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First Human Case of *Capillaria hepatica* Infection in Japan

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Abstract

A female of *Capillaria hepatica* (Bancroft, 1893) was detected in a granuloma formed in the liver of a 26-year-old Japanese man who had laparotomy for cholelithiasis. Identification of the worm is based on the morphology of the bacillary bands, stichosome, vulva and vagina. This is the first human case of *C. hepatica* infection in Japan.

Key words: *Capillaria hepatica*, human infection, granuloma, Japan

Introduction

Capillaria hepatica (Bancroft, 1893) (Trichinelloidea: Trichuridae: Capillariinae) is a zoonotic nematode which is normally parasitic in the liver of wide range of mammals, especially rats. Human infection with *C. hepatica* is rare: only about 20 confirmed clinical cases including 9 fatal ones have been recorded from various parts of the world (cf. Camain *et al.*, 1965; Beaver *et al.*, 1984; Gutierrez, 1990; Berger *et al.*, 1990). In addition, Šlais (1973) recorded 9 cases in which solitary liver granulomas caused by *C. hepatica* were found at autopsy. To our knowledge, there has been no report on human case of hepatic capillariasis from Japan. Recently, we experienced a case in which *C. hepatica* was detected in a tumor formed in the liver as reported herein.

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Case

T. H., 26-year-old Japanese male, employee of an international trading company, spending about one-third of a year abroad.

Chief Complaint: Abdominal pain.

Family History: Not contributory.

Past History: He had abdominal pain 2 years ago, and was transported by ambulance to a hospital in Tokyo, where he was treated with intravenous drip infusion for 5 days under the diagnosis of ureterolithiasis.

Present Illness: On 7 October 1990, he felt epigastric pain on his trip in China. After returned to Japan, he was admitted to the Nagaoka Red Cross Hospital on 26 November 1990. By ultrasonic examination gall stones were revealed. Extracorporeal shock wave lithotripsy (ESWL) was performed for two times, and his symptoms were disappeared. He was discharged on 8 December 1990. On 5 January 1991 he was readmitted for ultrasonic examination, by which gall stones and a renal cyst were revealed.

Laboratory Findings (28 January 1991): Height 169cm, weight 63kg, well nourished. RBC

$522 \times 10^4/mm^3$; hemoglobin 15.6mg/dl; hematocrit 46.9%; WBC $51 \times 10^2/mm^3$ (eosinophil 9%, stab neutrophil 3%, segmented neutrophil 54%, monocyte 9%, lymphocyte 25%); platelet $19.8 \times 10^4/mm^3$; fecal examination for parasite eggs was negative. It has been reported that the eosinophil ratio was 15% in October 1990, but gradually decreased to 1% on 6 February 1991.

Surgical Operation: Under the clinical diagnosis of cholelithiasis, laparotomy was performed on 30 January 1991. There was no adhesion of the viscera in the abdominal cavity. A tumor with clear margin, about 2 cm in diameter, was noticed in S4 region of the liver, and excised. By rapid pathological examination, the tumor was revealed to be non-malignant. Then, normograde cholecystectomy was performed. Postoperative course was uneventful and the patient was discharged.

