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【 CASE REPORT 】

Toxocariasis Suspected of Having Infiltrated Directly from the Liver to the Lung through the Diaphragm

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Abstract:
A 37-year-old woman presented to our hospital with mild abdominal pain experienced for 2 months and hepatic nodules in segments 3 and 8. Peripheral blood eosinophilia was observed, and toxocariasis was serologically diagnosed. Seventeen days after the first imaging evaluation, a new lesion was found in segment 9 of the right lung, which was contiguous through the diaphragm to the hepatic nodule in segment 8. After treatment with albendazole, the liver and lung nodules disappeared. We suspect that larvae had directly invaded the lung from the liver, through the diaphragm.

Key words: *Toxocara canis*, toxocariasis, liver nodule, pulmonary nodule, diaphragm

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Introduction

Toxocariasis is an important zoonotic disease caused by the dog ascarid, *Toxocara canis*, or the cat ascarid, *Toxocara cati*. Human infection occurs by the accidental ingestion of embryonated eggs in contaminated soil or from larvae in the tissues of infected paratenic hosts. After ingestion, the embryonated eggs or larvae penetrate the intestinal wall and are disseminated by the circulation to a variety of tissues, such as the liver, lung, central nervous system, and eyes, where they cause local reactions. Toxocariasis is clinically classified into four types: visceral larva migrans (VLM), neural larva migrans (NLM), ocular larva migrans (OLM), and covert type. Clinical manifestations of toxocariasis are varied, ranging from asymptomatic to severe, and depend on the number of ingested larvae. There are also some cases diagnosed from pulmonary or hepatic nodules on chest X-ray or abdominal ultrasonography done in periodic health examinations.

We herein report a case of VLM caused by *Toxocara canis* that was diagnosed from hepatic nodules, showing that it is possible for the larvae to directly migrate to the lung through the diaphragm.

Case Report

A 37-year-old Japanese woman was admitted to our hospital because of right upper quadrant abdominal pain experienced over the past 2 months. Ten months previously, she had been diagnosed with chronic hepatitis C in a preoperative examination for high-grade cervical dysplasia. After cervical conization had been performed, the patient had been treated with direct-acting antivirals for hepatitis C virus (HCV) and achieved a sustained virological response. Four months after the end of HCV treatment, the patient presented at the hospital in which she had undergone HCV treatment with mild abdominal pain in the right upper quadrant. An ill-defined, oval shaped, hypoechoic, 19×13-mm nodule was found in segment 3 (S3) of the liver by abdomi-

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Table. Laboratory Findings on Admission.

<Hematology>		<Biochemistry>		<Infection>	
WBC	9,050 /μL	TP	7.1 g/dL	HBsAg	negative
Neu	50.5 %	Alb	4.6 g/dL	HBcAb	negative
Lym	21.5 %	BUN	13 mg/dL	HBsAb	negative
Mon	1.5 %	Cr	0.58 mg/dL	HCV-RNA	negative
Eos	23 %	T-Bil	0.7 mg/dL		
Aty-L	0.5 %	AST	18 U/L	<Tumor marker>	
RBC	4.9×10^6 /μL	ALT	10 U/L	AFP	2.2 ng/mL
Hb	13.9 g/dL	CK	76 U/L	PIVKA II	22 mAU/mL
PLT	22.7×10^4 /μL	LDH	198 U/L	CEA	1.3 ng/mL
		ALP	199 U/L	CA19-9	7.4 U/mL
<Coagulation>		γ-GTP	12 U/L	sIL2-R	428 U/mL
PT%	117 %	Na	140 mmol/L		
APTT	33.4 sec	K	4.1 mmol/L		
		Cl	104 mmol/L		
		Type IV collagen	99 ng/mL		
		CRP	0.08 mg/dL		
		IgE	339 IU/mL		

WBC: white blood cell, Neu: neutrophil, Lym: lymphocyte, Mon: monocyte, Eos: eosinophil, Aty-L: atypical-lympocyte, RBC: red blood cell, Hb: hemoglobin, Ht: hematocrit, PLT: platelet, PT%: prothrombin time%, APTT: activated partial thromboplastin time, TP: total protein, Alb: albumin, BUN: blood urea nitrogen, Cr: creatinine, T-Bil: total bilirubin, AST: asparate aminotransferase, ALT: alanine aminotransferase, CK: creatine kinase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase, γ-GTP: γ-glutamyltransferase, Na: natrium, K: kalium, Cl: chlorine, CRP: C-reactive protein, IgE: immunoglobulin E, HBsAg: hepatitis B virus surface antigen, HBcAb: hepatitis B virus core antibody, HBsAb: hepatitis B virus surface antibody, HCV-RNA: hepatitis C virus RNA, AFP: α-fetoprotein, PIVKA II: protein induced by vitamin K absence or antagonist-2, CEA: carcinoembryonic antigen, CA19-9: carbohydrate antigen 19-9, sIL2-R: soluble interleukin-2 receptor

nal ultrasonography (23 days before admission to our hospital), and an ill-defined, oval, 20-mm nodule in S3 and 10-mm nodule in S8 were found on magnetic resonance imaging (MRI) (13 days before admission to our hospital). She was subsequently referred to our hospital because hepatocellular carcinoma (HCC) was suspected. She had no known allergies and had consumed approximately 900 mL of alcohol per day until the age of 32, and her father had chronic hepatitis C.

