

Echinococcus multilocularis infection presenting clinically as cholangiocarcinoma

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Abstract

Cases of alveolar echinococcosis (liver cyst) caused by *Echinococcus multilocularis* are rare in the UK, but are increasing secondary to migration and travel. We report a case of alveolar echinococcosis that presented clinically as a cholangiocarcinoma. At histology, vesicles unusually contained protoscoleces, a feature more commonly seen in cases of *Echinococcus granulosus*. PCR confirmed the organism as *E. multilocularis*, avoiding misdiagnosis and subsequent mismanagement.

Keywords alveolar echinococcosis; *Echinococcus multilocularis*; liver cyst

Case report

A 30 year old female, originally from Eastern Europe, presented to her GP with fatigue and alopecia. Blood tests revealed an elevated ALP and slightly raised ALT. Ultrasound of the liver showed a hilar Klatskin tumour with duct dilatation, compatible with cholangiocarcinoma, and this was confirmed by MRI. The patient underwent an extended right hemihepatectomy.

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Macroscopic examination revealed an unusual multi-vesicular lesion surrounded by firm yellow tissue and focal calcification (Figure 1a). No tumour mass suggestive of cholangiocarcinoma was identified. Histology revealed multiple small vesicles lined by collapsing laminated membranes, some with a retained germinal layer (Figures 1b and 1c). Occasional viable protoscoleces (the larval stage of a tapeworm), were noted (Figure 1d). Vesicles were surrounded by fibrosis, palisaded histiocytes forming granulomas and chronic inflammation including eosinophils (Figure 1c). Vesicles infiltrated the hepatic parenchyma, and were identified tracking along nerve fibres adjacent to an extrahepatic bile duct.

The case was referred to the Hospital for Tropical Diseases, London, for histological review and serological testing. PCR of the tissue confirmed the presence of *Echinococcus multilocularis* (*E. multilocularis*). Imaging excluded cerebral involvement. The patient received albendazole and is under long-term follow-up locally and by the National Hydatid MDT to monitor recurrence. Family members were screened.

Discussion

There are a number of *Echinococcus* species, of which four infect humans. Two species predominate: *Echinococcus granulosus* (*E. granulosus*), which causes Cystic Echinococcosis (CE), and *E. multilocularis*, which causes alveolar echinococcosis (AE). Histopathologists will be familiar with CE or the conventional 'hydatid cyst', which is still endemic in parts of the UK. However, *E. multilocularis* is not endemic to the UK, and has a lower worldwide incidence; cases of *E. multilocularis* are therefore rare and prone to misdiagnosis partly due to a lack of awareness.

E. multilocularis is a cestode (tapeworm) transmitted to humans from the definitive hosts foxes, dogs and cats, either through direct contact or indirectly through contaminated food or water (parasitic ova are excreted in faeces of the definitive host).¹ The worldwide incidence is estimated to be 18,235 new cases/year, with cases confined to the Northern hemisphere.² Approximately 90% of cases occur in China; other affected areas include certain central and eastern European countries (e.g. France, Switzerland, Austria, Germany), Asia, and parts of the USA and Canada.^{1,2}

Unlike *E. granulosus* which can involve almost any organ, *E. multilocularis* primarily affects the liver, although the disease can spread to other organs by direct infiltration or metastasis.³ Due to the infiltrative tumour-like growth pattern with irregular

