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【 CASE REPORT 】

Septic Meningitis and Liver Abscess due to Hypermucoviscous *Klebsiella pneumoniae* Complicated with Chronic Strongyloidiasis in a Human T-lymphotropic Virus 1 Carrier

Tomohiro Hosoda[1], Mitsuo Sakamoto[1], Hideki Orikasa[2], Akiko Kubomura[3], Takako Misaki[3] and Nobuhiko Okabe[3]

Abstract:

Recently, severe cases of infection due to hypermucoviscous *Klebsiella pneumonia* (hmKP) have been reported in Japan. The Amami Islands in Japan are also endemic regions for *Strongyloides stercoralis*. Disseminated strongyloidiasis strain often causes severe enterobacteria infection; however, whether or not chronic strongyloidiasis induces it remains unclear. We herein report a 71-year-old man who developed meningitis and liver abscess due to hmKP complicated with chronic strongyloidiasis. He died on the seventh hospital day. *Strongyloides stercoralis* were only found around the polyp in the cecum. Chronic strongyloidiasis can also induce severe infection due to enterobacteria, especially hypervirulent pathogens like hmKP, through the induction of mucosal rupture.

Key words: hypermucoviscous *Klebsiella pneumoniae*, meningitis, liver abscess, strongyloidiasis

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Introduction

Hypermucoviscous *Klebsiella pneumoniae* (hmKP), especially that with the K1 serotype, is a hypervirulent strain (1). HmKP induces severe infections with systemic abscess and central nervous system infection as well as liver abscess (1). Most cases of hmKP were reported in Southeast and East Asia, especially Taiwan, in the 1980s and 1990s (1). However, recently, an increasing number of hmKP-infected cases have been reported worldwide (2). Sporadic and family incident cases of hmKP infection have also been documented in Japan (3).

The reasons for the distribution of hmKP and the frequent development of their invasive infection in South East and East Asia including Taiwan and Japan remain to be fully elucidated (1). However, *K. pneumoniae* is the most commonly implicated pathogen in patients with community-acquired bacterial meningitis in Taiwan, an area with high endemicity for hmKP (4), although meningitis due to enterobacteria is relatively rare in Western countries (5-7).

Strongyloides stercoralis mainly infests the duodenum and jejunum in immunocompetent hosts. Chronic strongyloidiasis most frequently causes asymptomatic infection in immunocompetent individuals, but some patients may have diarrhea, constipation, or intermittent vomiting. Disseminated infection of this strain often causes severe enterobacteria infection especially in immunocompromised hosts, such as those who are human T-lymphotropic virus 1 (HTLV-1) or human immunodeficiency virus (HIV) carriers and those who have been administered systematic corticosteroids (8). Indeed, severe infections due to *S. stercoralis* have been mainly reported in the southwestern islands of Amami and *Okinawa* in Japan, where both *S. stercoralis* and HTLV-1 are endemic (9). However, the relationship between non-disseminated chronic strongyloidiasis and severe enterobacterial infection remains unclear.

We herein report a fatal case of septic meningitis due to

[1]Department of Infectious Disease, Kawasaki Municipal Kawasaki Hospital, Japan, [2]Department of Pathology, Kawasaki Municipal Kawasaki Hospital, Japan and [3]Kawasaki City Institute for Public Health, Japan
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Correspondence to Dr. Tomohiro Hosoda, ottotto723@gmail.com