At a physical examination on admission, she was afebrile, and her vital signs were normal. Her abdomen was flat and soft, and no tenderness or mass was observed, although she reported spontaneous pain in the right side of the abdomen. Her liver and spleen were not palpable. No skin rash was observed.

The findings of laboratory tests are shown in Table. Peripheral blood eosinophilia (2,082/μL) and slightly elevated serum immunoglobulin E (IgE) level (339 IU/mL) were observed. Her liver enzymes were normal, and C-reactive protein was not increased. Hepatitis B surface (HBs) antigen, Hepatitis B core (HBc) antibody, and HBs antibody were negative, and HCV RNA was not detected. Tumor markers, such as Alpha fetoprotein (AFP), protein induced by vitamin K absence or antagonist II (PIVKA-II), carcinoembryonic antigen (CEA), and carbohydrate antigen 19-9 (CA19-9), were within normal ranges. Non-contrast CT revealed ill-defined, oval-shaped, faint, low-density nodules of 20 and 10 mm in S3 and S8 of the liver, respectively, and contrast-enhanced CT revealed the nodules to be isodense in the arterial phase, low-density in the portal phase, and isodense in the equilibrium phase (Fig. 1). Portal vein penetration was observed in the S3 tumor in the portal-equilibrium phase. These findings on CT were not suggestive of HCC. No significant findings were observed on chest CT.

At this point, the laboratory findings pointed more toward a parasitic infection, including visceral larva migration, than to a malignant tumor. A serum multiple-dot enzyme-linked immunosorbent assay (ELISA) performed to screen for parasitic infections was positive for class II antibodies to *Dirofilaria immitis*, *Toxocara canis*, and *Ascaris suum*. A serum microplate ELISA revealed a high titer of antibody to *Toxocara canis*, and a confirmatory test by Western blotting was positive for *Toxocara canis*. A biopsy of the nodule on the liver at S3 showed marked infiltration of eosinophils without malignant cells or parasites. No eggs were detected in the stool, and no significant findings were observed on fundoscopy. Seventeen days after the first abdominal MRI examination and seven days after the CT examination, the hepatic nodule at S8 was seen at the surface of the right lobe, and a new lesion at S9 of the right lung was found on MRI that appeared to be contiguous with the hepatic nodule at S8 (Fig. 2).

The patient was treated with 600 mg of albendazole orally for 4 weeks, after which the symptoms improved and the number of eosinophils decreased to <500/μL. Two months after treatment, the antibody titer of *Toxocara canis*

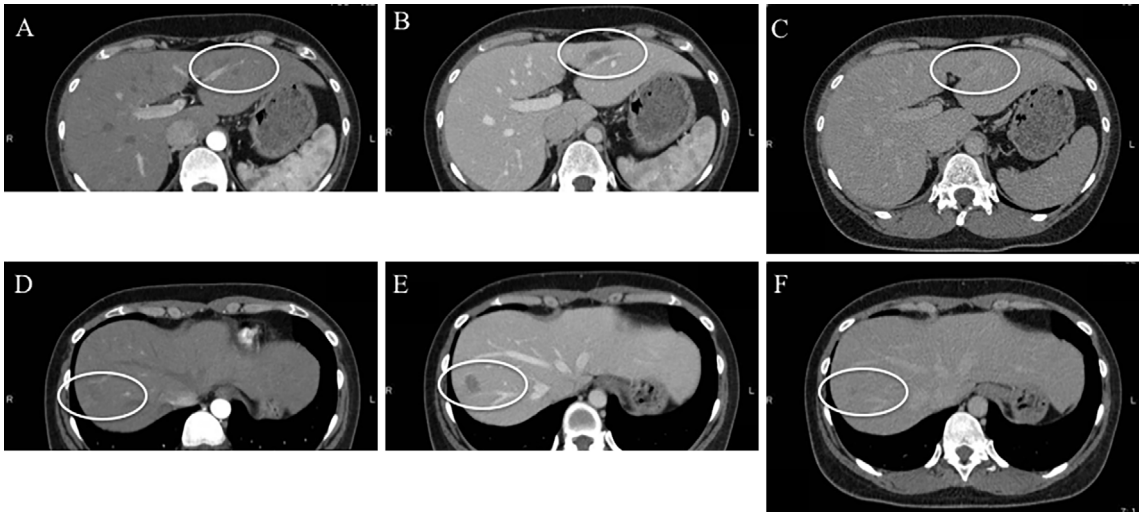

Figure 1. **Computed tomography (CT) findings four days before admission to our hospital. Contrast-enhanced arterial phase (A, D), portal phase (B, E), and equilibrium phase (C, F). CT findings show two oval nodules in the liver at segments 3 and 8.**

