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INTERNAL MEDICINE

CASE REPORT

Unusual Radiological Findings of *Fasciola Hepatica* Infection with Huge Cystic and Multilocular Lesions

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Abstract

This report describes a case of hepatic phase *Fasciola hepatica* infection presenting huge and multilocular lesions. The unique radiological findings mimicked hydatid diseases and also cystic liver neoplasm. Fascioliasis should be included in the differential diagnosis for cystic liver diseases.

Key words: *fasciola hepatica*, fascioliasis, eosinophilia, cystic, abscess, dot-ELISA

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Introduction

Fascioliasis is a widespread infectious disease caused by trematode *Fasciola hepatica* (*F. hepatica*) infection (1). Although the radiological diagnosis of human fascioliasis has been improved, consideration of the possibility in the differential diagnosis is lacking in many developed countries. Typical computed tomography (CT) findings for hepatic phase of fascioliasis include small or sometimes clustered hypodense nodules and tortuous linear tracks, which are predominantly in subcapsular area (2, 3).

Here, we report a case with a unique hepatic phase fascioliasis. The patient was free from the symptoms, but presented uncommon radiological findings; a huge cystic lesion located in the middle of the liver together with peripheral multiloculated lesions.

Case Report

A 61-year-old Japanese man was referred to our hospital for the evaluation of migrating hepatic masses in November 2005. He had been involved in the construction of a power plant in Myanmar from January to November 2004. He had had a health checkup at a pre-consulted hospital in January 2005, and had undergone blood tests and abdominal ultrasonography (US) imaging. Although the clinical and laboratory findings were unremarkable except for peripheral blood eosinophilia (3,200/ml), the abdominal US imaging demonstrated multiple hypo-echoic lesions in right hepatic lobe. A contrast-enhanced CT scan showed multiple hypodense lesions in the right hepatic lobe. In the anterior segment of the right lobe, a huge and low attenuated mass measuring up to 57 mm with regular margins and some tiny hypodense lesions were detected (Fig. 1a, b). Thickening of the common bile duct or biliary dilatation did not exist. Although histological examination of the liver biopsy demonstrated the differentiatios from neoplastic lesions including intrahepatic cholangiocarcinoma or bile duct cystadenocarcinoma, the specimens were consistent with inflammation characterized by the presence of fibrotic changes and no sludge was drained. He was followed without any treatment and was referred to our hospital in November 2005.

On admission, physical examinations revealed only slight

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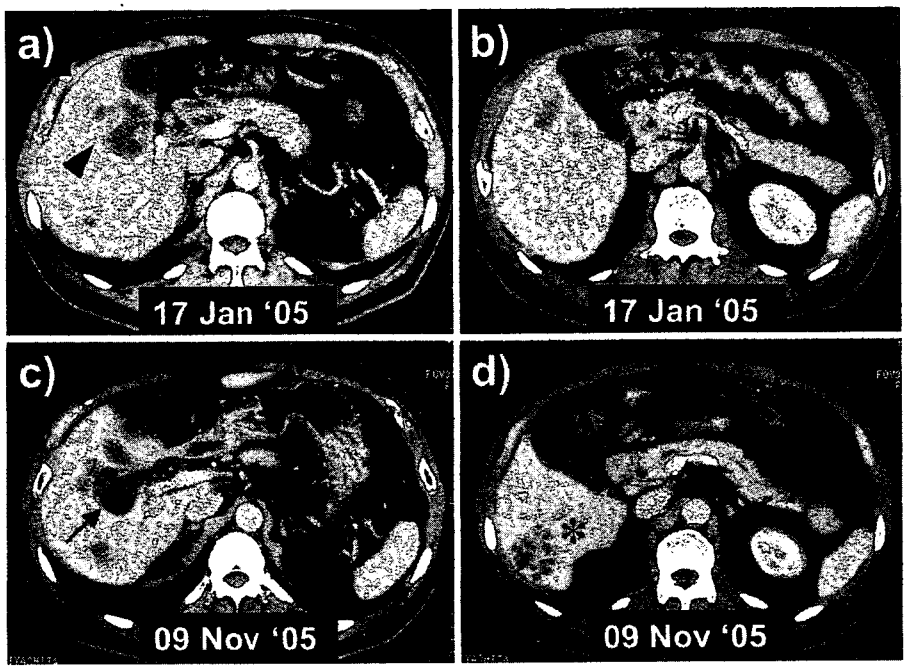