Table. **Laboratory Findings on Admission.**

Hematology		Coagulation	
WBC	15,530 /μL	PT-INR	1.18
RBC	499×10⁴ /μL	APTT	30.2 Sec
Hb	17.6 g/dL	Fib	628 mg/dL
Ht	47.4 %	D-dimer	19 μg/mL
PLT	1.2×10⁴ /μL	Infection	
Biochemistry		HBsAg/Ab	(+)/(-)
TP	7 g/dL	HBeAg/Ab	(-)/(+)
Alb	3 g/dL	HBcAb	(+)
T-Bil	2.4 mg/dL	HBV genotype	C
D-Bil	1.3 mg/dL	HBV-DNA	(-)
AST	280 IU/L	HCVAb	(-)
ALT	88 IU/L	HTLV-1 (WB)	(+)
LDH	569 IU/L	HIV Ag/Ab	(-)
ALP	853 IU/L	Entamoeba histolytica IgG	(-)
BUN	76 mg/dL	Cerebrospinal fluid (CSF)	
Cr	2 mg/dL	CSF pressure	25 cmH_2O
UA	10.2 mg/dL	Cell	7 /3μL
Na	136 mEq/L	N/L	1/6
K	3.3 mEq/L	Pro	556 mg/dL
Cl	95 mEq/L	Glu	1 mg/dL
CK	1,626 IU/L	Gram's stain	Gram negative rods
HbA1c	5.9 %	Culture	
Lac	6.3 mEq/L	Blood	*K. pneumoniae*
CRP	35.26 mg/dL	CSF	*K. pneumoniae*

hmKP complicated with chronic strongyloidiasis in an HTLV-1 carrier.

Case Report

A 71-year-old Japanese man presented with a 7-day history of right upper quadrant abdominal pain, a 5-day history of exacerbation of chronic diarrhea for about 6 months, a 2-day history of a fever and headache, and disturbance of consciousness and was admitted to the emergency room. His birthplace was the Amami Islands in Japan, and he had frequently visited Okinawa in his childhood. He also had a history of frequent travel to the Solomon Islands on business over 40 years ago. His other medical history included hepatitis B virus and HTLV-1 carrier status, and he had a history of chronic alcohol abuse.

A physical examination on admission revealed a temperature of 36.0 ℃, blood pressure of 117/85 mmHg, pulse rate of 95 beats per minute, respiratory rate of 24 per minute, oxygen saturation of 94% while breathing 5 liters/min of oxygen, neck rigidity, and whole abdominal pain with the most severe tenderness in the right upper quadrant. Laboratory data showed severe thrombocytopenia and elevated liver enzyme levels, and an enhanced computed tomography (CT) scan showed liver abscess (Table, Fig. 1a).

A lumbar puncture was performed to determine the cause of the worsened consciousness and signs of meningeal irritation. The result of cerebrospinal fluid tests revealed a significant reduction in the glucose level, an elevated protein level, and Gram-negative rods. He was diagnosed with a pyogenic liver abscess and bacterial meningitis due to Gram-negative rods and was administered meropenem. He received intensive care including respirator support in the intensive-care unit (ICU) because of his deteriorated mental status. On the fourth day of admission, blood and cerebrospinal fluid cultures revealed string test-positive *K. pneumoniae* (Fig. 2). Direct microscopy of the stool showed rhabditiform larvae of *S. stercoralis* with peristaltic movement (Fig. 3). Excretion of the larvae in his stool continued despite the administration of daily ivermectin through a nasogastric tube for the treatment of strongyloidiasis. His coma did not improve after discontinuation of the sedation drugs. On the sixth day of admission, his electroencephalogram revealed flat brain waves, and head CT revealed pseudo-subarachnoid hemorrhaging signs associated with severe cerebral edema (Fig. 1b). The patient died of cardiopulmonary arrest on the seventh day of admission.

An autopsy was performed. A pathomicrograph of the liver tissue showed necrosis with neutrophil infiltration. A pathomicrograph of the brain tissue showed neutrophil infiltration not only in the meninges but also in the cerebral parenchyma. No *S. stercoralis* larvae were observed in the liver or brain tissue. There were no regions of mucosal rupture except for a polyp in his cecum. Several rhabditiform larvae of *S. stercoralis* were found only around the polyp (Fig. 4), with none found in any other part of the intestinal tract, including the duodenum. No filariform larvae were found in the gastrointestinal tract. Based on the autopsy