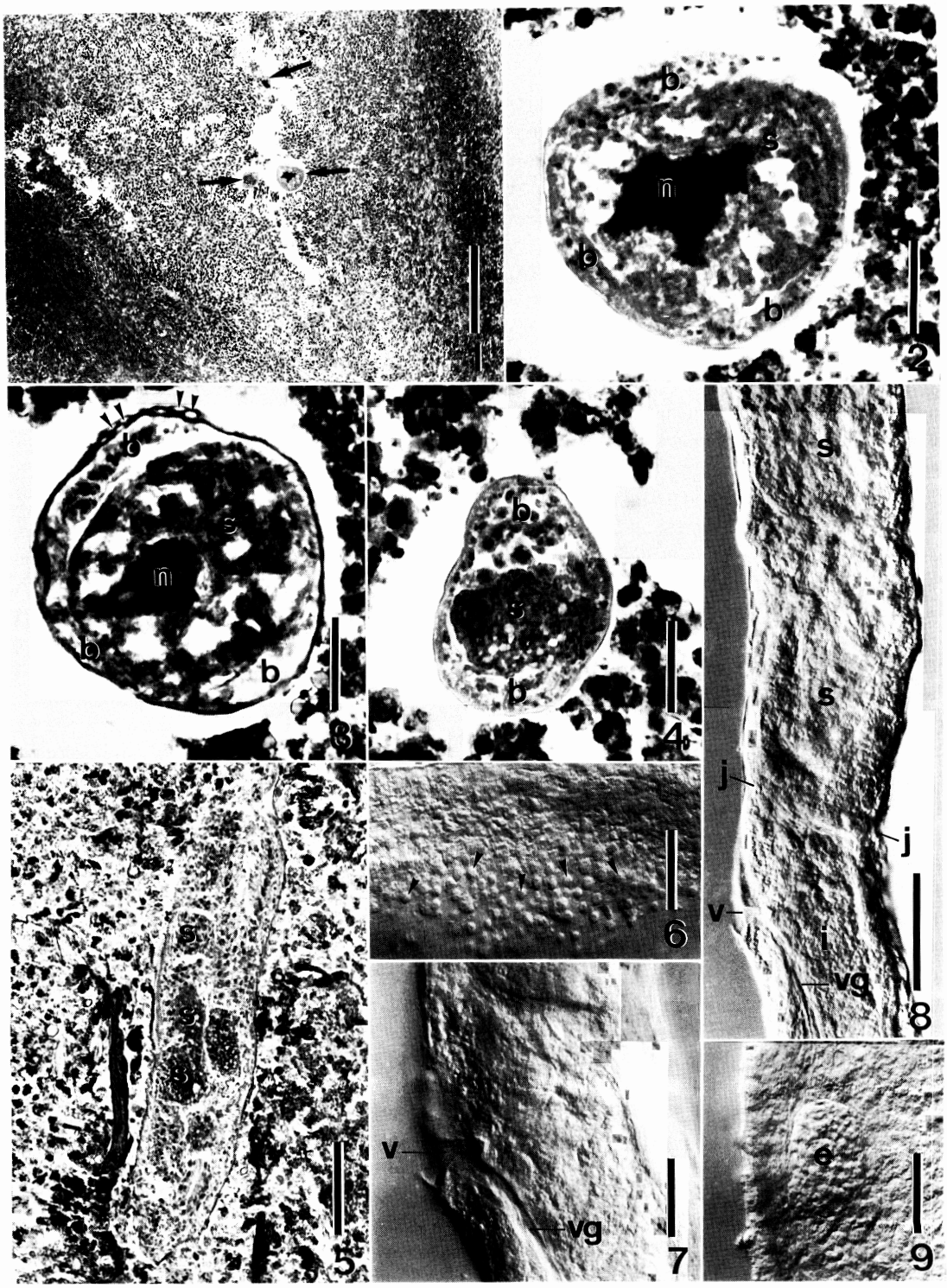
Pathological Examination of Dissected Tissues: The gall bladder showed typical chronic cholecystitis. The tumor resected from the liver was a granuloma with massive infiltration of eosinophils, monocytes, lymphocytes, plasma cells and foreign body giant cells (Figs. 1–5). Numerous Charcot-Leyden crystals were scattered in the granuloma. In the center of the tumor two cross and three oblique sections of a nematode were observed (Fig. 1). The remaining paraffin block of the tumor was melted at 60°C, soaked in xylene and in a descending series of ethanol. Then, the tissue was carefully minced in 70% ethanol with fine forceps to recover fragments of the worm. The collected fragments were cleared in a glycerin-alcohol solution, mounted with a glycerin solution for microscopic observation.

Parasite

Sectioned Worm: The cross sections were $70 \times 65\,\mu m$ and $50 \times 40\,\mu m$, and the oblique sections were 125 to 284 μm long with maximum width of 56 μm (Figs. 2–5). The worm was considerably decomposed. The cuticle was thin (about 1 μm). The somatic musculature was highly degenerated, and the type of musculature was not identifiable. In the cross sections two large glandular cell masses were seen in lateral sides, and each mass occupied about one-fourth of the circumference (Figs. 2–4). In addition, a small mass of glandular cells was also present in the larger cross section, so that the somatic musculature was divided into one wide and two narrow fields (Fig. 2). These glandular cell masses corresponded to the bacillary bands. In the larger cross section stained by silver implegnation (Watanabe's method), the cuticle covering one of the bacillary bands was slightly turned up, showing large pits on the cuticle (Fig. 3). The cavity encircled by the somatic musculature and the glandular cell masses was occupied by a large cell, i.e. stichocyte (Figs. 2–4). In the larger cross section, a large degenerated nucleus with irregular outline, stained darkly with both hematoxylin and silver, was seen in the stichocyte (Figs. 2, 3). In one of the oblique sections, the stichocytes of which cytoplasm was stained with eosin were seen in row (Fig. 5). Genital organs were not observed in the sections.

Fragments Collected from Granuloma: Two fragments were recovered. They were about 2.6mm long by 70 μm wide and 1.6mm long by 70 μm wide. Many infiltrated cells and Charcot-Leyden crystals adhered on the surface obscuring the surface morphology of the cuticle. Two wide and one narrow bacillary bands were observed. Secreted materials were seen as droplets on the pits of bacillary bands (Fig. 6). Inner structure of the worm was highly decomposed. However, three stichocytes, intestine, vulva and vagina were discernible, indicating that this portion was the esophago-intestinal junction level of the worm (Figs. 7, 8). Mature egg was not seen in the vagina, though three round masses, probably unfertilized eggs, were observed (Fig. 9).

Identification: The bacillary bands and stichocytes indicate that this worm belongs to the superfamily Trichinelloidea. Moreover, the size and arrangement of the pits of the bacillary bands are identical with those observed in *Capillaria hepatica* collected from the liver of a brown rat, *Rattus norvegicus,* in Niigata, Japan. *Capillaria hepatica* has three bacillary bands, two wide and one narrow, as in the present worm (cf.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Gutierrez, 1990). Thus the worm is identified as a female of *C. hepatica* (Bancroft, 1893). The presence of unfertilized egg-like masses may indicate solitary infection.

