

This article is licensed under the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC) (<http://www.karger.com/Services/OpenAccessLicense>). Usage and distribution for commercial purposes requires written permission.

Single Case

Alveolar Echinococcosis Mimicking a Hepatic Neoplasm with Lymph Node Metastasis: A Case Report

Takahiro Amano^a Shiro Hayashi^a Tsutomu Nishida^a
Tokuhiro Matsubara^a Kei Takahashi^a Dai Nakamatsu^a
Yoshito Tomimaru^b Masashi Yamamoto^a Sachiko Nakajima^a
Koji Fukui^a Hiromi Tamura^c Shiro Adachi^c Keizo Dono^b
Masami Inada^a

^aDepartment of Gastroenterology, Toyonaka Municipal Hospital, Toyonaka, Japan;

^bDepartment of Surgery, Toyonaka Municipal Hospital, Toyonaka, Japan; ^cDepartment of Pathology, Toyonaka Municipal Hospital, Toyonaka, Japan

Keywords

Alveolar echinococcosis · *Echinococcus multilocularis* · Endoscopic ultrasonography fine-needle aspiration

Abstract

A 37-year-old man had an asymptomatic 17-mm mass in the liver by health check with ultrasonography. Five years later, he was referred to our hospital because the mass was slightly enlarged with a peripancreatic lymph node. We performed endoscopic ultrasonography fine-needle aspiration (EUS-FNA) to evaluate a lymph node, but it showed amorphous eosinophilic material and eosinophilic infiltrate in necrotic tissue of toothpaste-like white specimen. However, we diagnosed as potentially malignant liver mass with lymph node metastasis because of 2-deoxy-2-(fluorine-18) fluorodeoxyglucose uptake. We then performed hepatectomy and enucleation of the pancreas. DNA polymerase chain reaction analysis revealed *Echinococcus*

multilocularis infection. Retrospectively, we could find a part of *Echinococcus* in the specimens of EUS-FNA.

© 2018 The Author(s)
Published by S. Karger AG, Basel

Introduction

Alveolar echinococcosis (AE) is a parasitic infestation that is caused by the larval stage of *Echinococcus multilocularis* spreading in the majority of the northern hemisphere [1, 2]. The main hosts are dogs, foxes, or related species that pass eggs into their feces, and humans can accidentally be an intermediate host in the life cycle of *E. multilocularis* [1]. It was reported that a high prevalence in foxes with *E. multilocularis* was recognized in the Hokkaido area, Japan. The larval form enters the lymphatic circulation by penetrating the intestinal mucosa [3], and AE is commonly located in the liver [4]. Since hydatid cysts grow slowly, many affected patients may remain asymptomatic for years. Ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), endoscopic US (EUS), and serological test are routinely used to diagnose AE [5, 6]. However, in nonendemic area, it is not always easy to differentiate AE from other neoplasms by these images and serological test [4, 5]. EUS fine-needle aspiration (EUS-FNA) to diagnose AE is contraindicated because it may cause seeding and because of the risk of anaphylaxis from spillage or leak of cystic fluid during FNA [7, 8]. There are, therefore, few reports of patients who had no other alternative but to be diagnosed as having AE with EUS-FNA [9–11]. We here report a case of an uncommon AE who underwent EUS-FNA in a nonendemic area.