Figure 1. The contrast-enhanced CT image presented huge cystic and multilocular lesions. a, b) In the anterior segment of the right lobe, a huge and low-attenuated mass (arrowhead) and some tiny hypodense lesions were detected. c) The corresponding lesion in the anterior segment migrated into the center of the right lobe (arrow). d) A multilocular lesion (asterisk) was newly detected in the posterior segment of the right lobe.

hepatomegaly. Laboratory data showed the white blood cell count of 7,030/ml with a differential of 14.8% eosinophils. Serum IgE level was 438 U/ml (normal range; <250 U/ml). Neither ova nor larvae of any parasites were found in his stool. Contrast enhanced CT scans in November 2005, demonstrated mainly two types of masses in the right hepatic lobe. One of the masses, which had been detected in January but migrated during ten months, was located in the anterior segment and showed cyst-like hypodense lesion measuring up to 45 mm (Fig. 1c). The other mass, which could not be detected in January 2005, was located in the posterior segment and multiloculated (Fig. 1d). Because it was ineffective to distinguish between solid and cystic materials constructing these hypodense lesions with CT and ultrasonographic examinations, magnetic resonance imaging (MRI) was performed. The corresponding lesions proved to be hypointense on T1-weighted images (Fig. 2a), hyperintense on T2-weighted images (Fig. 2b, c), and extremely hypointensive foci on inverted diffusion-weighted images (Fig. 2d). These MR images suggested that these hepatic lesions consisted of necrotic or abscess-forming materials. MR cholangiopancreatography showed normal presentation.

The diagnosis was made by serologic tests. Because of the presence of eosinophilia and radiological changes of those lesions, we suspected that he suffered from some a type of parasitic infection. We conducted a screening test for parasitic antibodies in the patient's serum using a multiple dot enzyme-linked immunosorbent assay (dot-ELISA) (4). The antibody against *F. hepatica* was strongly positive by dot-ELISA. We also performed plate-ELISA and the ouchterlony double-diffusion test for confirmation. The ELISA titer for the antibody to *F. hepatica* was highly increased and the ouchterlony test showed a strong precipitin band against crude antigen of *F. hepatica* (Fig. 3). The antibody to *Echinococcus multiocularis* was negative in plate-ELISA. The patient was treated with triclabendazole (5). After 6 weeks, abdominal CT revealed a significant decrease in the size of the huge cystic lesion as well as the satellite lesions.

Discussion

F. hepatica is a trematode parasite that naturally infects cattle or sheep, and causes fascioliasis in almost every country around the world (1). Humans are an accidental reservoir host and could be infected by the ingestion of metacercaria-laden water plants. The infected young fluke, hatched from metacercaria, migrates in the peritoneal cavity and penetrates through the liver to the bile ducts causing acute hepatic phase of fascioliasis. In the later stage, the fluke matures and lodges in the bile duct resulting in chronic biliary disorder. In the acute hepatic phase, most patients note right upper quadrant pain, fever and malaise with eosinophilia, but a few cases remain asymptomatic like the case presented here (6). Although the diagnosis of fascioliasis is fundamentally made by the detection of the ova or fluke in the bile duct or stool, it is difficult to obtain such evidence until the patient advances to the chronic biliary phase.

