CASE REPORT

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

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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

(Intern Med 59: 129-133, 2020) (DOI: 10.2169/internalmedicine.3403-19)

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 systemic 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

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Received: May 28, 2019; Accepted: July 4, 2019; Advance Publication by J-STAGE: August 21, 2019

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Table. Laboratory Findings on Admission.

| Hematology          | Coagulation     |
|---------------------|-----------------|
| WBC 15,530 /μL     | PT-INR 1.18     |
| RBC 499x10⁴ /μL    | APTT 30.2 Sec   |
| Hb 17.6 g/dL       | Fib 628 mg/dL   |
| Ht 47.4 %          | D-dimer 19 μg/mL|
| PLT 1.2x10⁴ /μL    |                 |
| Biochemistry        |                 |
| TP 7 g/dL          | HBsAg/Ab (+)(-)|
| Alb 3 g/dL         | HBeAg/Ab (-)(+) |
| T-Bil 2.4 mg/dL    | HbcAb (+)       |
| 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 cmH₂O |
| 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    |
| HbA1c 5.9 %        | Culture Gram negative rods |
| 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 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 ivmectin 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
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 Kp 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 Kp 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 Kp bacteremia in clinical disorders include diabetes mellitus (15, 16), cancer (16)
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 meningocencephalitis.

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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