Case Report

A 37-year-old man had an asymptomatic 17-mm mass in the liver by health check with US. Further noninvasive imaging led to the diagnosis of the mass as an inflammatory pseudotumor, and he was annually followed by US at a previous hospital. After that, he was referred to our hospital at the age of 42 because the liver mass was slightly enlarged and an enlargement of the lymph node adjacent to the head of the pancreas was newly detected. He had a medical history of viral meningitis, right clavicular fracture, and appendectomy due to appendicitis. He had no smoking or drinking habit. He had no resident history in the endemic areas of AE, but had been to the Hokkaido area more than 20 times. His physical examination and laboratory studies including tumor markers showed everything to be in the normal range (Table 1). We did not investigate with serologic assay for AE because we did not consider differential diagnosis. We evaluated the mass using contrast-enhanced CT, MRI, and EUS. Contrast-enhanced CT showed a 27-mm mass without enhancement and with dotted calcifications in liver segment 3 (Fig. 1a, b) and a 35-mm mass adjacent to the head of the pancreas (Fig. 1c, d) in a similar fashion to the former. MRI revealed masses with low intensity on T1-weighted images, slightly high intensity on T2-weighted images, and decreasing diffusion (Fig. 2) and no enhancement in the dynamic study. EUS (Olympus GF-UCT 260; Olympus Corp., Tokyo, Japan) showed the mass adjacent to the head of the pancreas with isoechoic, well-circumscribed, and mixed patterned with small cystic lesions (Fig. 3). In addition, to evaluate ma-

lignancy, we performed positron emission tomography with 2-deoxy-2-(fluorine-18) fluoro-deoxyglucose integrated with CT (^{18}F -FDG PET/CT) that showed uptake in both masses with a maximum standardized uptake value of 6 (Fig. 4). Based on the above findings, we suspected that those masses were malignant neoplastic lesions. We then performed EUS-FNA on the mass adjacent to the head of the pancreas through a transgastric approach using a 22-gauge needle (Expect®, Boston Scientific Co. Ltd.) for two punctures. Microscopic examination showed amorphous eosinophilic material and eosinophilic infiltrate in necrotic tissue of toothpaste-like white specimen obtained by EUS-FNA. It was difficult to differentiate definitively whether both masses were neoplastic or not. Comprehensively, we diagnosed them as a potentially malignant liver mass with a necrotic lymph node because it had showed slow enlargement with ^{18}F -FDG uptake. We did not perform target biopsy on the mass in liver segment 3 because it was located on the surface of the liver.

Obtaining the patient's informed consent, we planned partial hepatectomy with lymph node dissection adjacent to the head of the pancreas. First, diagnostic laparoscopy findings showed that there were no findings suggesting malignancy such as peritoneal dissemination and intraoperative rapid tissue diagnosis of the lymph node. Then, we performed the planned procedure. Macroscopic findings of the resected lesions revealed that there were a lot of small cysts including transparent mucus in both liver and peripancreatic masses (Fig. 5). Histological examination of the cystic lesion showed a floating acellular laminated cuticle with eosinophilic infiltrate, which is a characteristic of echinococcosis. DNA polymerase chain reaction analysis of tissue sections confirmed *E. multilocularis* infection. *E. multilocularis* was confirmed in a specimen of EUS-FNA by retrospective review (Fig. 6). There were no remnant findings with resected specimens. We finally diagnosed the patient as having AE of the liver with lymph node metastasis. He was discharged on the 7th postoperative day. He has had no recurrence without medication for 3 years and 3 months.

Discussion

Human echinococcosis is known as a zoonotic disease caused by the *Echinococcus* parasite. The most common species encountered in humans are *E. granulosus* and *E. multilocularis*, which cause cystic echinococcosis and AE, respectively [12]. AE is endemic in certain parts of the world, especially in Europe, Northern America, and Central Asia [1]. In Japan, the AE-endemic area is restricted to the Hokkaido area, although sporadic human cases have been rarely reported in other areas of Japan [13]. AE is usually asymptomatic and the clinical presentation depends on the size and the location [4]. It is difficult to differentiate it from any other malignant lesions of the liver in nonendemic areas [4, 5]. Furthermore, the growth of AE is slow (1–3 cm per year), similar to that of other liver tumors [4, 5]. In the present case, it was very difficult to diagnose AE and differentiate it from other neoplasms because of no resident history in endemic areas, but we finally considered he had acquired AE during his visiting to the Hokkaido area.

Serology findings and multiple images are necessary to differentiate AE from other tumors. In the present case eosinophilia, which is present in just 10% of cases, was not observed, and we did not examine specific IgG antibodies by ELISA, which confirms diagnosis in the majority of patients, because we could not give AE to differentiation before operation [4].