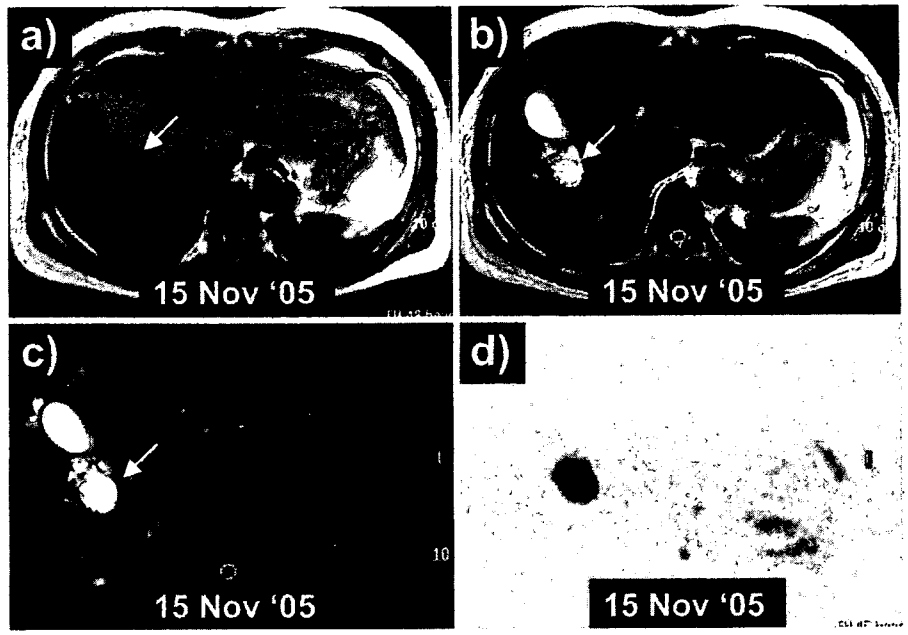

Figure 2. The corresponding MR image showed necrotic or abscess-forming lesions (arrows); a) T1-weighted images, b) T2-weighted images, c) fat-suppressed T2-weighted image, d) inverted diffusion-weighted images.

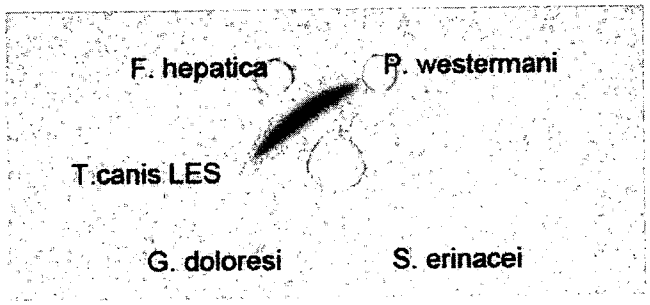

Figure 3. The ouchterlony double-diffusion test showed a strong precipitin band against crude antigen on *Fasciola hepatica*. The positions of antigens; F. hepatica, *Fasciola hepatica*; P. westermani, *Paragonimus westermani*; T. canis LES, Larval excretory and secretory antigen of *Toxocara canis*; G. doloresi, *Gnathostoma doloresi*; S. erinacei, *Spirometra erinacei*.

Typical CT findings for hepatic fascioliasis are nodular or tubular hypodense lesions up to 20-30 mm in diameter particularly in the subcapsular area (2, 7) because the infected form of metacercariae penetrates through the liver capsule and could cause subcapsular hemorrhage and frank hepatic necrosis before the biliary stage (8). However, some atypical radiographic findings have also been observed during acute or chronic fascioliasis (9, 10). In the present case, a huge abscess-forming lesion and asymptomatic physical presentations with eosinophilia mimicked hepatic unilocular hydatid disease (11) but that etiology is unknown. Usually, unilocular hydatid disease is caused by *Echinococcus granulosus* infection that produces unilocular and huge cystic lesions without any obvious symptoms. Although *Fasciola* and *Echinococcus* are quite different parasites, these parasitic diseases may present similar radiological appearances. Kim and colleagues reported confusing radiological findings of fascioliasis exhibiting huge abscess lesions without eosinophilia (9). That lesion was considered as an abscess-forming lesion with distinct thick wall and therefore as chronic biliary phase fascioliasis. These radiological and laboratory findings were not exhibited in the present case of hepatic phase fascioliasis; therefore our case was different from those in previous reports.

