scan eight months after the operation showed no sign of relapse.

The patient grew up in an urban area in Denmark. The family had a pet dog, but no livestock or *e.g.* home slaughtering of animals. The patient had no longer-term stays abroad, only short-term tourist travels to Tunisia, Thailand, Turkey, and several European countries. A full overview of the patient's travel history from more than ten years prior to onset of symptoms is shown in Table 1.

Discussion

This is the first CE case reported in international literature from Denmark where the causative parasite was identified to species and genotype level. There are no reports on *E. granulosus sensu stricto* G1 having been detected in animal hosts from Denmark. Surprisingly, the patient had only been on short-term tourist holidays abroad prior to admission. However, she had visited areas where *E. granulosus sensu stricto* G1 is endemic. None of her travel companions had reported any

Table 1
Self-reported travel history of the patient diagnosed with cystic echinococcosis.

Years before onset of symptoms	Destination	Duration	Accommodation	Main purpose
1 year	Holland, Amsterdam	4 days	No data	Sightseeing and shopping
2 years	South of France, Antheor	7 days	Camping	Sunbathing
	South of France, different cities	5 days	Hostels	Sightseeing
	Spain, Barcelona	1 day	AirBnB	Sightseeing
	Germany, Berlin	3 days	AirBnB	Sightseeing
3 years	Holland, Amsterdam	3 days	Hotel	Sightseeing
	Germany, Hamburg	3 days	Hotel	Sightseeing
4 years	Holland, Rotterdam	3 days	Rented apartment	Sightseeing
	The Canary Islands, Tenerife and Puerto De La Cruz	7days	Hotel	Sunbathing on the beach and at the pool
5 years	Austria, Zell Am See	7 days	Hotel	Skiing holiday
	Turkey, Alanya	7 days	Hotel	Sunbathing on the beach and at the pool
	Italy, Passo Tonale	7 days	Rented apartment	Skiing holiday
	Italy, Canazei	10 days	Rented apartment	Skiing holiday
6 years	Greece, Rhodes	7 days	Hotel	Sunbathing on the beach and at the pool
7 years	Greece, Crete	7 days	Hotel	Sunbathing on the beach and at the pool
8 years	Turkey, Fethiye	7 days	Hotel	Sunbathing on the beach and at the pool
9 years	Turkey, Alanya	10 days	Hotel	Sunbathing on the beach and at the pool
	Austria	7 days	No data	Kayaking, mountain biking, hiking, canyoning, climbing in mountains
10 years	Thailand, Bangkok, Phuket and Koh Samui	21 days	Stayed at hotels, a beach cabin and a river cabin	Sightseeing, visiting temples, street kitchens and food markets, sunbathing at the pool, river boat trip, hiking
11 years	France	10 days	No data	Sightseeing, kayaking, canyoning
	Austria	7 days	Cabin	Skiing holiday
12 years	France, Paris	7 days	Hotel	Sightseeing
	Tunisia	10 days	Stayed in clay huts, caves in the Sahara Desert and hotels	Camel riding, visiting markets
	Norway	7 days	Cabin	Skiing holiday

symptoms. CE develops slowly, and infected individuals can remain asymptomatic for years.

Echinococcus granulosus sensu stricto G1 strain is globally common. Therefore, based on the genotype, the size of the cyst and her travels to endemic areas it is not possible to determine where and when she was infected. A literature search identified one previous published case of CE presumably acquired during a tourist travel: A 32-year-old woman, born and grown up in the Netherlands, was diagnosed with CE in the lungs and the liver. She had probably been infected seven years earlier on a holiday in Turkey [6].

This case highlights the importance of reaching the diagnosis at species-level and further genotyping. Data on species and genotypes of *Echinococcus* spp. need to be gathered using a One Health approach – from human cases, animal hosts, food and environmental samples – to enable source attribution and to inform interventions and advice. Because *E. granulosus sensu stricto* G1 has not been identified in animal hosts nor in food or environmental samples from Denmark, it was concluded that the patient most likely acquired the infection during a tourist travel abroad. As humans are dead-end hosts for the parasite, there is no further transmission when the infection is imported by a human hosting it. Key advice for avoiding the infection during travels is covered by general hygiene and food hygiene advice: washing hands and washing or cooking food items that could be contaminated by faeces of infected definitive hosts.

In this case, CE was not initially considered a differential diagnosis, and the diagnosis of CE was reached postoperatively upon histopathological examination. Earlier diagnosis was challenged, as the serological tests were negative. It is well known that negative serologic test results do not rule out CE, and specifically for patients with pulmonary CE, the serological responses tend to be lower, with negative serology being observed in about third of the cases [5]. What could have been done to reach the diagnosis a bit earlier is direct microscopy of the cyst contents during or immediately after the operation.

Surgery is the recommended treatment for CE in the lungs, with adjunctive drug therapy four weeks prior to surgery as well as four weeks postoperatively to avoid seeding of protoscoleces during the procedure. The World Health Organization recommends albendazole to be avoided during the first trimester but endorses treatment of pregnant women in the second and third trimester if clinically indicated [7]. In this case, the pathologist was definite in their description, and treatment was initiated before the diagnosis was confirmed by molecular methods. It was decided to initiate treatment with albendazole and to complete postoperative regimen of four weeks treatment.

This case emphasises the challenge of diagnosing CE. It highlights the limitation of serology in the diagnostics and the importance of collaborations across specialist fields. CE is a neglected zoonotic disease [9], and knowledge and awareness about CE is important for differential diagnostics, also in non-endemic areas. CE should be considered also in patients from non-endemic areas, who have travelled to endemic countries, that are diagnosed with liver or lung cyst.

Ethical approval

Nothing to declare.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of Competing Interest

The authors declare no conflict of interests regarding the publication of this paper.

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