Abdominal US is considered the most sensitive tool for detecting floating membranes, hydatid sand, and floating daughter cysts. Presence of daughter cyst and plaque-like calcifications in the cystic wall detected by CT is also highly suggestive of hydatid cysts. However, in nonendemic areas, it is not always easy to differentiate AE from metastatic carcinoma, other primary liver tumors, and benign liver lesions such as hemangioma, focal nodular hyperplasia, and hepatocellular adenoma by these images [4–6].

EUS was recently reported to be among the effective modalities to differentiate AE from other cystic neoplasms [7, 14]. These images can help in the diagnosis of AE and its differentiation from other malignant lesions, and it has been reported that surgery remains the only definitive diagnostic and therapeutic tool [3, 7]. However, EUS-FNA for AE has the risk of seeding and anaphylaxis from spillage or leak of cystic fluid [7, 8]. Consequently, EUS-FNA is generally thought to be contraindicated [14]. There are few reports that EUS-FNA contributes to the differentiation of AE from other neoplasms [9–11]. Unfortunately, we preoperatively diagnosed these as a liver tumor with lymph node metastasis and did not reach a definitive diagnosis of AE in the present case. We performed a retrospective review, and it would have been possible to preoperatively differentiate lymph node AE behind the pancreas from other neoplasms by EUS-FNA. Fortunately, the patient has had no recurrence without medication for 3 years and 3 months after EUS-FNA. We should have to consider to differentiate AE in this case based on his history of visiting the Hokkaido area, but we think this case can be helpful when differentiating AE from other neoplasms.

Acknowledgment

We thank Yasuyuki Morishima, PhD, National Institute of Infectious Diseases, Tokyo for analyzing the nucleic acids purified from tissue sections and for confirming *E. multilocularis* infection.

Statement of Ethics

All procedures were performed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. The patient was not required to give informed consent for this case report because institutional review board approval was not required for a retrospective analysis of one case.

Disclosure Statement

The authors declare that they have no conflicts of interest.

