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CASE REPORT

A case of hemorrhagic colitis after influenza A infection

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The pandemic (H1N1) influenza virus continues to be the predominant circulating virus in both the northern and southern hemispheres. In February 2009, during the early stage of the world-wide H1N1 influenza virus (influenza A) pandemic, we experienced a case of hemorrhagic colitis after infection with influenza A. A 21-year-old man with no serious disease in his past history visited our hospital with chief complaints of a high body temperature and pharyngeal pain. A diagnosis of influenza A was made using a rapid diagnosis kit (Capilia Flu A+B), and the patient was admitted to our hospital. After admission, the patient complained of a lower abdominal pain, diarrhea, and hematochezia. An emergency colonoscopy revealed active bleeding colitis from the sigmoid to descending colon. Hemorrhagic colitis was confirmed by the pathological findings of a punch biopsy specimen. After the administration of an antiviral drug, zanamivir hydrate (10 mg/d), the patient's general condition and colonoscopic findings improved significantly. The findings of both sequential colonoscopies and intestinal histology strongly suggested that infection with influenza A could induce hemorrhagic colitis, though the incidence is quite low.

Introduction

In seasonal influenza, gastrointestinal symptoms, such as diarrhea, vomiting, and abdominal pain, are sometimes observed.[1] Hemorrhagic gastritis in children was reported during the influenza A epidemic of 1988 in Australia.[2] Diarrhea occurred in 18.4% of the children infected with influenza A virus who required hospitalization in Taiwan.[3]

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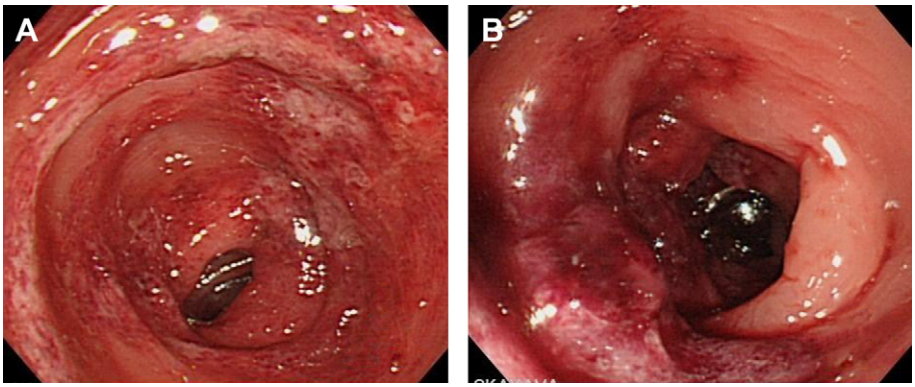

Figure 1. An emergency colonoscopy performed on the day of admission revealed redness and multiple edemas from the descending colon (A) to the sigmoid colon (B). An irregularly shaped ulcer and longitudinal ulcers were observed. Contact bleeding and spontaneous bleeding were also seen.

Influenza A virus is considered to be agent of acute gastroenteritis.[4] However, the pathogenesis of virus-induced acute gastroenteritis remains to be elucidated.

Currently, the novel swine influenza A (H1N1) virus is causing a pandemic and is a serious threat for all generations. Among patients infected with H1N1 in the United States, about 25% reportedly suffer from digestive conditions, including diarrhea.[5]

Some reports of gastrointestinal symptoms in patients with avian flu have been made. Diarrhea is an important presentation of avian influenza (H5N1) and might imply a poor prognosis.[6] A report of bleeding enteritis as a result of influenza has not been previously reported.

We experienced a case of hemorrhagic colitis after infection with influenza A. This is a rare case of a patient with hemorrhagic colitis after infection with seasonal influenza virus.

Case report

A 21-year-old man visited our hospital because of a high body temperature of 39.5°C and pharyngeal pain on February 18, 2009. A diagnosis of infection with influenza A was made using a rapid diagnosis kit (Capilia Flu A+B; TAUNS, Tokyo, Japan). A polymerase chain reaction assay of a nasal swab was not performed. The patient was treated with zanamivir hydrate (20 mg/d).