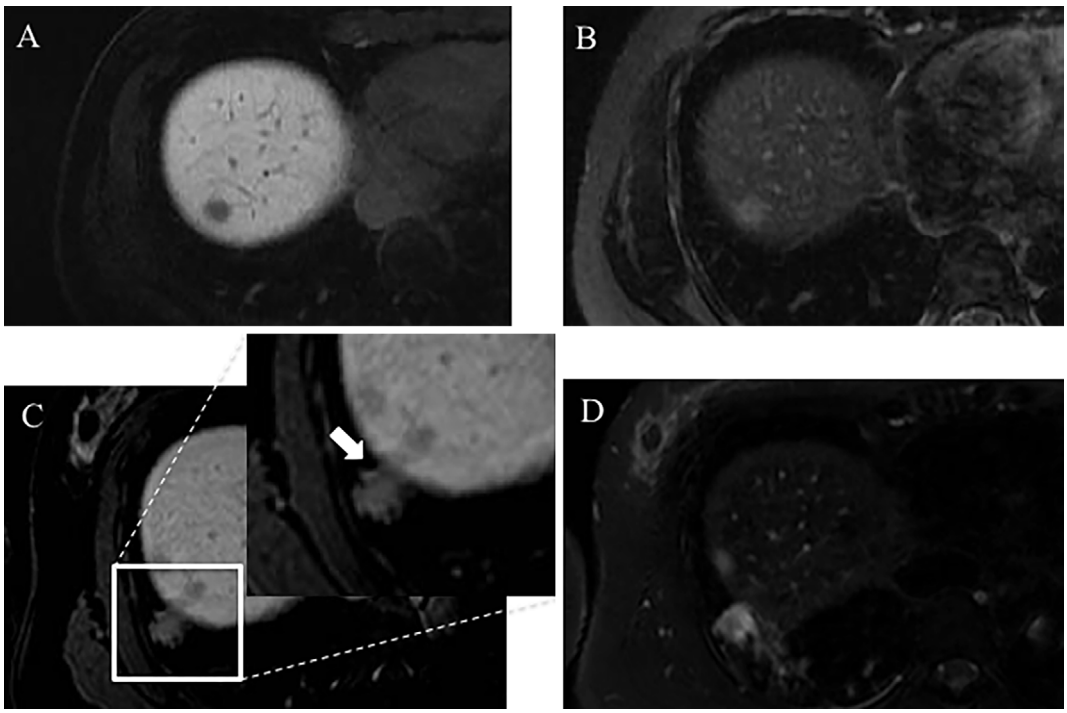

Figure 2. **Magnetic resonance imaging (MRI) findings. On non-contrast MRI 13 days before admission to our hospital, an ill-defined oval-shaped hepatic nodule in S8 showed low intensity on T1-weighted images (A) and high intensity on T2-weighted images (B). Larvae had not yet invaded the lung from the liver. MRI 17 days after the first abdominal MRI examination showed a new pulmonary lesion in the bottom of the right lung at S9 in addition to the hepatic lesions on T1 (C)- and T2 (D)-weighted images. The hepatic nodule in S8 moved toward the surface of the liver and appeared to be contiguous, through the diaphragm, with the pulmonary lesion (arrowhead).**

had remarkably decreased compared with that before treatment, and the Western blot band for *Toxocara canis* disappeared. Furthermore, the liver and lung nodules disappeared on contrast-enhanced CT.

After the patient was diagnosed with Toxocariasis, she remembered that she had eaten raw beef liver at a restaurant seven months before the symptoms presented. Her peripheral blood eosinophils had since gradually increased in number (Fig. 3).

