


# Simultaneous occurrence of hepatic alveolar and cystic echinococcosis

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## Short Communication

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## Abstract

The co-occurrence of hepatic cystic echinococcosis (CE) and alveolar echinococcosis (AE) is extremely rare. Here, we present the clinical manifestations and treatment outcomes of three cases with co-occurring CE and AE in the liver. Computed tomography (CT), magnetic resonance imaging and  $^{18}\text{F}$ Fluorodeoxyglucose Positron Emission Tomography-CT were used for preoperative diagnosis. Specimens were taken intraoperatively and sent for pathological studies to confirm the coexistence of CE and AE by laminated membrane, daughter cysts or germinal layer and infiltration structure. Albendazole was prescribed after operation for 12 months. All patients were completely recovered and showed no recurrence at last follow-up. Therefore, surgical intervention and postoperative application of albendazole are recommended for patients with concurrence of hepatic AE and CE.

## Introduction

Echinococcosis is a zoonotic disease caused by the larval stage of tapeworms of *Echinococcus* spp. including *Echinococcus granulosus* and *E. multilocularis*, causing cystic echinococcosis (CE) and alveolar echinococcosis (AE), respectively (Wen *et al.*, 2019). AE is a rare but life-threatening disease. *Echinococcus multilocularis* grows slowly at the larval stage and progressively develops in human livers, which is similar to the growth pattern of liver tumours (Vuitton & Bresson-Hadni, 2014). CE cysts are often round, unilocular fluid-filled bladders (Wen *et al.*, 2019).

Echinococcosis often leads to considerable morbidity and mortality, especially AE, with a high fatality rate if not managed properly. CE is globally distributed in most pastoral farming areas with high endemic regions, including countries around the Mediterranean, in northern Africa, southern and east Europe, South America and Central Asia including western China (Deplazes *et al.*, 2017). AE only distributes in the Northern Hemisphere, with high endemic rates in western China, Russia and central Europe (Deplazes *et al.*, 2017).

Although both diseases are endemic in China's western region, the concurrence of CE and AE in the same patient is exceptionally rare, as also reported by other Chinese researchers (Wen *et al.*, 1992; Yu *et al.*, 2006). Approximately 3750 patients have been admitted to our hospital with a diagnosis of CE for surgery in the past decade. Among them, only three cases presented with the concurrence of AE and CE. In this study, the diagnosis and treatment strategies of these cases are presented.

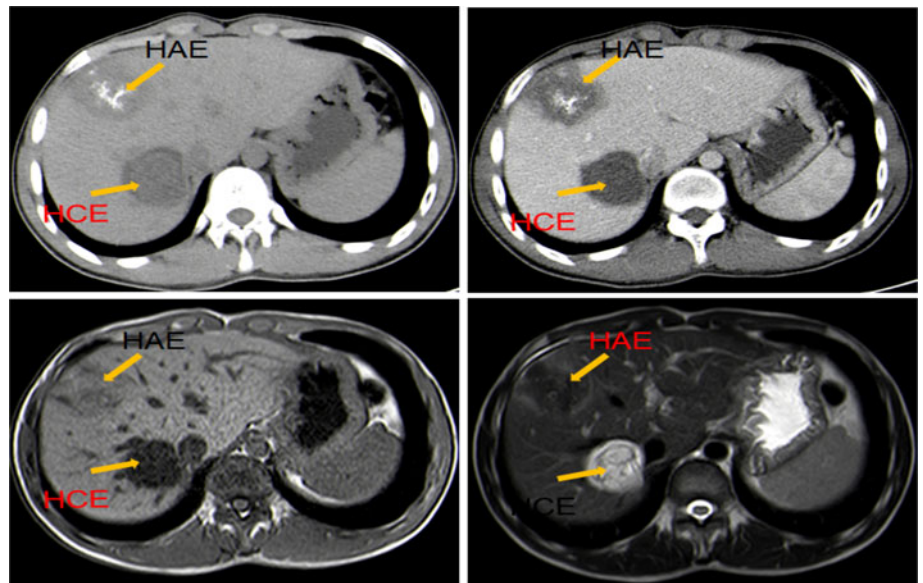
## Material and methods

### Ethical approval

The publication of patients' data in the report was approved by the Ethical Committees of the First Affiliated Hospital of Xinjiang Medical University (approval number 20080731-3) and written informed consent was obtained from each patient. All patients in this study were retrospectively enrolled from January 2009 to January 2019.