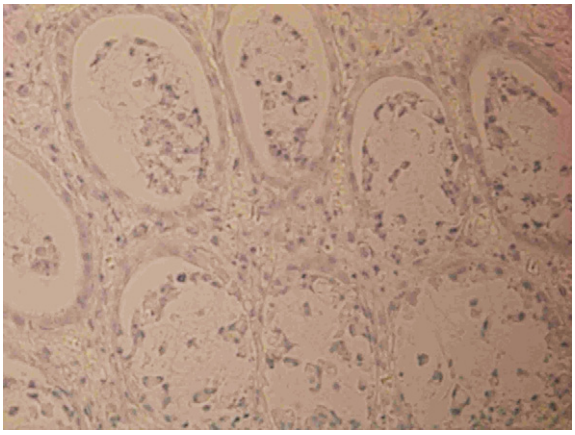

Figure 3. Immunohistochemical staining of our tissue specimen for the detection of influenza A antigen was negative (×200).

Five hours after being admitted to our hospital, he developed abdominal pain, diarrhea, and hematochezia. His body temperature was maintained at a level of 39°C. Chest and abdominal X-rays showed no abnormal shadow. The laboratory data showed mild inflammatory change (white blood cell count, 6,913/μL; Stab neutrophil, 6.0%; Segmented neutrophil, 57.0%; lymphocyte (lym), 24.0%;

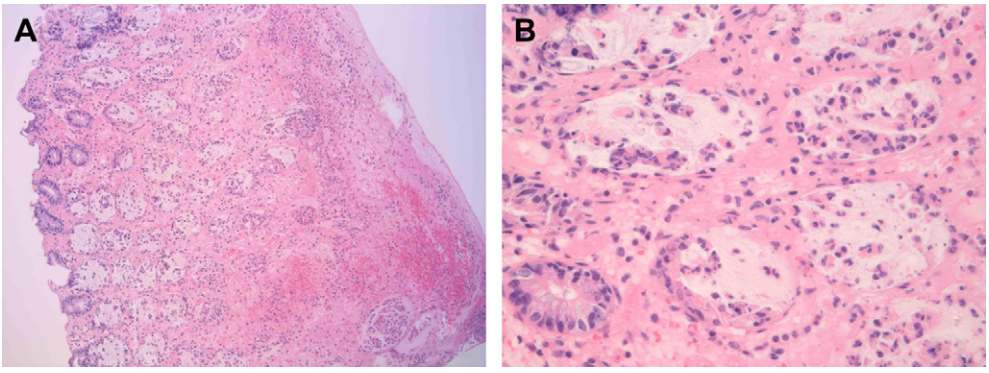

Figure 2. In the hematoxylin—eosin staining specimen, (A) moderate edema, uneven blood filling, and stasis in the small vessels were observed. (B) An increase in histiocytes, lymphocytes, and neutrophils, and acute crypt necrosis were also visible.

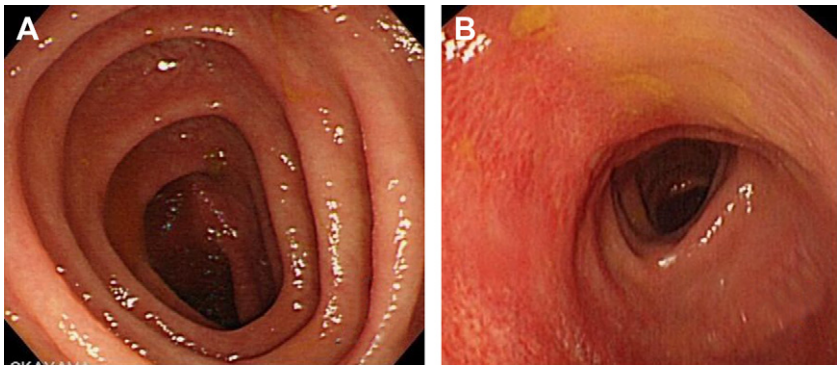

Figure 4. Endoscopic findings obtained 7 days after discharge. (A) In the descending colon, the mucosal edema and redness had improved remarkably. (B) Scattered or longitudinal areas of redness were seen in the sigmoid colon.

monocyte, 13.0%; hemoglobin, 16.1 g/dL; C reactive protein, 1.42 mg/dL).