References

- 1 Torgerson PR, Keller K, Magnotta M, Ragland N. The global burden of alveolar echinococcosis. *PLoS Negl Trop Dis*. 2010 Jun;4(6):e722.
- 2 Nonaka N, Kamiya M, Oku Y. Towards the control of Echinococcus multilocularis in the definitive host in Japan. *Parasitol Int*. 2006;55 Suppl:S263–6.
- 3 Buttenschoen K, Kern P, Reuter S, Barth TF: Hepatic infestation of Echinococcus multilocularis with extension to regional lymph nodes. *Langenbecks Arch Surg*. 2009 Jul;394(4):699–704.
- 4 Pohnan R, Ryska M, Hytych V, Matej R, Hrabal P, Pudil J. Echinococcosis mimicking liver malignancy: A case report. *Int J Surg Case Rep*. 2017;36:55–8.
- 5 Sade R, Kantarci M, Genc B, Ogul H, Gundogdu B, Yilmaz O. Computed Tomography Perfusion Imaging for the Diagnosis of Hepatic Alveolar Echinococcosis. *Eurasian J Med*. 2018 Feb;50(1):1–5.
- 6 Marrero JA, Ahn J, Rajender Reddy K; American College of Gastroenterology. ACG clinical guideline: the diagnosis and management of focal liver lesions. *Am J Gastroenterol*. 2014 Sep;109(9):1328–47; quiz 1348.
- 7 Chatterjee S, Roy MK, Banerjee S, Mukhopadhya S, Sen S, Mallath MK: Hydatid cyst mimicking cystic neoplasm of the pancreatic tail: an endoscopic ultrasound diagnosis. *Endoscopy*. 2014;46 Suppl 1 UCTN: E318–9.
- 8 Neumayr A, Troia G, de Bernardis C, Tamarozzi F, Goblirsch S, Piccoli L, et al. Justified concern or exaggerated fear: the risk of anaphylaxis in percutaneous treatment of cystic echinococcosis – a systematic literature review. *PLoS Negl Trop Dis*. 2011 Jun;5(6):e1154.
- 9 Kawakami H, Kuwatani M, Sakamoto N: Hepatobiliary alveolar echinococcosis infiltration of the hepatic hilum diagnosed by endoscopic ultrasonography-guided fine-needle aspiration. *Dig Endosc*. 2013 May;25(3):339–40.
- 10 Lopes CV, Dedavid E Silva TL, Coelho NH, Santos GO. The value of endoscopic ultrasound-fine needle aspiration in the suspicion of pancreatic hydatid cyst in endemic areas with negative serology (with video). *Endosc Ultrasound*. 2017 Sep–Oct;6(5):350–1.
- 11 Moriichi K, Fujiya M, Goto T, Okumura T. Echinococcosis infection diagnosed based on the histological findings of a lymph node involvement obtained by EUS-FNA. *Endosc Ultrasound*. 2018 May–Jun;7(3):210–1.
- 12 Akbulut S, Yavuz R, Sogutcu N, Kaya B, Hatipoglu S, Senol A, et al. Hydatid cyst of the pancreas: report of an undiagnosed case of pancreatic hydatid cyst and brief literature review. *World J Gastrointest Surg*. 2014 Oct;6(10):190–200.
- 13 Doi R, Nakao M, Nihei N, Kutsumi H. [Epidemiology of alveolar hydatid disease (AHD) and estimation of infected period of AHD in Rebun Island, Hokkaido]. *Nihon Kosshu Eisei Zasshi*. 2000 Feb;47(2):145–52.
- 14 Sharma M, Somasundaram A, Pathak A, Simon EG, Cloa MM. Endoscopic ultrasound in hepatobiliary hydatid disease. *Endoscopy*. 2010;42 Suppl 2:E56–7.