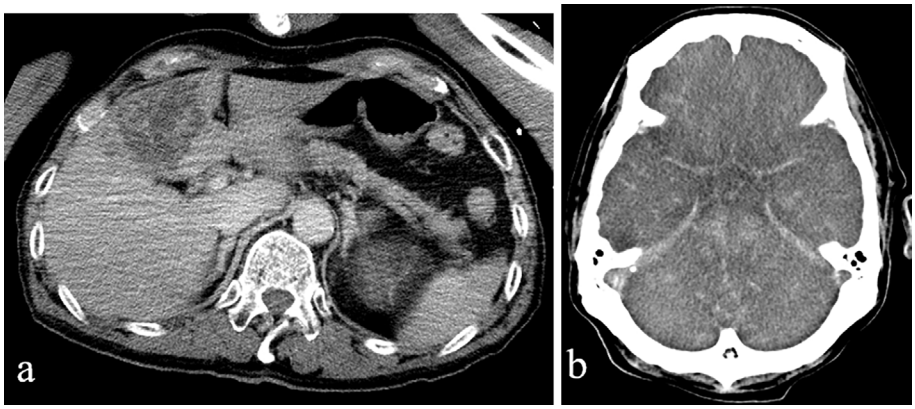

Figure 1. **a) Contrast-enhanced abdominal computed tomography (CT) on admission. A single mass-like solidity region with heterogeneous contrast is visible in the right hepatic lobe. b) Non-contrast-enhanced brain CT on the sixth day of admission. Pseudo-subarachnoid hemorrhaging signs due to severe cerebral edema can be observed.**

Figure 2. **A colony of *Klebsiella pneumoniae* on a blood agar plate cultured from cerebrospinal fluid. The string test is positive, with a pull of more than 5 mm.**

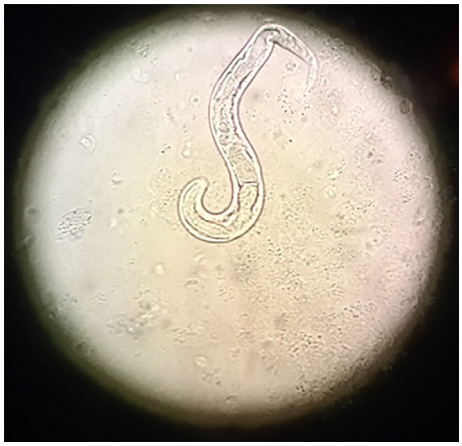

Figure 3. **Direct microscopy of a stool sample on the fourth hospital day of admission. Rhabditiform larvae of *Strongyloides stercoralis* with motility are visible.**

findings, we concluded that the cause of death was brainstem compression secondary to meningoencephalitis due to *K. pneumoniae* infection. The patient was also diagnosed with chronic, but not disseminated, strongyloidiasis.

The capsular serotype of the *K. pneumoniae* isolated in this case was K1, and it belonged to ST23, as determined by multilocus sequence typing (10). The isolate was positive for the following virulence factors: *magA*, *rmpA*, *iutA fimH*, *aerobactin*, and *iroN* by polymerase chain reaction using specific primers (11).

Discussion

The present case study highlighted two important clinical topics. First, even chronic strongyloidiasis can allow hmKP to invade the intestinal mucosa and induce severe infection due to enterobacteria, similar to disseminated strongyloidiasis. *S. stercoralis* infect the intestinal mucosa, and chronic infection of this pathogen induces inflammation of the intestinal mucosa (12). HTLV-1 carriers, such as in the present case, are at a high risk for disseminated strongyloidiasis and hyperinfection of *S. stercoralis* because of an impaired production of IL-4, IL-5, total IgE, and *S. stercoralis*-specific IgE (9). Nutman proposed that larvae in non-disseminated hyperinfection were increased in numbers but confined to the organs normally involved in the autoinfective cycle (e.g. gastrointestinal tract), although enteric bacteria (e.g. *Escherichia coli*, *K. pneumoniae*, *Proteus mirabilis, Enterococcus faecalis, Streptococcus bovis*) that could gain systemic access through intestinal ulcers were able to affect any organ system (13). In the present case, chronic diarrhea and its acute exacerbation before admission indicated the worsening of the chronic strongyloidiasis, i.e. "hyperinfection". *S. stercoralis* larvae were found in the cecum polyp, which was the only site of mucous membrane collapse of the intestinal tract according to the pathological autopsy.