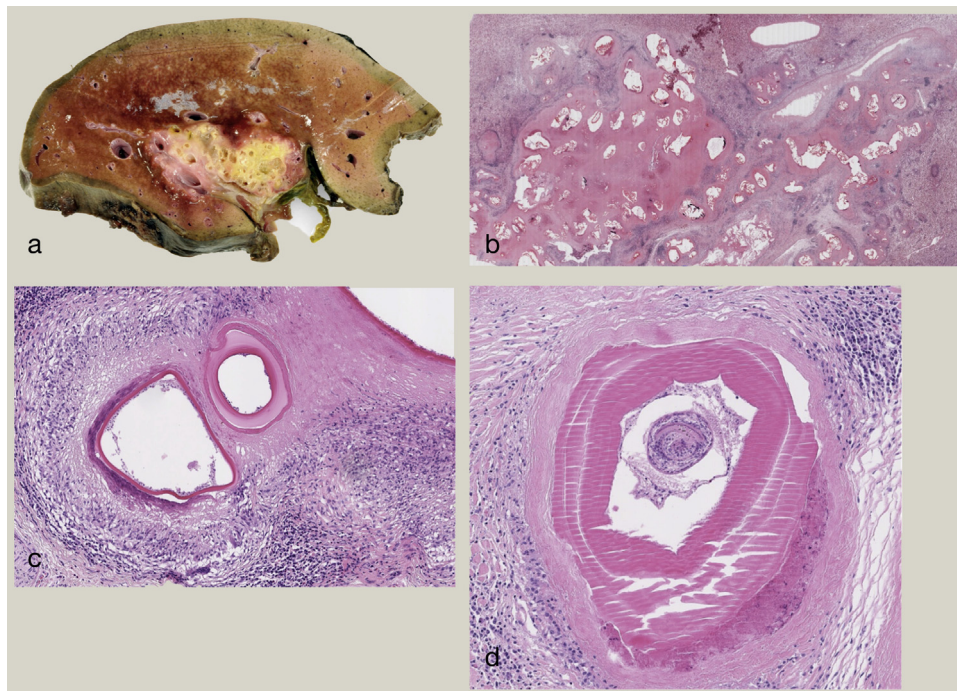


Figure 1 (a) Macroscopic image of pale multivesicular central area within a right extended hemihepatectomy specimen. (b) Low power histology (x0.5) showing multiple variably sized vesicular spaces infiltrating into the liver parenchyma, giving rise to the description 'alveolar pattern'. (c) High power view (x20) of vesicles with laminated membrane and surrounding periparasitic granuloma and chronic inflammation with eosinophils. (d) Histology (x20) of a viable protoscolex within a vesicle; this is an unusual finding in cases of *E. multilocularis*.

margins, cases are often misdiagnosed on imaging as hepatocellular carcinoma or cholangiocarcinoma. The latency period is 10–15 years⁴; the majority of patients are asymptomatic until the late stages of the disease, when they may present with abdominal pain, cholestatic jaundice, or liver failure.³ Patients should ideally be managed by a centralized specialist MDT. Treatment is with surgery and long term or life-long antiparasitic treatment with a benzimidazole, usually albendazole. Life expectancy at diagnosis is 20 years.^{1,3}

The histological features of *E. multilocularis* infection include variably sized (<1 mm up to 30 mm) parasitic vesicles lined by laminated membrane, surrounded by granulomas.¹ Lesions are arranged in an alveolar pattern and can be set within a collagenous and necrotic stroma. Lesions may infiltrate adjacent parenchyma and track along nerves.

Management of patients with Echinococcus should be planned by a multidisciplinary team approach, which is often regional or national (in the UK this is hosted by the Hospital for Tropical Diseases in London). Patients with *E. granulosus* can be managed in a number of ways, including percutaneous treatment, surgery, drugs such as benzimidazoles, or watchful waiting, depending on the stage of the disease. By comparison the management of *E. multilocularis* is much more complex. Ideally, early diagnosis with radical resection followed by long term management with benzimidazoles (e.g. albendazole) is recommended; however treatment with lifelong benzimidazoles is required for inoperable cases or those with suboptimal resection margins. These patients also require long term follow up to assess for recurrences.^{1,3}

Our case was unusual as vesicles contained protoscolexes, which are frequently present in cases of *E. granulosus* but are present in only 3% of cases of *E. multilocularis*.^{1,5,6} Expert review is recommended, and PCR can be performed to confirm the diagnosis. It is vital that histopathologists appreciate that protoscolexes may rarely occur in cases of *E. multilocularis*, in order to avoid misdiagnosis as *E. granulosus* with subsequent mismanagement which could prove fatal. This is particularly relevant, as cases of *E. multilocularis* are increasing in the UK, secondary to migration from endemic countries including Europe. ◆

Practice points

- With migration, cases of *E. multilocularis* are increasing in the UK.
- Clinically, such cases may mimic hepatocellular carcinoma or cholangiocarcinoma.
- Protoscolexes, which are frequently present in cases of *E. granulosus*, may rarely be seen in cases of *E. multilocularis*; histopathologists should be aware of this, to avoid misdiagnosis as *E. granulosus* and subsequent mismanagement.
- Diagnosis should be confirmed by expert review, and PCR may be required.

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Self-assessment

In which of the following countries is *E. multilocularis* endemic

- A UK
- B Switzerland
- C Peru
- D Argentina
- E Australia

Answer: B Switzerland

In what percentage of *E. multilocularis* cases do the vesicles include protoscoleces

- A 0%
- B < 5%
- C 50%
- D 80%
- E 100%

Answer: B <5%

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