Journal of Medical Sciences. 23 Nov, 2023 - Volume 11 | Issue 6. Electronic - ISSN: 2345-0592
Medical Sciences 2023 Vol. 11 (6), p. 45-52, https://doi.org/10.53453/ms.2023.11.6

e-ISSN: 2345-0592
Online issue
Indexed in *Index Copernicus*

Medical Sciences

Official website:
www.medicsciences.com

Case report of hepatic alveolar echinococcosis

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Abstract

Background. Hepatic alveolar echinococcosis (HAE) is a parasitic disease, caused by Echinococcus multilocularis. HAE may be a challenging diagnosis, as it often resembles a malignant liver lesion upon initial investigation. Diagnosis of HAE as a malignancy may result in surgical overtreatment or progression to a stage in which resection may no longer be available and in some cases critical delay in growth-inhibiting benzimidazole treatment.

Case presentation. We present a case of HAE and its differential diagnostic work-up from cholangiocarcinoma (CCA), with thorough radiological work-up being the primary diagnostic tool. Our patient, a 65-year-old male was admitted to the emergency department (ED) with complaints of pruritus and jaundice. An abdominal ultrasound (US) performed in the ED revealed an irregular heterogeneous necrotic mass. Laboratory work-up showed conjugated hyperbilirubinemia, slightly elevated liver transaminases and significantly increased cholestatic markers. Following this, the patient was transferred to the gastroenterology department. A contrast-enhanced chest abdomen-pelvis computerized tomography (CT) scan was performed. The images detected a tumorlike heterogeneous hepatic mass with a liquefied necrotic area. Abdominal US ruled out cholangiocarcinoma (CCA) and a positive anti-echinococcus IgG antibody test confirmed the diagnosis of HAE. After alleviating obstructive cholestasis with biliary stenting using endoscopic retrograde cholangiopancreatography, treatment with albendazole was initiated and the patient was discharged. At 1 month follow-up, cholestatic serum markers had improved with no reported side effects of anthelmintic treatment.

Conclusion. Despite diagnostic and treatment innovations, HAE still causes high mortality in the Baltic region. Thus, gastroenterologists should be aware of the relevance of HAE as a differential diagnosis in infiltrating liver lesions.

Keywords: hepatic alveolar echinococcosis, echinococcus multilocularis, case report, ultrasonography, computerized tomography, cholangiocarcinoma.

1. Introduction

Hepatic alveolar echinococcosis (HAE) is a parasitic disease, caused by Echinococcus multilocularis (E. multilocularis) [1]. Humans contract echinococcosis by petting or handling infected animals (e.g. fox, wolf, raccoon dog) or ingesting food contaminated with their faeces [2]. In one study, E. multilocularis was detected in 58.7 % of red foxes examined in various areas of Lithuania [3]. Despite diagnostic and treatment innovations, HAE still causes high mortality in the Baltic region. From 1997 to 2013, the survival in 35.4 % of registered HAE cases in Lithuania was less than one year from initial diagnosis, due to the advanced stage of the disease [4]. Moreover, HAE may be a challenging diagnosis, as it often resembles a malignant liver lesion upon initial investigation, which may lead to an inappropriate treatment strategy [5]. We present a case of HAE and its differential diagnostic work-up from cholangiocarcinoma (CCA).

2. Case presentation

A 65-year-old man was admitted to the emergency department (ED) with complaints of pruritus and jaundice. The patient noted passing putty-coloured stools and decreased appetite, having lost about 2 kg during a couple of weeks. During physical examination, no abdominal symptoms were observed. The patient had no previous history of liver disease or other underlying conditions. An abdominal ultrasound (US) in the ED revealed an irregular heterogeneous mass with a large area of necrosis, peripheral hyperechogenicity and dilated biliary tree. Laboratory work-up showed conjugated hyperbilirubinemia, slightly elevated liver transaminases and significantly increased cholestatic markers (Table 1).