However, it is generally believed that hmKP colonize the gastrointestinal tract of humans and can invade the intestinal mucosa and portal venous flow to develop invasive infections (14). Known risk factors of hmKP bacteremia in clinical disorders include diabetes mellitus (15, 16), cancer (16)

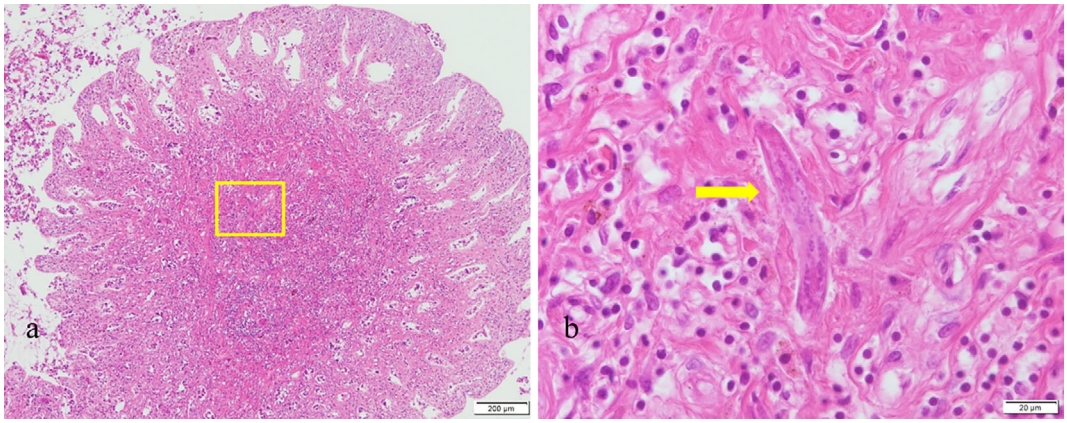

Figure 4. Hematoxylin and Eosin staining: Histopathologic features of the cecum showing a polyp with several rhabditiform larvae of *Strongyloides stercoralis* (arrow).

and alcoholic hepatitis (17). The present findings suggested that larvae had caused intense inflammation of the cecum, which allowed hmKP to invade the intestine without disseminated strongyloidiasis. In addition, we believe that because of the hypervirulence of the hmKP strain itself and the patient's history of daily alcohol use, he likely developed fatal liver abscess and meningoencephalitis.

Second, we believe that cases such as the present one are not rare in areas endemic for HTLV-1, *S. stercoralis* and hmKP, including Taiwan and Japan. *S. stercoralis* is endemic in the southwestern islands of Amami and Okinawa in Japan (18). As in Japan, the prevalence of both HTLV-1 carriers and patients infected with *S. stercoralis* is also relatively high in Taiwan (19, 20). A number of case reports of severe hmKP infection with high mortality rates, including liver abscess and septic meningitis, have been reported in Taiwan (1); the main hmKP sequence type isolated in Taiwan, ST23, was also detected in the present case. Some of these patients may also have chronic *S. stercoralis* infection and be HTLV-1 carriers, as in the present case, or may be complicated with disseminated strongyloidiasis. Strongyloidiasis should not be underdiagnosed, as a specific treatment with antiparasitic drugs is available. We should perform direct microscopy of the stool to detect *S. stercoralis* in patients who develop severe enterobacterial infections, including hypervirulent *K. pneumoniae*, especially in areas endemic for these pathogens.

In conclusion, chronic *S. stercoralis* infection can be a risk factor for severe infection due to hypermucoviscous *K. pneumoniae* in endemic areas in Japan and Taiwan.

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

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