In the past decade, substantial progress in the radiological diagnosis of human fascioliasis has been achieved and some reports on the MR imaging have been well documented (12, 13). Cevikol and colleagues (12) reviewed the MR observations of hepatic fascioliasis and classified them into five types. In their article, hypointense lesions on T1-weighted images and brightly hyperintense lesions on T2-weighted images could be classified as one of the type of lesion. However, the appearance of the lesions in our case, i.e., huge and multiloculated masses, was not referred to as a usual pattern of hepatic fascioliasis. Intrahepatic cholangiocarcinoma or biliary cystadenocarcinoma could demonstrate the same signal patterns on T1-weighted and T2-weighted images, but the diffusion-weighted image is quite useful to distinguish solid neoplasms and necrotic cysts caused by fascioliasis as in the present case (14). Bacterial abscess also shows similar MR images, therefore, it is not possible to confirm the diagnosis based on MR images and thus examinations of other laboratory findings, serology and aspiration

specimens are necessary.

In conclusion, we emphasize here that hepatic fascioliasis can present a variety of lesions in the liver and huge cystic liver masses can also be produced. It is important to keep these findings in mind.

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Identification of Human Herpesvirus 6 in a Patient With Severe Unilateral Panuveitis

Human herpesvirus 6 (HHV-6) is a member of the HHV family[1] and has been associated with immunodeficiency disorders and neurologic diseases.[2] This widespread virus can be classified into 2 groups: variant A (HHV-6A) and variant B (HHV-6B).[2] Although HHV-6B is the known causative agent in exanthema subitum,[3] the association of HHV-6A with clinical entities is still unknown. We describe a patient with severe right-sided panuveitis and multiple subretinal lesions. The *HHV-6A* genome was detected in the ocular fluid of this patient.

Report of a Case. A 75-year-old man developed a sudden decrease in vision in the right eye in 2005. Slit-lamp examination of the right eye disclosed ciliary hyperemia, moderate mutton-fat keratic precipitates, and severely inflamed anterior chamber cells with hypopyon. Funduscopic examination of the right eye revealed dense vitreous opacities, optic disc swelling, yellowish-white massive retinal lesions measuring approximately 1.5 optic disc diameters, and whitish retinal exudates (**Figure 1**). The left eye was normal. Results of all systemic examinations, including serologic testing for human immunodeficiency virus, were negative, and results of serologic testing for HHVs (herpes simplex virus, varicella zoster virus, Epstein-Barr virus, cytomegalovirus, and HHV-6) were positive except for varicella zoster virus. On the basis of the ocular manifestations, a viral infection was suspected. After informed consent was obtained, an aliquot of aqueous humor and an aliquot of peripheral blood were collected and examined for further investigations. Immunoglobulin G for *Toxocara* larval excretory-secretory antigen in the aqueous humor and serum was detected using an anti-*Toxocara* antibody detection kit.[4] A multiplex polymerase chain reaction demonstrated HHV-6 genomic DNA in both samples but not other HHVs (herpes simplex virus type 1 or 2, varicella zoster virus, Epstein-Barr virus, cytomegalovirus, HHV-7, or HHV-8). To acquire quantitative data, a real-time polymerase chain reaction was performed at different stages of the clinical course. In the acute phase with active inflammation, a high copy number for the HHV-6 DNA was detected in the samples (aqueous humor: 2.4×10^6 copies/mL; serum: 5.4×10^6 copies/mL). Because the patient indicated that there was progression of intraocular inflammation, right eye diagnostic pars plana vitrectomy was performed. A high copy number for the *HHV-6* genome was detected in the vitreous fluid, retinal membrane, and peripheral blood mononuclear cells. In addition, IgG for *Toxocara* larval excretory-secretory antigen in the vitreous was also detected. These data led us to make the diagnosis of panuveitis related to a *Toxocara canis* larva or an HHV-6 infection. Next we examined whether the HHV-6 infection was indicative of variant A or variant B. A high number of copies of HHV-6A was detected in the samples, and the *HHV-6A* genome decreased after antiviral valganciclovir hydrochloride treatment associated with systemic corticosteroids, whereas the *HHV-6B* genome was not detected (**Figure 2**). After treatment, funduscopic examination of the right eye revealed resolution of the vitreous opacities, optic disc swelling, and retinal exudates.