Table 1. *Laboratory blood analysis with signs of cholestasis.*

Laboratory analysis		
Parameter	**Value**	**Reference value**
Total bilirubin	241.98 μmol/L	5-21 μmol/L
Direct bilirubin	145.01μmol/L	0-3,4 μmol/L
Alanine aminotransaminase	75.0 U/L	1-50 IU/I
Aspartate aminotransferase	84.0 U/L	1-50 IU/I
Alkaline phosphatase	621.0 U/L	30-120 IU/I
Gamma-glutamyl transferase	781.0 U/L	1-39 I/UI

Following this, the patient was transferred to the gastroenterology department. A contrast-enhanced chest abdomen-pelvis computerized tomography (CT) scan was performed. The images detected a tumorlike heterogeneous hepatic mass, infiltrating the hilum and right liver lobe, where it had formed a liquefied necrotic area (Figure 1).

To differentiate between HAE lesion and CCA, a throughout abdominal US was performed. The pseudocyst pattern located in the right liver lobe, containing ~1460 ml of liquid, supported the high possibility of echinococcus parasitic tissue (Figure 2).

Figure 1. *Contrast-enhanced CT reveals heterogeneous hepatic mass infiltrating the hilum and right liver lobe (15.7 × 13.4 × 16.7 cm).*

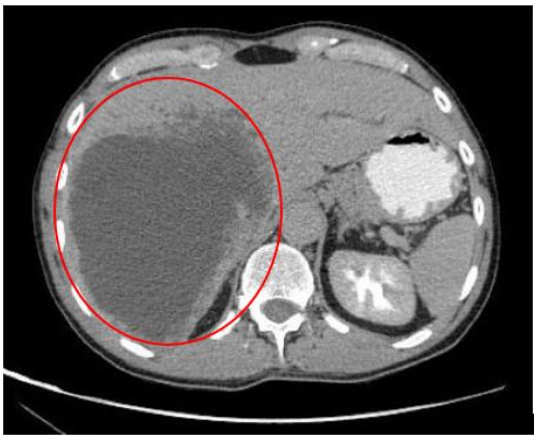
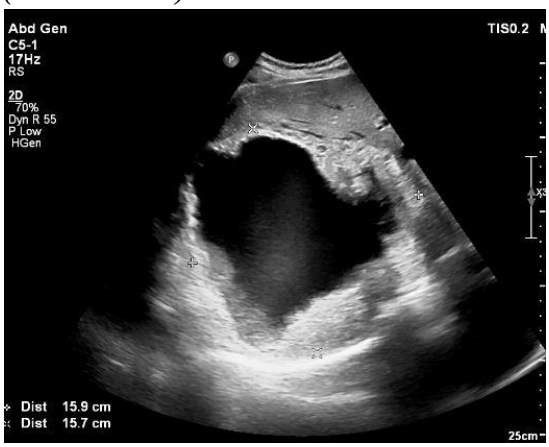


Figure 2. *The abdominal US showcases a pseudocyst with a large area of central necrosis surrounded by an irregular region of hyperechogenicity representing fibrous tissue (15.9 × 15.7 cm).*



Biopsy of the lesion was avoided due to the possible spread of echinococcosis. An immunoserologic analysis for anti-echinococcus IgG antibody came back positive, supporting the diagnosis. According to clarified environmental anamnesis, the patient is an agricultural worker and noted having contact with non-domesticated red foxes two years before current hospitalization. The patient's further treatment plan was discussed by a multidisciplinary team. It was decided that the formation was too large for successful radical surgical resection. After alleviating obstructive cholestasis with biliary stenting using endoscopic retrograde cholangiopancreatography, treatment with albendazole 400 mg twice daily was initiated and the patient was discharged.

During a follow-up after a month, the patient reported no abdominal symptoms or other side effects (e.g. toxic hepatitis) of anthelmintic treatment. Moreover, a blood work-up revealed markedly improved bilirubin and liver enzyme levels. Thus, a choice to continue the treatment with albendazole for at least two years was made.

3. Discussion

Diagnostic strategy. The diagnosis of HAE is based on the patient's clinical-epidemiological history, radiological imaging, serologic and histopathologic analyses [6]. At least two of the following findings are needed to confirm a case of HAE: 1) typical lesion pattern confirmed with imaging; 2) positive Echinococcus spp. serologic test; 3) E. multilocularis histopathologic features; and 4) E. multilocularis DNA identification in a clinical specimen [7].