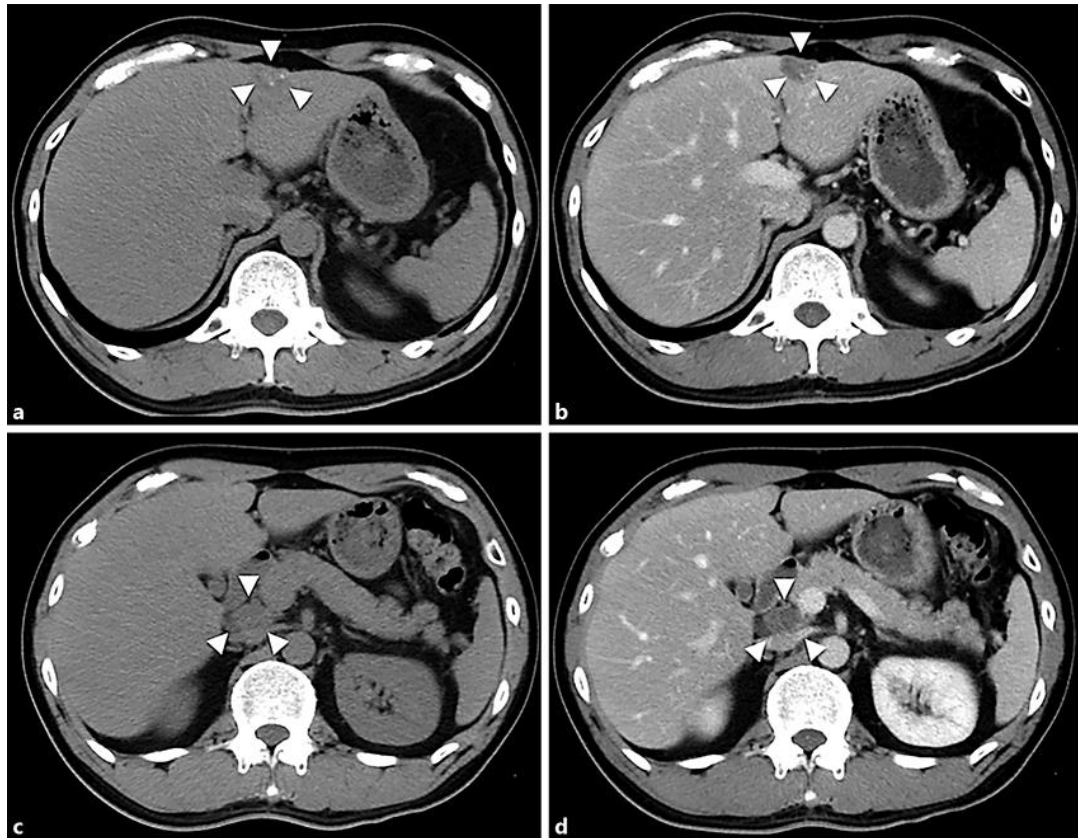


Fig. 1. Noncontrast computed tomography showing a 27-mm mass with dotted calcifications in liver segment 3 (a) and a 35-mm mass adjacent to the head of the pancreas in a similar fashion (c), and contrast-enhanced computed tomography showing those masses without enhancement (b, d).

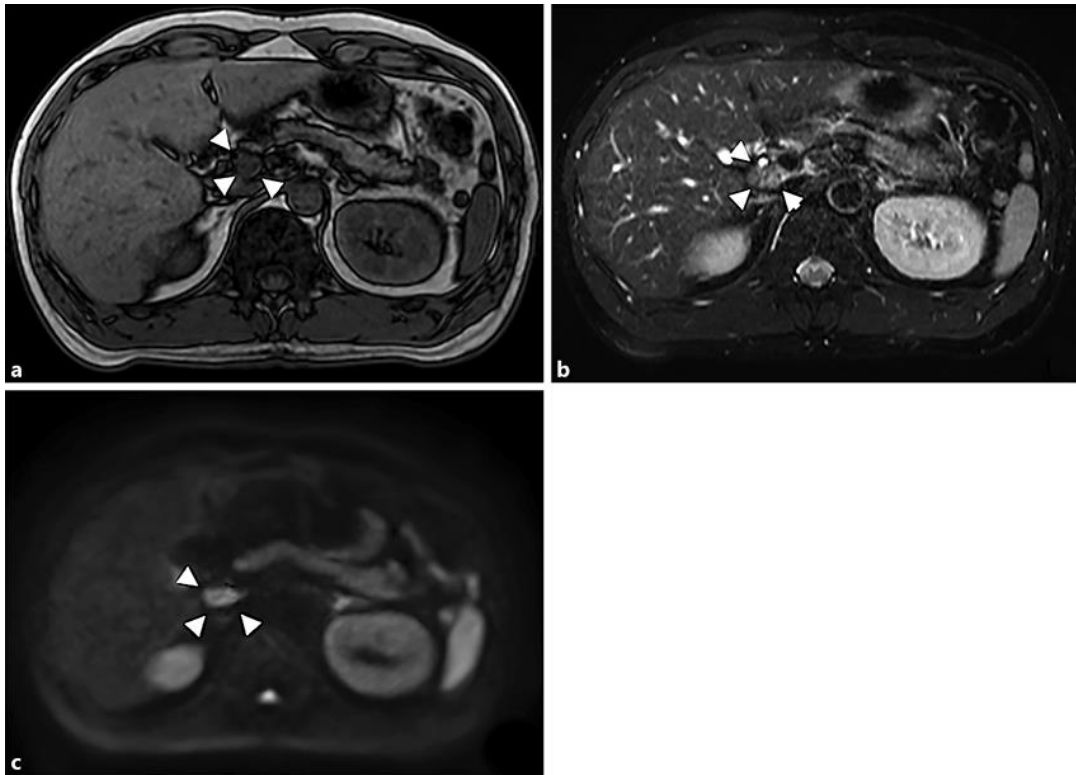


Fig. 2. Magnetic resonance imaging revealing a low-intensity peripancreatic mass on T1-weighted image (a) and a slightly high-intensity mass on T2-weighted image (b), with decreasing diffusion on the diffusion-weighted image (c). The same imaging was shown in a mass of liver segment 3.