### Preoperative assessment

The size and location of the lesion, parenchymal, vascular and biliary extension were evaluated by computed tomography (CT), liver magnetic resonance imaging (MRI) and  $^{18}\text{F}$ Fluorodeoxyglucose Positron Emission Tomography (FDG-PET)-CT preoperatively (figs 1–3). The dot immune-gold filtration assay (DIGFA) was used to detect the serum echinococcosis specific antibodies (Feng *et al.*, 2010; Siles-Lucas *et al.*, 2017). Disease staging of these patients was categorized according to the World Health Organization Informal



**Fig. 1.** Typical CT and MRI imaging. Preoperative imaging demonstrates hepatic alveolar echinococcosis (HAE) and hepatic cystic echinococcosis (HCE) of a 17-year-old Tibetan patient who was found with co-occurrence of AE and CE.

Working Group on Echinococcosis P: parasite mass in the liver, N: involvement of neighboring organs, M: distance metastasis (PNM) classification system (Kern *et al.*, 2017). Specimens were taken intraoperatively and sent for pathological studies to confirm the coexistence of CE and AE by laminated membrane, daughter cysts or germinal layer and infiltration structure.

### Case reports

#### Case 1

A 17-year-old Tibetan man was admitted to our hospital with chief complaint of a recurrent pain in the right upper-abdominal region. Physical examination of the abdominal region was unremarkable. Both MRI and CT showed a solid lesion with ill-defined contours in the right posterior lobe of the liver, which was suspected as hepatic AE. In addition, a cystic lesion with a collapsed capsule in the right anterior lobe of the liver was suspected as hepatic CE (fig. 1). Laboratory tests including complete blood count, C-reactive protein level, kidney and liver function were normal. DIGFA showed *EgCF* and *Em2* positive, whereas *EgP* and *EgB* were negative. The patient disclosed that he had frequent contact with dogs, yaks and sheep. The staging of the AE lesion indicated P1N0M0 for AE and CE4/T4D8C0 for CE according to the World Health Organization Informal Working group on Echinococcosis classification system. Laparoscopic partial hepatectomy and subtotal peri-cystectomy were applied for the treatment. The patient recovered well and was successfully discharged five days after operation.

#### Case 2

A 25-year-old female from a village in Tibet was admitted to our department with chief complaint of abdominal pain in the right upper-quadrant region. Routine laboratory tests were unremarkable. CT and MRI showed multiple lesions and daughter cysts in the liver, which was suspected as CE, while other lesions with irregular appearance demonstrated mixed density, which was suspected as AE (fig. 2). An  $^{18}\text{F}$ FDG PET-CT scan showed that the lesion in the caudate lobe had circular low-density shadows and clear boundaries, with no  $^{18}\text{F}$ FDG uptake, which highly indicated a CE lesion. Other lesions with nodular and

circumferential calcification had higher FDG uptake and were also considered as AE. DIGFA showed weakly positive against *EgCF* and *EgP* and negative against *EgB* and *Em2*. Staging of the diseases was P1N0M0 for AE and CE3b/T3D6C0 for CE. The patient underwent laparotomic partial hepatectomy and total peri-cystectomy.

