CASE REPORT

Cytomegalovirus-associated gastric ulcer: a diagnostic challenge in a patient of fulminant hepatitis with steroid pulse therapy

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SUMMARY

A 69-year-old woman presented with malaise. She had had organising pneumonia with the treatment of prednisolone. A diagnosis of fulminant hepatitis was made and steroid pulse therapy was initiated. Ten days later, a colonic resection with a colostomy was performed because of the perforated diverticulitis of the sigmoid colon. She presented with epigastric pain and melena after surgery. Despite the administration of the proton pump inhibitor, an endoscopy revealed multiple deep, punched-out ulcers of the stomach. Biopsy specimen showed cytomegalovirus (CMV) infection. The melena and CMV antigenemia was improved with ganciclovir; however the patient died from worsening of hepatic failure. We emphasise that CMV-associated gastric ulcers should be considered in the differential diagnosis of gastric ulcers in patients treated with immunosuppressive drugs.

BACKGROUND

Cytomegalovirus (CMV) is a very common viral pathogen that usually causes an asymptomatic infection in normal hosts. However in immunocompromised hosts primary or reactivated infection often causes serious damage to systemic organs, including the gastrointestinal (GI) tract. As shown in this case, CMV-associated gastric ulcers should be considered in the differential diagnosis of gastric ulcers in patients treated with immunosuppressive drugs.

CASE PRESENTATION

A 69-year-old woman presented with malaise for a week. Diagnosis of organising pneumonia had been made based on the findings of bronchoscopy and transbronchial lung biopsy, and she had been treated with prednisolone for 6 months. Tests for CMV were not performed at the bronchoscopy. Her medical history included osteoporosis, fracture of the rib and cholecystectomy. On examination, she was alert and had jaundice. She was admitted because of the elevated serum bilirubin at 17 mg/dL, aminotransferase at 847 IU/L and alanine transaminase 426 IU/L. Her antinuclear antibody titre was positive with a titre >160. Her anti-CMV IgG and IgM antibodies were a previously infected pattern (IgG 110.0 C.O.I, IgM 0.3 C.O.I). The image of MR cholangiopancreatography revealed no extrahepatic cholestasis. The liver biopsy specimen revealed features compatible with autoimmune hepatitis (AIH). Diagnosis of fulminant hepatitis due to AIH

was made and steroid pulse therapy (methylprednisolone 1000 mg/day) was initiated because steroid pulse therapy has been widely used for fulminant hepatitis due to AIH in Japan. She presented sudden abdominal pain 10 days later, and a perforated diverticulitis of the sigmoid colon was diagnosed. A colonic resection with colostomy was performed. She presented with epigastric pain and melena 16 days after surgery.

INVESTIGATIONS

Her laboratory test results were as follows: white cell count 6300 cells/ μ L (neutrophils 83.1%, monocytes 2.5%, lymphocytes 13.4%, eosinophils 0.8% and basophils 0.2%), haemoglobin 8.7 g/dL, and platelets 120 000 cells/ μ L. Her anti-HIV antibody test was negative. Serum CMV pp65 antigenemia was positive ($29/1.5 \times 10^5$ leucocytes). Despite the administration of the proton pump inhibitor, an endoscopy revealed multiple deep, punched-out ulcers, in the antrum of the stomach (figure 1). Histopathological examinations of the biopsy specimen showed large epithelial cells with enlarged nuclei and peripheral halos (owl's eye sign; figure 2). Immunohistochemical staining was positive for CMV (figure 3).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis might have included peptic ulcer, acute gastric mucosal lesion.

Figure 1 Endoscopic view of multiple deep, punched-out ulcers in the antrum of the stomach.

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Figure 2 Histological image of characteristic 'owl's-eye' cells with enlarged nuclei and peripheral halos in the gastric epithelial cells (H&E staining, ×200).

TREATMENT

The patient was treated with ganciclovir.

OUTCOME AND FOLLOW-UP

Melena and CMV antigenemia was improved with ganciclovir, however colonic diverticular haemorrhage occurred, resulting in worsening of the hepatic failure. The patient died 2 months after admission.

DISCUSSION

CMV-associated gastric ulcer is common in the patients with immunosuppressive therapy. But the accurate endoscopic diagnosis of CMV ulcers is not easy because of the absence of characteristic morphological features.¹ In general, CMV-associated gastric ulcers might cause multiple and deeper lesions in the upper GI tract.² Lin *et al*³ investigated 20 cases of GI CMV disease, and classified macroscopic features into inflammatory mucosa alone, ulceration alone, inflammatory mucosa associated with ulcer and submucosal tumour with ulcer. Tsuji⁴ reported the case of polypoid lesion caused by CMV infection. Thus endoscopic features of CMV gastritis are quite variable, but the

Figure 3 Immunohistochemical staining showing multiple cytomegalovirus (CMV)-positive cells (CMV immunostaining, ×200).

endoscopic feature of our patient was the typical multiple deep, punched-out ulcers.

The most common site of a CMV infection in the GI tract is the colon (55%), while the stomach is involved in 40% of the cases, and oesophagus is rare (5%).³ As we did not perform video capsule endoscopy and colonoscopy, our patient might have not only gastric lesions but also small intestinal and/or colonic lesions.

The presence of cytomegalic cells with viral inclusions in tissue biopsies is considered the gold standard for establishing a diagnosis of CMV gastritis.⁵ The CMV antigenemia assay is widely used for detection of reactivation of CMV infection in a variety of clinical settings. Because of the low assay sensitive (54%), the CMV antigenemia assay is not useful to exclude CMV GI disease, and the results need to be interpreted in the context of clinical presentation and other diagnostic test results.⁶ In our patient, CMV-associated gastric ulcer was suspected due to the presence of gastric ulcers despite the administration of proton pump inhibitor. CMV-associated gastric ulcer could be diagnosed by the means of pathological cytomegalic cells and positive CMV antigenemia. Therefore, CMV-associated gastric ulcers should be considered in the different diagnosis of gastric ulcers in patients treated with immunosuppressive drugs.

Learning points

- ▶ In immunocompromised hosts, primary or reactivated infection of cytomegalovirus (CMV) often causes serious damage to systemic organs, including the gastrointestinal tract.
- ▶ The presence of cytomegalic cells with viral inclusions in tissue biopsies is considered the gold standard for establishing a diagnosis of a CMV-associated gastric disease.
- ▶ CMV-associated gastric ulcers should be considered in the different diagnosis of gastric ulcers in patients treated with immunosuppressive drugs.

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Competing interests None.

Patient consent Obtained.

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