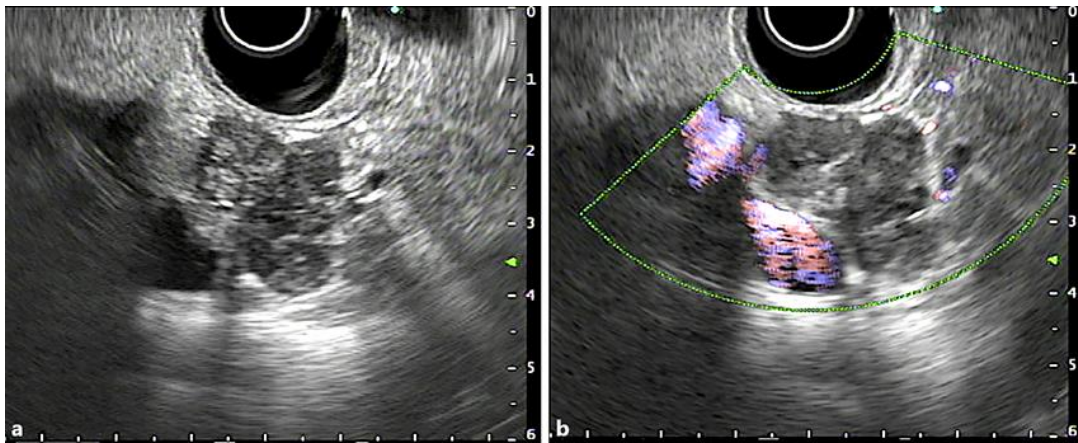


Fig. 3. Endoscopic ultrasonography (EUS) appearance of the peripancreatic mass: a 35-mm well-circumscribed, isoechoic mass with mixed pattern accompanying solid and small cystic component (a), and Doppler EUS did not show blood flow signals in the tumor (b) and EUS fine-needle aspiration was safely done without complication.

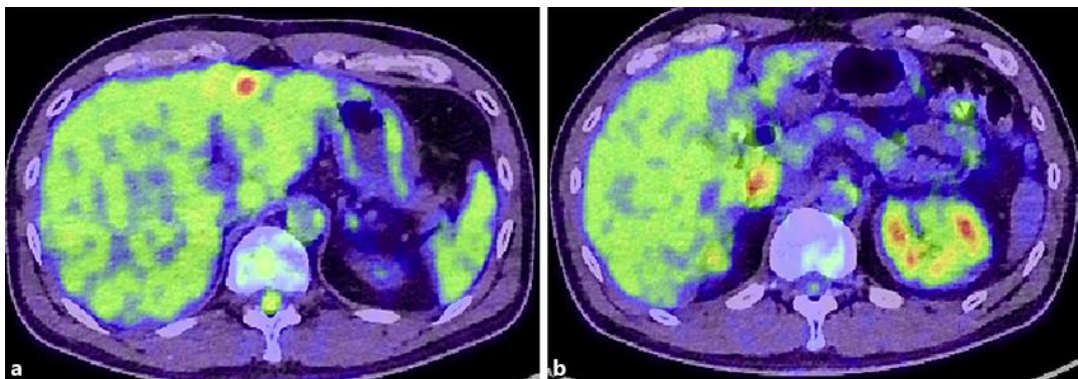


Fig. 4. Positron emission tomography with 2-deoxy-2-(fluorine-18) fluorodeoxyglucose integrated with computed tomography (^{18}F -FDG PET/CT) showed a maximum standardized uptake value of 6, both in the liver mass (a) and a peripancreatic mass (b).



Fig. 5. Macroscopic findings of the resected lesions revealed that there were a lot of small cysts including transparent mucus and not nodules in the peripancreatic mass, and their content was transparent viscous and necrosis-like. It was same in the liver.