#### Case 3

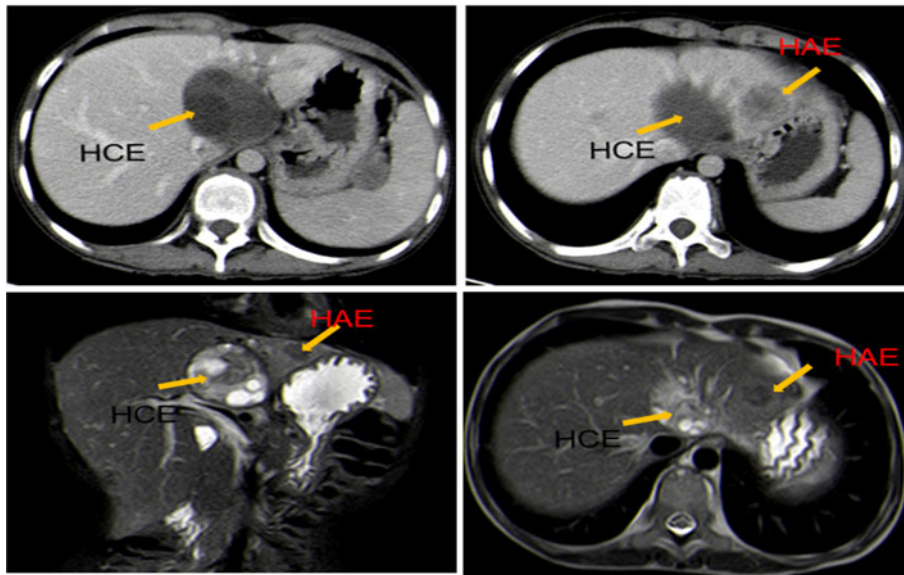
A 29-year-old Mongolian male presented with cystic and solid lesions in his liver during a routine physical check-up at his local hospital. Past medical history revealed that he underwent surgery for hepatic AE six years ago. Physical examination was normal. CT and MRI revealed a lesion in the right liver lobe with irregular appearance, peripheral calcification, mixed density and invasion of the diaphragm, which was suspected as AE recurrence. Meanwhile, the daughter cystic lesion on the left lateral lobe with clear boundaries was suspected as CE (fig. 3). DIGFA showed weakly positive against *EgCF*, *EgP* and *EgB*, and negative against *Em2*. Staging of the disease was P2N1M0 for AE and CE4/T4D8C0 for CE. The patient underwent laparotomic partial hepatectomy with phrenectomy and total peri-cystectomy.

#### Post-operative follow-up

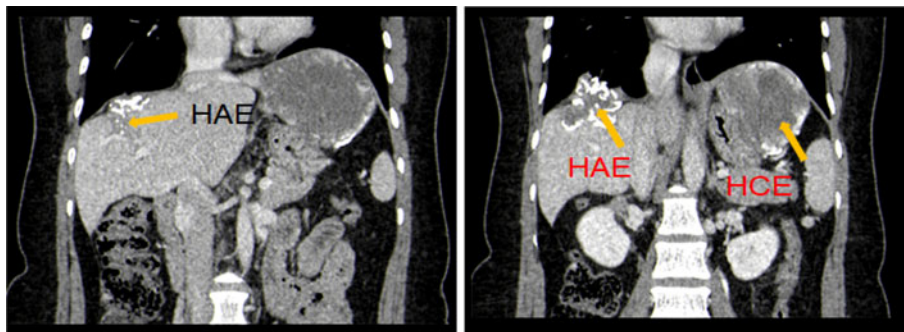
All patients were prescribed with albendazole for 12 months after successful removal of the AE and CE lesions (Kern *et al.*, 2017), and were closely followed-up for one year at an outpatient clinic for any possible recurrence.

#### Results and discussion

All patients received a standardized protocol of albendazole for 12 months after surgery and no recurrence has been recorded at one-year follow-up. Some researchers have reported the concurrence of AE and CE in the Qinghai-Tibetan Plateaus by ultrasonography for epidemiological surveys (Feng *et al.*, 2010; Li *et al.*, 2010); however, their cases have not been confirmed by intraoperative findings or pathological studies. Our study presents cases with the concurrence of AE and CE, as confirmed by surgery and pathological studies.



**Fig. 2.** Representative preoperative imaging. Typical imaging shows hepatic alveolar echinococcosis (HAE) and hepatic cystic echinococcosis (HCE) of 25-year-old female patient with co-occurrence of AE and CE.



**Fig. 3.** Typical preoperative imaging. This imaging indicates hepatic alveolar echinococcosis (HAE) and hepatic cystic echinococcosis (HCE) of 29-year-old Mongolian male patient with co-occurrence of AE and CE.