Comment. It is difficult to be certain whether HHV-6 was the causative agent in intraocular inflammation in this patient. Anti-*Toxocara* antibodies were also detected in serum and aqueous humor and vitreous samples, the significance of which is difficult to interpret. Another hypothesis could be that HHV-6 favored *Toxocara*-generated inflammation. However, the vi-

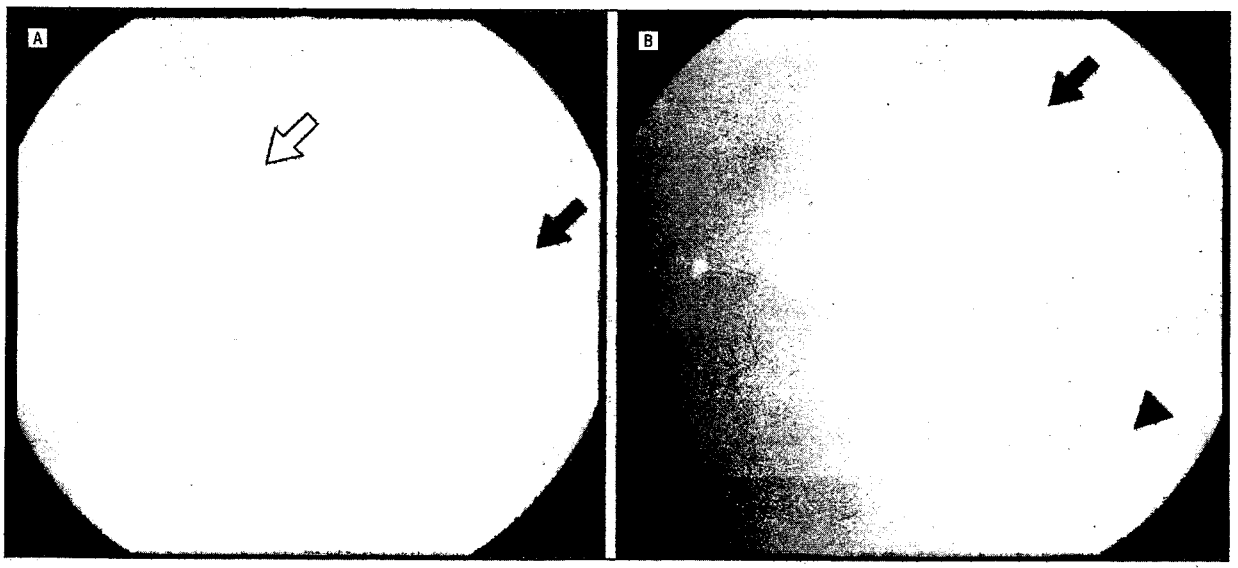

Figure 1. Fundus photographs of the right eye of a patient with a human herpesvirus 6 variant A infection. A, Whitish retinal exudates (white arrow), optic disc swelling (black arrow), and dense vitreous opacities are seen. B, Retinal yellowish-white massive lesions (black arrowhead) and optic disc swelling (black arrow) are seen.