The main method of HAE diagnosis is radiological imaging, while serologic examination (Echinococcus spp. and E. multilocularis IgG ELISA) is used to support the diagnosis or rule it out [8]. In cases of ambiguous radiological and serological test results, percutaneous fine needle aspiration (FNA) biopsy may be considered [9]. However, it is not usually recommended due to the potential spread of daughter cysts. In rare cases of FNA, prophylactic treatment with albendazole for 4 days prior to the procedure and continuation for one month after, is recommended [10]. Ultrasonography is the initial diagnostic method of

HAE [11]. The World Health Organization Informal Working Group on Echinococcosis (WHO-IWGE) proposed an imaging classification that groups HAE lesions into different PNM (parasite lesion, neighbour organs, metastases) types to help with determining further treatment strategies [12]. E. multilocularis Ulm classification-ultrasound (EMUC-US) distinguishes five different lesion patterns: hailstorm, pseudocystic, hemangioma-like, metastasis-like and ossification [13]. However, about 70 % of cases present as a mixed echogenicity hepatic mass with irregular margins, dispersed calcification foci, and a pseudocyst with central necrosis surrounded with a rim of hyperechogenicity [8,11]. Contrast-enhanced ultrasonography (CEUS) is another promising diagnostic technique, as it visualizes the parenchymal microvasculature of HAE lesions [14]. It is proven, that CEUS can accurately differentiate HAE from tumors, such as CCA and hemangiomas [14,15]. Fluorodeoxyglucose positron emission tomography (FDG-PET) is the recommended HAE metabolic activity evaluation tool, as the FDG uptake in HAE lesions is higher than in unaffected liver areas [16]. However, previous studies report that CEUS can assess the activity of HAE, similar to FDG-PET [17]. Magnetic resonance imaging (MRI) may provide a more precise evaluation of the parasitic lesion [8]. However, in cases of diagnostic uncertainty and pre-operative evaluation, computed tomography (CT) remains the modality of choice, as it evaluates vascular, biliary, and extrahepatic infiltration of the mass, which is valuable when considering lesion resectability [18]. A simplified diagnostic algorithm is depicted in Figure 3.

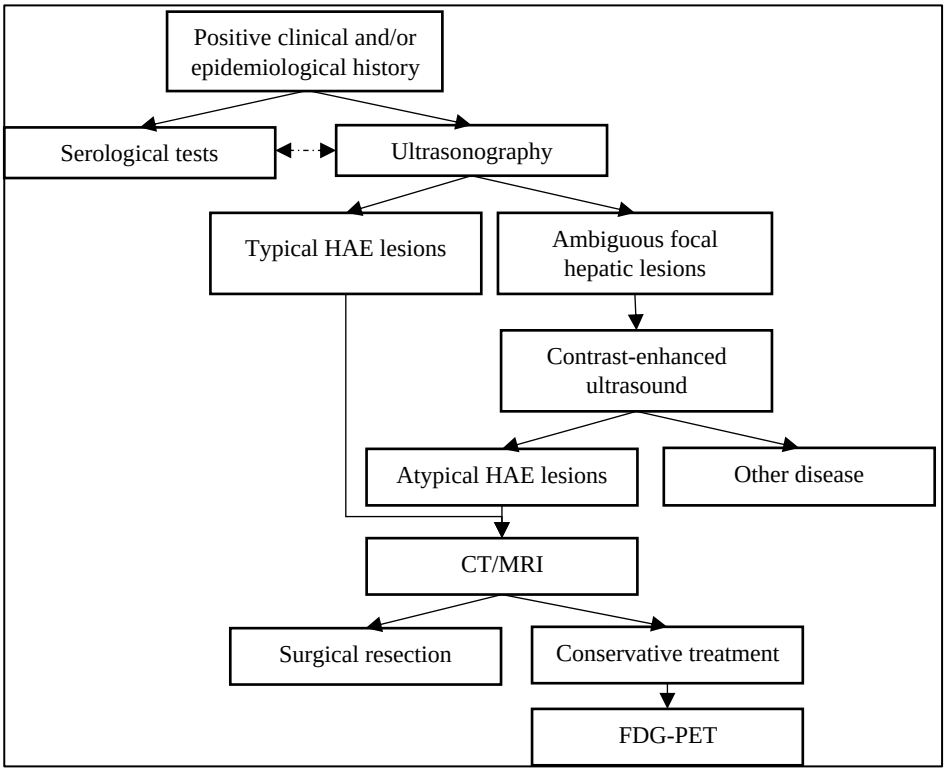
Nonetheless, differentiating HAE from other hepatic masses can be a challenging task, as many cases are diagnosed incorrectly as CCA or other liver malignancies [5,19]. In one study, 32.5 % of HAE patients were initially given the wrong diagnosis, while HAE was mistaken for CCA in 19.2 % of the cases [5]. Considering the clinical significance of misclassifying HAE as CCA, a scoring system based on typical features of conventional US and CEUS has been proposed, with the sensitivity and specificity of 80.0 % and 81.3% respectively [14]. The extensive diagnostic examination of HAE is important, as misclassifying it as a malignancy may result in surgical overtreatment or progression to a stage in which resection may no longer be available and in some cases critical delay in growth-inhibiting benzimidazole treatment [5,20]. Thus, gastroenterologists should be aware of the relevance of HAE as a differential diagnosis in infiltrating liver lesions.