The concurrence of AE with CE in the same patient is rare. The low co-infectious rate in high-endemic areas indicates that they may prevent any progression of each other. However, our cases of concurrence may indicate that the mutual preventive mechanism of disease progression was compromised.

Image examination (CT, MRI and  $^{18}\text{F}$ FDG-PET-CT) plays an important role in the diagnosis and differential diagnosis of the concurrence of AE and CE. Ultrasonography is usually the first-line examination tool for CE and complemented by CT and/or MRI for further confirmation of the concurrence of AE and CE (Brunetti *et al.*, 2010; Kern *et al.*, 2017). Ultrasonography actually works better for CE diagnosis, especially in the case of CE3a or CE3b cysts (Pawłowski *et al.*, 2001; McManus *et al.*, 2012). CT depicts the characteristic calcification pattern of AE and water-like density with daughter cysts of CE, while in some AE cases with a large irregular cyst without solid components, MRI may show the characteristic multi-vesicular appearance of AE lesions more accurately (Bece *et al.*, 2014).  $^{18}\text{F}$ FDG PET-CT imaging can display all the lesions at the same time. It can not only detect the invasion, morphology, number, boundary, internal calcification and surrounding tissues of hepatic hydatid echinococcosis, but also observe dynamic changes in hepatic echinococcal cysts (Qin *et al.*, 2016). In this study, the second case, which presented with multiple lesions located in the caudate lobe and typical daughter cysts, can be clearly diagnosed as CE by ultrasonography and CT scan, while the rest of the liver lesions appeared on CT

and MRI as peripheral calcification and internal necrosis, which demonstrated atypical AE. In addition,  $^{18}\text{F}$ FDG PET-CT showed a high  $^{18}\text{F}$ FDG uptake of all lesions except the caudate lobe, which confirmed the diagnosis of AE and CE concurrence. The CT image of the third patient indicated that the lesion with regular appearance and collapsed cysts in the left lobe was diagnosed as CE, while the lesion in the right posterior lobe presented irregular calcification in the periphery and necrotic lesions in the left interior lobe, which was difficult to confirm as AE. MRI showed the characteristic multi-vesicular appearance of AE lesions. For the diagnosis of the concurrence of AE and CE, we propose that MRI and ultrasonography are the best preoperative diagnostic tool, while CT scanning can be used as a reference to the preoperative plan. If making a diagnosis is difficult based on the aforementioned approach,  $^{18}\text{F}$ FDG PET-CT can be applied for confirmatory diagnosis.

Serological tests are also useful in the diagnosis, which can be applied in differential diagnosis. The sensitivity of a serological test is dependent on the cystic stage, size, location, host immunity, local epidemiology and the test methodology (Siles-Lucas *et al.*, 2017). Serological tests are commonly employed for the diagnosis of CE to look for antibodies directed against a particular antigen, and this is the reason why patients may have a positive antigen for several years after surgery. In this study, the dot immune-gold filtration assay (DIGFA) was used to detect specific antibodies in the serum of these patients. However, the results showed that



all patients were serologically negative against *E. multilocularis* antigen, and two patients were weak positive against *E. granulosus* antigens. Based on these serological results, DIFA was not recommended in the diagnosis of the concurrence of AE and CE.

The treatment of hepatic echinococcosis depends on the stage, size and form of cyst/metacestode of *Echinococcus* (McManus *et al.*, 2012; Wen *et al.*, 2019), and surgical intervention is effective in selected cases (Brunetti *et al.*, 2010). In this study, in order to identify the location and invasion of the lesion, the three-dimensional laparoscopic technique was used for the first patient, which made operation easier for the surgeon than the two-dimensional procedure. The laparoscopic technique is superior in terms of blood loss, analgesic requirements, hospital stay and convalescence compared to traditional open surgery.

In summary, the surgical removal of AE and CE lesions, with 12 months of albendazole prescribed post operation, has shown to have a curative effect, and we propose that MRI is the best pre-operative diagnostic method for detecting the concurrence of AE and CE.

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**Conflicts of interest.** None.

**Ethical standards.** The authors assert that all procedures contributing to this work comply with the Ethical Committees of the First Affiliated Hospital of Xinjiang Medical University. Written informed consent was obtained from all patients for publication of the clinical data.

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