

Acute and extremely severe necrotic esophagitis accompanied by hyperglycemic hyperosmolar syndrome in a subject with type 2 diabetes mellitus

Acute necrotic esophagitis is characterized by blacking in the esophageal mucosa and is very rarely observed among the huge number of the population with diabetes mellitus, especially under severe hyperglycemic conditions^{1–3}. Here we show a very rare case of a patient who had acute and extremely severe necrotic esophagitis accompanied by hyperglycemic hyperosmolar syndrome.

A 62-year-old Japanese male had type 2 diabetes mellitus (duration of diabetes: approximately 10 years). Hemoglobin A1c (HbA1c) was around 6%. For several weeks, he had repeated vomiting and suffered from poor oral intake. Nonetheless, he continued to drink too much alcohol (300 g in ethanol equivalents). One day, he vomited a black residue. His glycemic control worsened drastically; his blood glucose level increased up to 600 mg/dL. During gastroscopy, acute esophagitis was observed and he was hospitalized in our institution.

On admission, the plasma glucose level was 471 mg/dL, whereas the HbA1c level was not very high (6.2%), indicating that glycemic control had worsened drastically in a short period. Ketone body levels were markedly increased: total ketone bodies, 16,220 $\mu\text{mol/L}$; acetoacetate, 4,080 $\mu\text{mol/L}$; 3-hydroxybutyrate, 1144.0 $\mu\text{mol/L}$. Blood gas data showed metabolic acidosis: pH 7.363, HCO_3^- 12.1 mEq/L, base excess -11.0 mEq/L. Renal dysfunction was observed probably due to

dehydration (creatinine, 1.23 mg/dL; blood urea nitrogen, 45 mg/dL), and liver dysfunction was also observed probably due to drinking too much alcohol (AST, 47 U/L; ALT, 40 U/L; g-GTP 194 U/L). Inflammatory markers were moderately increased: CRP, 4.66 mg/mL, WBC 8700/ μL . Abdominal computed tomography (CT) revealed a thickening of the esophageal wall spreading continuously from the central to the lower esophagus, liquid storage inside the esophageal lumen, and severe fatty liver (Figure 1a). During gastroscopy, almost the entire circumference of the whole esophagus was shown to have turned black (Figure 1b). Thereby, we diagnosed him as having acute necrotic esophagitis complicated by hyperglycemic hyperosmolar syndrome.

We stopped oral intake and started fluid replacement therapy. Also, we started intravenous insulin therapy to obtain good glycemic control. During gastroscopy 7 days after admission, the black necrotic mucosa had disappeared but a geographic ulcer was observed in the middle and lower esophagus (Figure 1b). After this, he started oral intake and intensive insulin therapy. During gastroscopy 14 days after admission, the esophageal mucosa was improved drastically, although erosion and an ulcer running vertically were observed (Figure 1b). Since we confirmed that endogenous insulin secretion was preserved (C-peptide 1.4 ng/mL; CPR index, 1.08), we stopped insulin therapy and started metformin (500 mg/day) and sitagliptin (50 mg/day).

We think that there are several possible reasons for such severe necrotic esophagitis. First, the percentage of the onset of acute necrotic esophagitis is very

low among the large number of the population with diabetes mellitus, but many subjects with acute necrotic esophagitis had diabetes mellitus^{3,4}. Therefore, we think that the presence of diabetes mellitus was, at least in part, associated with the development of severe necrotic esophagitis in this subject. It is also possible that ketoacidosis and oxidative stress together with hyperglycemia and dehydration due to poor oral intake and drinking too much alcohol were likely involved in this process. Second, since atherosclerotic change was observed around the celiac artery in the abdominal CT, peripheral circulatory failure in the upper gastrointestinal mucosa was also likely to be involved. Third, repeated vomiting could lead to an increase of esophageal pressure which was also likely to be involved. Fourth, since multiple duodenal ulcers were observed in gastroscopy and the serum gastrin level was as high as 757 pg/mL (reference range: 42–200 pg/mL) probably due to drinking too much alcohol, it is likely that this subject had gastric hyperacidity which also might have been involved in the development of severe acute esophagitis. Fifth, in general it is possible that virus or candida infection is involved in the development of severe necrotic esophagitis. However, there were no findings indicating herpes esophagitis or esophageal candidiasis in gastroscopy. In addition, β -glucan was negative in this subject. Furthermore, while generally it is rare that cytomegalovirus (CMV) esophagitis is observed in subjects without human immunodeficiency virus (HIV) infection, anti-HIV antibody was negative in this subject. Therefore, we assume that