An emergency colonoscopy was performed. It revealed constriction with mucosal edema and multiple areas of redness from the sigmoid colon to the descending colon (Fig. 1). An irregularly shaped ulcer and longitudinal ulcers were observed. The transverse colon and ascending colon presented with a normal mucosa, but the area of bleeding exhibited an ischemic colitis-like appearance. The histological findings showed moderate infiltration of inflammatory cells, consisting of neutrophils, lyms, and histiocytes, in the proprial mucosa. Cryptic necrosis was evident. Moderate edema and uneven blood filling were also seen (Fig. 2). Immunoperoxidase staining using a monoclonal antibody against the nucleoprotein of influenza A virus failed to detect the viral antigen of influenza A (Fig. 3).

A fecal culture test showed normal flora. A drug-induced lym stimulation test was negative for zanamivir hydrate. The blood was negative for antiamoebic antibodies.

The patient was treated using peripheral parenteral nutrition. Nonsteroidal anti-inflammatory drugs, antibiotics, and other drugs were not used. The administration of zanamivir hydrate was continued. The abdominal pain, diarrhea, and hematochezia disappeared on the third day after admission. During the subsequent 5 days, his general condition improved. The patient was discharged from our hospital 1 week after hospitalization. His colonoscopic findings had improved remarkably at 7 days after discharge (Fig. 4).

Discussion

Declared a global pandemic in June 2009, the H1N1 virus has since become even more widespread and remains unpredictable. Under the influences of both seasonal A and H1N1 influenza, more than 2 billion people worldwide were infected, and thousands of schools were closed by the end of 2009.

Digestive symptoms, such as diarrhea and vomiting, in patients with seasonal influenza infections are often reported. Although, several gastrointestinal symptoms were frequently observed in patients infected with the avian influenza virus, few reports on hemorrhagic colitis complications in any type of influenza infection have been reported. In the present case, the colonoscopic findings were typical of hemorrhagic colitis with an ischemic appearance. Irregular-shaped ulcers were distributed longitudinally in the area from the descending colon to the sigmoid colon. We report here a rare case in which bleeding enteritis suddenly occurred in a patient infected with influenza A. The patient was treated with zanamivir hydrate (Relenza; Glaxo SmithKline, Middlesex, United Kingdom) after emergency admission. The patient's general and digestive symptoms improved in parallel with the colonoscopic findings, thereby denying a possibility of drug-induced colitis.

Hematoxylin—eosin staining of specimens obtained during an endoscopic examination showed evidence of severe inflammation and crypt necrosis in the mucosal layer. These findings were more significant than those typically observed for drug-induced or general colitis. The pathogenesis of intestinal symptoms as a result of infection with influenza virus is controversial. An irrelevant cytokine action inducing apoptotic lyms is likely to be one of the key mechanisms responsible for the direct action of the virus on digestive organs.[7] The viral RNA of seasonal influenza A (H3N2) was often detected in stool specimens.[1,4,8] On one hand, immunohistochemical staining of our tissue specimen for the detection of influenza A antigen was negative. However, several studies have indicated that influenza virus antigens were not directly detected in the organs of infected patients.[9,10] The hemorrhagic colitis could be induced by many other factors. Therefore, a precise understanding of intestinal complications can be drawn from *in situ* hybridization or polymerase chain reaction of the infected tissues, although these are not routine examinations in a general clinic, especially during a pandemic situation. Although the exact mechanism of hemorrhagic colitis during infection with influenza A remains to be elucidated, it is important to be aware that influenza infection can induce severe intestinal complications as reported in this article.

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