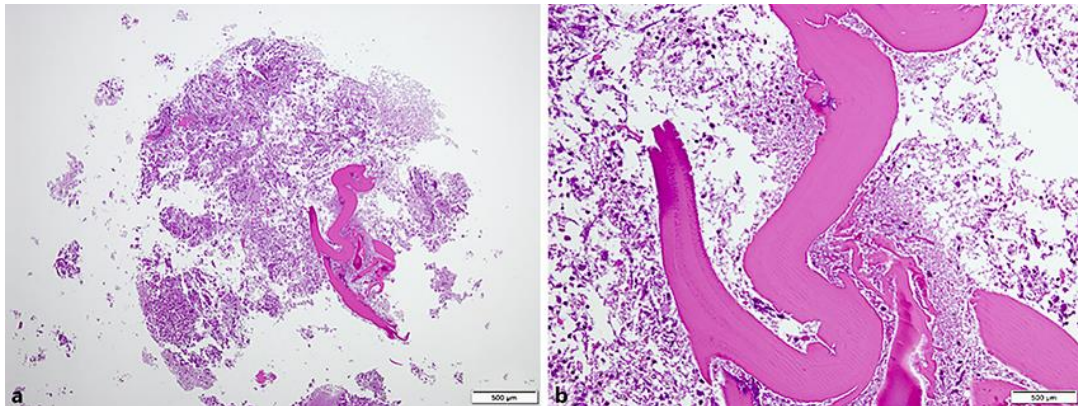


Fig. 6. Histological findings of an endoscopic ultrasonography fine-needle aspiration specimen from the peripancreatic lymph node (hematoxylin and eosin staining). Eosinophilic laminated cuticle, low-power field (a) and high-power field (b). We retrospectively confirmed them as *Echinococcus multilocularis*.

Table 1. Laboratory data on admission

<i>Biochemical data</i>		<i>Viral markers</i>	
WBC, / μ L	4,500	HIVAb	–
Eosinophils, / μ L	130.5	HBsAg, IU/mL	0.02
Basophils, / μ L	31.5	HCVAb	–
Lymphocytes, / μ L	1,922		
RBC, $\times 10^4$ / μ L	475	<i>Tumor markers</i>	
Hemoglobin, g/dL	14.4	AFP, ng/mL	2.6
Platelets, $\times 10^4$ / μ L	20.3	AFP-L3, %	<0.5
PT-INR	1.03	PIVKA-II, mAU/mL	25
Albumin, g/dL	5.0	CEA, ng/mL	0.7
Total protein, g/dL	7.9	CA19-9, U/mL	2
AST, U/L	27	SCC, ng/mL	0.7
ALT, U/L	42	SPan-1, U/mL	1.7
T-Bil, mg/dL	0.54	DUPAN-2, U/mL	≤ 25
ALP, U/L	218	NSE, ng/mL	8.6
γ -GTP, U/L	125	Elastase, ng/dL	<80
Amylase, U/L	43		
BUN, mg/dL	14		
Creatine, mg/dL	0.69		
Sodium, mEq/L	142		
Potassium, mEq/L	4.2		
CRP, mg/dL	0.10		

AFP, α -fetoprotein; AFP-L3, α -fetoprotein-lectin 3; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; CRP, C-reactive protein; DUPAN-2, Duke pancreas-2 antigen; γ -GTP, gamma-glutamyl transpeptidase; HBsAg, hepatitis B surface antigen; HCVAb, hepatitis C virus antibody; HIVAb, human immunodeficiency virus antibody; INR, international normalized ratio; NSE, neuron-specific enolase; PIVKA-II, protein induced by vitamin K absence or antagonist-II; PT, prothrombin time; RBC, red blood cells; SCC, squamous cell carcinoma-associated antigen; SPan-1, s-pancreas-1 antigen; T-Bil, total bilirubin; WBC, white blood cells.