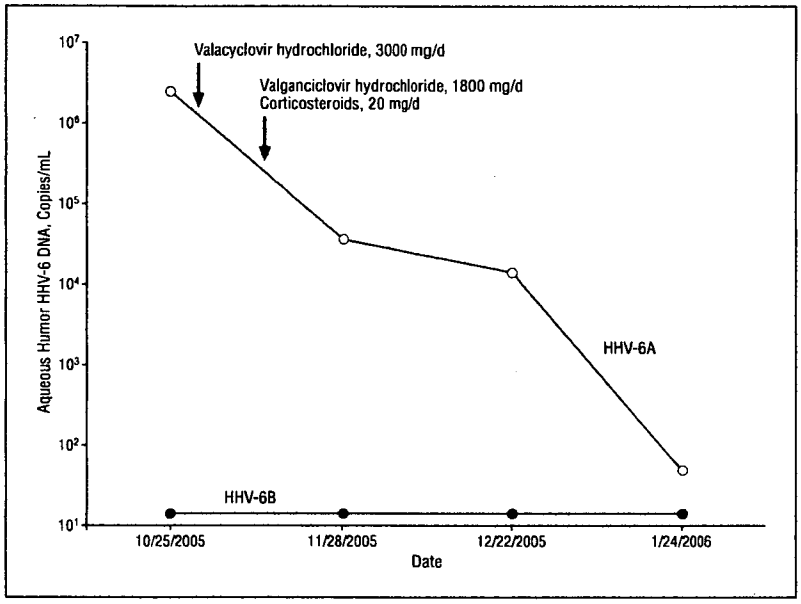

Figure 2. Serial measurement of aqueous humor human herpesvirus 6 variant A (HHV-6A) and variant B (HHV-6B) DNA levels by means of real-time polymerase chain reaction..

ral DNA and intraocular inflammation decreased in response to antiviral agents, suggesting that HHV-6A has some role in the pathogenesis of the ocular inflammation. To our knowledge, this is the first report of a case of HHV-6A associated with intraocular inflammation. These observations suggest that HHV-6A infection may have a role as a causative agent in severe intraocular inflammation.

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Severe Darkening of a Facial Skin Graft From Latanoprost

Latanoprost is a 17 phenyl–substituted analogue of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), which decreases intraocular pressure by increasing uveoscleral outflow. Since its introduction as a topical eye medication, several authors have reported adverse effects, like subtle hyperpigmentation of periocular skin and eyelid-margin hyperemia.[1] Herein, we present a case of a patient using latanoprost who developed severe darkening in a facial skin graft.

Report of a Case. A 68-year-old woman was diagnosed with primary open-angle glaucoma in September 2002. Topical latanoprost was commenced in both eyes, with a good control of intraocular pressure. In April 2005, a malignant melanoma was surgically excised from the left side of the patient's face and skin was grafted to this area from her neck behind the ear. Histology confirmed a low-risk, superficial, spreading malignant melanoma in situ, which was excised with adequate margins. In September 2005, severe darkening of the skin graft was noted together with subtle bilateral periocular hyperpigmentation and eyelid-margin hyperemia (**Figure 1**). Her medication was switched from latanoprost to topical brinzolamide in both eyes with a good control of the intraocular pressure. One month after stopping latanoprost, the skin graft had lightened significantly and the subtle bilateral periocular hyperpigmentation and eyelid-margin hyperemia had resolved (**Figure 2**).

Comment. Prostaglandins increase both melanocyte dendricity and melanin synthesis in the skin. Prostaglandin $F_{2\alpha}$ stimulates the activity and expression of tyrosinase, the rate-limiting enzyme in melanin synthesis, and the $PGF_{2\alpha}$ receptor has been shown to be up-regulated by UV radiation in melanocytes in vitro and in human skin in vivo.[2] Researchers have shown how proteinase-activated receptor 2 in keratinocytes plays an important role in skin pigmentation. Activation stimulates uptake of melanosomes through phagocytosis and also stimulates release of prostaglandin E_1 and $PGF_{2\alpha}$, which stimulate melanocyte dendricity.[3] Prostaglandins have also been implicated in postinflammatory skin hyperpigmentation.[4]

Significant lightening of the skin graft together with the resolution of subtle bilateral periocular hyperpigmentation and eyelid-margin hyperemia 1 month after stopping latanoprost implies that a local adverse drug reaction to latanoprost occurred in this patient. Absorption of latanoprost into facial skin is likely to occur from tear spillover during topical application. The severe dark-

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