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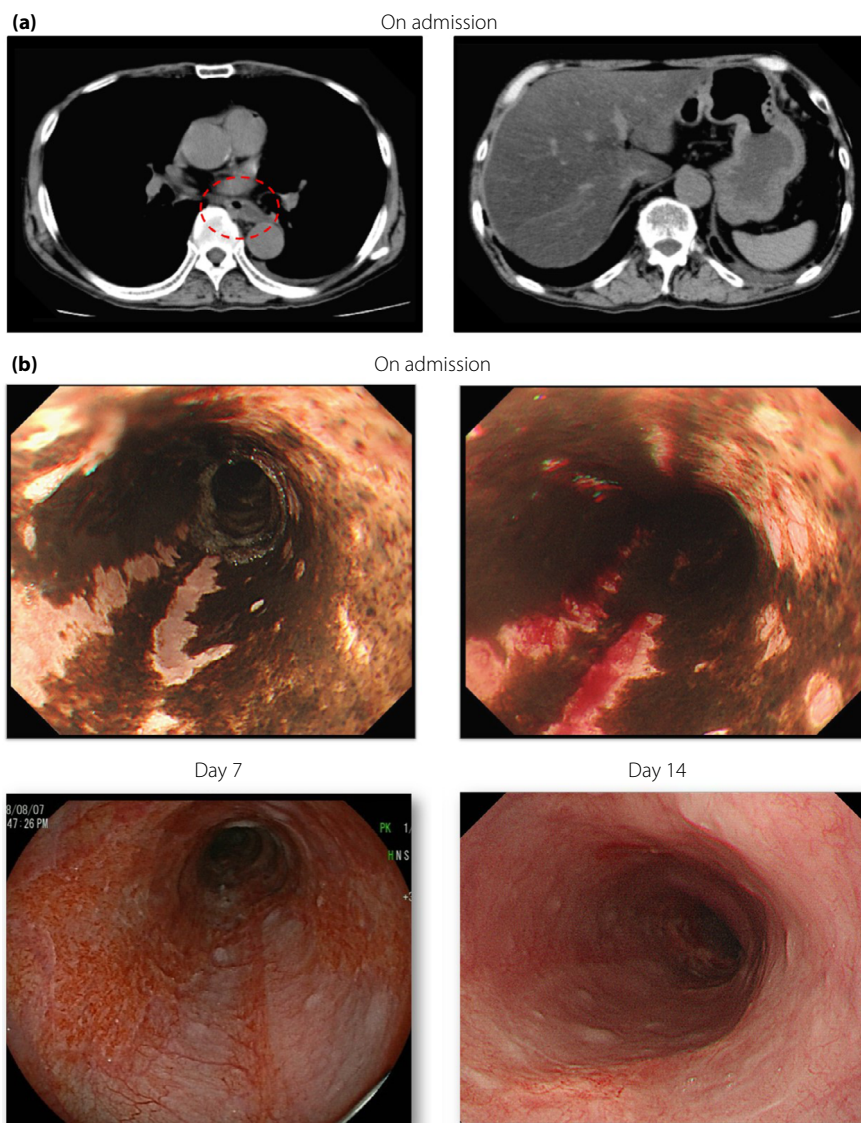




Figure 1 | (a) Abdominal computed tomography revealed thickening of the esophageal wall spreading continuously from the central to the lower esophagus, liquid storage inside the esophageal lumen (red dotted line) (left panel), and severe fatty liver (right panel). (b) During gastroscopy on admission, almost the entire circumference of the whole esophagus had turned black (upper panels). During gastroscopy 7 days after admission, the black necrotic mucosa had disappeared but a geographic ulcer was observed in the middle and lower esophagus (lower, left panel). During gastroscopy 14 days after admission, the esophageal mucosa was drastically improved, although erosion and an ulcer running vertically were observed (lower, right panel)

candida or CMV infection was not highly involved in the development of severe necrotic esophagitis in this subject. In addition, since it was possible that the sodium-glucose cotransporter 2 (SGLT2) inhibitor facilitated dehydration and ketoacidosis, we did not restart the SGLT2 inhibitor.

Taken together, we should bear in mind the possibility of acute necrotic esophagitis especially when acute aggravation of glycemic control and vomiting of black residue are observed in subjects with diabetes mellitus.

DISCLOSURE

The authors declare no conflict of interest.

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