Treatment and management.

The therapeutic strategy of HAE requires a multidisciplinary approach, as it is based on radiological evaluation with an MRI and (or) FDG-PET, the general status of the patient, and the technical capabilities of the surgical department [2]. HAE is often diagnosed in its advanced stage and is located in the right liver lobe, involving vascular and biliary structures. Thus, surgical liver resection cannot be performed safely [21]. In cases, with metabolically inactive lesions, which are calcified and/or negative by FDG-PET "watch-and-wait" approach can be used [2]. If the lesion is metabolically active and considered operable, the gold standard surgical treatment is radical

hepatectomy combined with adjuvant albendazole therapy for at least 2 years postoperatively [22]. Reduction surgery has been proposed as an alternative in some advanced cases. However, it does not appear to provide an advantage over anthelmintic therapy alone and has worse overall survival and progression-free survival outcomes than radical resection [23]. Liver transplantation (LT) may be considered for very advanced cases with a high risk of life-threatening complications [2]. Aydinli et al. presented their own experience with LT for HAE patients, with the overall survival rate being 77.8 % and the most common cause of death – sepsis [24]. Although the prognosis after LT for HAE is considered good, disease recurrence remains a risk due to immunosuppressive therapy [25]. Considering this, the WHO does not recommend LT in patients with AE metastases [1]. Ex vivo liver resection with auto-transplantation in end-stage HAE has been proposed as a palliative surgical option [2]. Aji et al. evaluated this surgical modality in a prospective study with 69 patients, the 30-day mortality and overall mortality being 7.24 % and 11.5 % respectively [26]. If surgical treatment is not possible, reducing the proliferation of E.multilocularis with long-term anthelmintic medication is recommended [2]. Albendazole is usually chosen to treat HAE, as it has been proven to be more efficient than mebendazole [27]. In a study conducted by Zavoikin et al., albendazole inhibited HAE progression in 60 % of patients with unresectable lesions [28]. However, considering that albendazole is only parasitostatic, further clinical trials are needed to investigate drugs (e.g. protease or immune checkpoint inhibitors) that could achieve a parasitocidal effect [29].

Figure 3. *Diagnostic algorithm for HAE.*



Another important aspect of HAE management is the treatment of complications, such as cholangitis, bile duct obstruction and bacterial infection of the necrotic cavity. The previous two are alleviated with endoscopic bile duct lavage/stenting and percutaneous drainage [2].

The recommended follow-up after diagnosis and initiation of albendazole is at 1, 4, and 12 weeks for the first 3 months. Then, every 3 months for the first year and every 6 months for the second year. The assessment should include abdominal US, complete blood count, transaminases, E.multilocularis serology, and albendazole sulfoxide (an active metabolite of albendazole) [30]. FDG-PET is performed at the end of the second year. However, anthelmintic treatment can only be withdrawn after two negative FDG-PET and E.multilocularis serology results [2,30].

4. Conclusions

HAE is a zoonotic parasitic infection primarily affecting the liver. Treatment strategy of HAE mainly consists of three options: (1) surgical approach (resection or transplantation) with combination albendazole therapy, (2) long-term monotherapy with albendazole, and (3) alleviation of possible complications. However, surgery is often deemed unsafe, as HAE tends to be diagnosed in an advanced stage. Moreover, due to diagnostic challenges, HAE is quite often misinterpreted as a malignancy. Thus, a high degree of clinical suspicion needs to be maintained, especially in endemic areas and a thorough investigation should be performed. A detailed patient history, radiological work-up and serology are the primary diagnostic tools with histology being reserved for the more challenging cases.

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