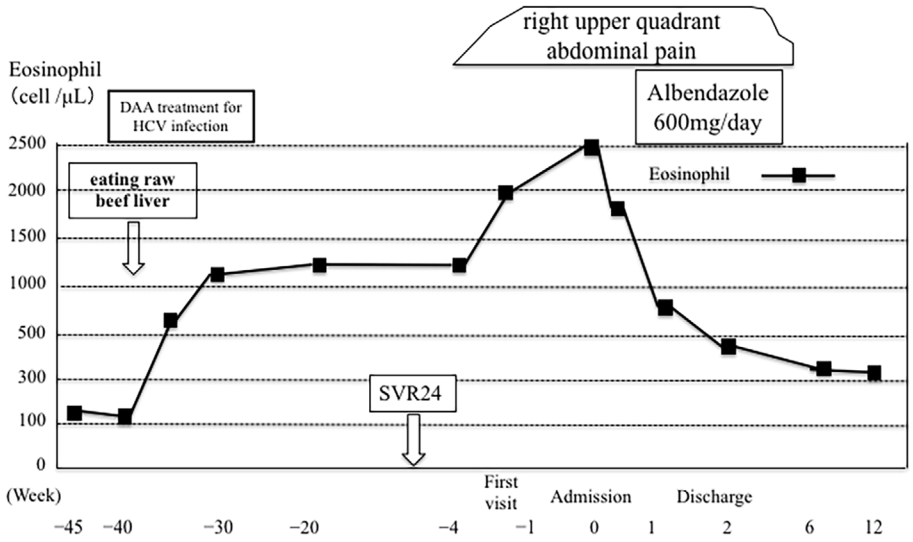

Figure 3. **Clinical course. DAA: direct-acting antivirals, HCV: hepatitis C virus, SVR24: sustained virological response at 24 weeks after the end of HCV treatment**

Discussion

Larvae frequently localize in the liver. Hepatic toxocariasis show hepatomegaly or nodular lesions that can be mistaken for primary or metastatic tumors (1-3). Toxocariasis induces eosinophilic inflammation, such as eosinophilic abscess or granuloma, in the liver or lung. On abdominal ultrasonography, hepatic lesions are seen as multiple, small, oval hypoechoic lesions in the liver parenchyma. On contrast-enhanced CT or MRI, the lesions are seen as multiple, ill-defined, oval lesions that measure 1.0-1.5 cm in diameter, usually best seen in the portal venous phase on dynamic contrast-enhanced CT and MRI: the lesions are either not seen or only faintly seen in the arterial and equilibrium phases (4). These findings and the presence of eosinophilia are helpful for differentiating toxocariasis from other diseases. In the present patient, a parasitic infection rather than HCC was suspected because of the peripheral blood eosinophilia and imaging findings, so serological testing for a parasitic infection was performed.

Histological findings of hepatic toxocariasis show eosinophilic infiltration, granuloma formation, or eosinophilic abscesses, reflecting the host inflammatory response to the migration of larvae, as was seen in our patient. It is extremely rare to detect the larvae in the tissue because they are small and move quickly (5).

In our patient, a new pulmonary lesion was found on MRI in the bottom of the right lung at S9, which appeared to be contiguous with the hepatic nodule in the liver at S8. This pulmonary lesion was not found on CT 8 days before or MRI 17 days before. Furthermore, the hepatic nodule in the liver at S8 expanded toward the periphery of the liver and was contiguous with the pulmonary lesion, suggesting that the larvae was able to directly invade the lung from the liver through the diaphragm. In human toxocariasis, it is thought that the larvae do not migrate to other tissues through the celomic cavities after being disseminated hematogenously to a variety of tissues, such as the liver or lung, although several studies have reported that the larvae can migrate through the tissues and celomic cavities of mice and monkeys (6-8). To our knowledge, our case is the first in which imaging findings showed that toxocariasis larvae in humans can migrate through a celomic cavity to other tissues.

Although most cases of toxocariasis are self-limiting and treatment varies according to symptoms and the location of the larvae, albendazole is widely accepted as the first-choice agent for treatment. In Japan, the recommended treatment is the oral administration of albendazole 10-15 mg/kg/day for 4 to 8 weeks and a follow-up evaluation with post-treatment serological tests. The regimen has been reported to have 78% efficacy, with 15% of patients experiencing side effects (9). In Europe and the US, albendazole is given at 400 mg twice a day for 5 days, but it was reported that the clinical cure rate with this regimen is 32% (10). Our patient took albendazole 600 mg/day for 4 weeks without side effects and achieved a clinical and serological cure of toxocariasis.

In Japan, most adult patients who suffer from toxocariasis are suspected of having ingested larvae through contaminated foods, such as raw meat, as in our case. Although the sale or provision of raw beef liver was prohibited in Japan in 2012 by an amendment to the Food Sanitation Law, foodborne parasitic diseases, including toxocariasis, still occur sporadically. Therefore, it is necessary to understand the clinical features of parasite infections and be able to differentiate them from other diseases.

In conclusion, we herein described a case of hepatic and pulmonary toxocariasis in a patient with suspected HCC after the successful treatment of chronic HCV. Parasitic diseases, including toxocariasis, should be considered for patients who have hepatic nodular lesions with eosinophilia. In

our case, the larvae migrated from the liver to the lung through the diaphragm, which is considered to be extremely rare.

The authors state that they have no Conflict of Interest (COI).

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