Discussion

Human hepatic capillariasis cases are generally symptomatic, sometimes even fatal (MacArthur, 1924; McQuown, 1950; Otto *et al.*, 1954; Ewing and Tilden, 1956; Ward and Dent, 1959; Kallichurum and Elsdon-Dew, 1961; Piazza *et al.*, 1963; Camain *et al.*, 1965). The seriousness of symptoms depends on the intensity of infestation, and subclinical infection with *C. hepatica* may not be so rare especially in persons with eosinophilia of unknown etiology (cf. Ward and Dent, 1959; Cislaghi and Radice, 1970). Šlais (1973) reported that the parasites apparently provoked no significant symptom and had few relation with the cause of death in the 9 cases of *C. hepatica* infections found as a solitary liver granuloma at autopsy in Czechoslovakia. The present case most resembles the case no. 7 of Šlais (1973), in which a female worm with unfertilized eggs was detected. The symptoms of the present patient were apparently due to ureterolithiasis and cholelithiasis, suggesting that the worm had hardly caused any symptoms.

The life history of *C. hepatica* is unique (cf. Beaver *et al.*, 1984): it lays eggs in the liver tissue of the host, but the eggs are not excreted from the host. When the liver containing eggs is eaten by other animals, the eggs are liberated from the liver tissue by digestion, and excreted with feces, and then become infective in a humid environment. Human is infected with *C. hepatica* by ingesting water or foods contaminated with eggs containing infective larvae. Thus, infection occurs among people residing in poor sanitary condition, especially among children with habit of eating dirt (cf. Ewing and Tilden, 1956; Cochrane *et al.*, 1957; Silverman *et al.*, 1973). In the present case, the patient had spent about one-third of the year abroad, and had visited many developing countries. Thus, the present patient might be infected during his trip in the developing countries. However, the possibility of indigenous infection in Japan may not be excluded because this parasite is also very common in Japanese rats.

The clinical features of hepatic capillariasis resemble those of the visceral larva migrans, especially toxocariasis, in having eosinophilia, hepatomegaly and fever (Šlais, 1974; Kumar *et al.*, 1985). Šlais (1974) considered that the case diagnosed as visceral larva migrans by Sumner and Tinner (1967) was hepatic capillariasis. *Capillaria hepatica* infection should be suspected in the cases which show clinical signs of visceral larva migrans but are serologically negative against *Toxocara* antigens. An immunological test with specific antigens of *Trichinella spiralis*, which is phylogenetically close to *C. hepatica*, may be valuable for diagnosis (Šlais, 1974).

In most of the human cases with hepatic

Fig. 1 Granuloma formed in the liver showing three nematode sections (arrows). (HE, Scale bar = 200 μm)

Fig. 2 Larger cross section of the nematode. The bacillary bands (b) and stichocyte (s) with nucleus (n) are seen. (HE, Scale bar = 20 μm)

Fig. 3 Larger cross section of the nematode. The bacillary bands (b) with pits (arrowheads) and stichocyte (s) with nucleus (n) are seen. (Silver, Scale bar = 20 μm)

Fig. 4 Smaller cross sections of the nematode. The bacillary bands (b) and stichocyte (s) are seen. (HE, Scale bar = 20 μm)

Fig. 5 Oblique section of the nematode. A row of stichocytes (s) is seen. (HE, Scale bar = 50 μm)

Fig. 6 Surface of the bacillary band of the nematode recovered from the granuloma, showing secreted droplets (arrowheads) on the pits. (Nomarski interference-contrast; Scale bar = 20 μm)

Fig. 7 Vulval portion of the nematode recovered from the granuloma, showing vulva (v) and vagina (vg). (Nomarski interference-contrast; Scale bar = 20 μm)

Fig. 8 Esophago-intestinal junction level of the nematode recovered from the granuloma, showing stichocytes (s), esophago-intestinal junction (j-j), intestine (i), vulva (v) and vagina (vg). (Nomarski interference-contrast; Scale bar = 50 μm)

Fig. 9. Unfertilized egg-like mass (e) in degenerated uterus. (Nomarski interference-contrast; Scale bar = 20 μm)

capillariasis, the presence of eggs in the liver tissue is a definite evidence for identification. If eggs are not seen, the presence of bacillary bands in the cross section of worms is one of the key characteristics. Since the pits of bacillary bands on the cuticle are hardly discernible in tissue sections stained with hematoxylin and eosin, silver impregnation method is recommended to demonstrate the orifices as shown in this report. In the present case the stichocytes and vulva were demonstrated in the fragment of the worm recovered from the paraffin block. Thus, if a nematode having decent size is found in a tissue section, efforts should be paid to recover the rest of the worm (cf. Ogata *et al.*, 1988). It is not recommended to make serial sections of the tissue because such slicing makes it almost impossible to visualize the external and third-dimensional morphology of the worm.

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