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Extremely rare case of necrotizing gastritis in a patient with autoimmune hepatitis: A case report

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Abstract

BACKGROUND

Autoimmune hepatitis can cause liver fibrosis, liver cirrhosis, and hepatocellular carcinoma. Its treatment option include the use of steroids and/or immunosuppressive agents such as azathioprine. However, these drugs have some side effects. Thus, close follow-up is needed during treatment. Here, we present an extremely rare case of a patient with an autoimmune hepatitis who died from necrotizing gastritis during immunosuppressive treatment.

CASE SUMMARY

A 52-year-old female patient was diagnosed with autoimmune hepatitis. We treated this patient with immunosuppressive agents. High-dose steroid treatment was initially started. Then azathioprine treatment was added while steroid was tapering. Five weeks after the start of treatment, she visited the emergency room due to generalized abdominal pain and vomiting. After computed tomography scan, the patient was diagnosed with necrotizing gastritis and the patient progressed to septic shock. Treatment for sepsis was continued in the intensive care unit. However, the patient died at 6 h after admission to the emergency room.

CONCLUSION

In patients with autoimmune infections undergoing immunosuppressant therapy, rare complications such as necrotizing gastritis may occur, thus requiring clinical attention.

Key Words: Autoimmune hepatitis; Azathioprine; Case report

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Core Tip: Primary treatment for autoimmune hepatitis is using immunosuppressants such as steroids and azathioprine. When using immunosuppressants, various side effects may occur. Thus, close observation is necessary. This case report is the first one to describe the occurrence of necrotizing gastritis, a very rare complication of immunosuppressants, in a patient with autoimmune hepatitis.

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INTRODUCTION

Autoimmune hepatitis is a rare liver disorder presenting persistent inflammation of the liver parenchyma. It is characterized by interfacial hepatitis, elevated liver enzyme levels, hypergammaglobulinemia, and the appearance of autoimmune antibodies[1,2]. If autoimmune hepatitis is not well controlled, it can continuously cause liver fibrosis and progress to liver cirrhosis and/or hepatocellular carcinoma[3,4]. The 2019 American Association for the Study of the Liver practice guideline recommends prednisolone and azathioprine combination therapy as a first-line drug in patients without cirrhosis, acute severe autoimmune hepatitis, or acute liver failure[5-7]. In particular, prednisolone is recommended to be used at an amount of 1 mg or more per 1 kg of body weight at the beginning of treatment. Screening for its various side effects such as infection and bone marrow suppression are essential[5,6,8,9]. Azathioprine is used in maintenance treatment. It is also a type of immunosuppressant that can cause various side effects. Here, we report an extremely rare case of a patient who died due to a sudden onset of necrotizing gastritis as a side effect of an immunosuppressant.

CASE PRESENTATION

Chief complaints

A 52-year-old female visited the emergency room of our hospital (Soonchunhyang University Bucheon Hospital) due to abdominal pain nausea and vomiting.

History of present illness

Five weeks before visiting the emergency room, she visited our outpatient clinic of gastroenterology department due to an increased level of liver enzyme alanine aminotransferase (ALT) (at 320 U/mL) that was accidentally found at a health screening test. Blood test showed positive autoimmune antibody (anti-nuclear antibody 1:1280 and anti-mitochondrial antibody positive). Her immunoglobulin G was elevated to 1577 mg/dL. Abdominal ultrasound and computed tomography (CT) showed coarse liver surface, indicating that she had chronic liver disease (Figure 1A). Therefore, a liver biopsy was performed and the patient was finally diagnosed with an overlap syndrome predominantly with features of an autoimmune hepatitis. After the biopsy, the patient started to take high dose of ursodeoxycholic acid (15 mg/kg) plus prednisolone 40 mg daily for two weeks. After two weeks from the initial treatment, the dose of ursodeoxycholic acid was maintained and prednisolone was reduced by 10 mg every week. Six days before the emergency room visit, prednisolone was reduced to 5 mg and azathioprine 50 mg was maintained.

From two days before visiting the emergency room, the patient had symptoms of mild heartburn and abdominal pain. One day before the emergency room visit, her abdominal pain worsened to the point that it interfered with her sleep. In addition, she had more symptoms of nausea, vomiting, and diarrhea. Thus, she finally visited the emergency room.

History of past illness

The patient had an unremarkable past medical history except for an overlap syndrome described above.

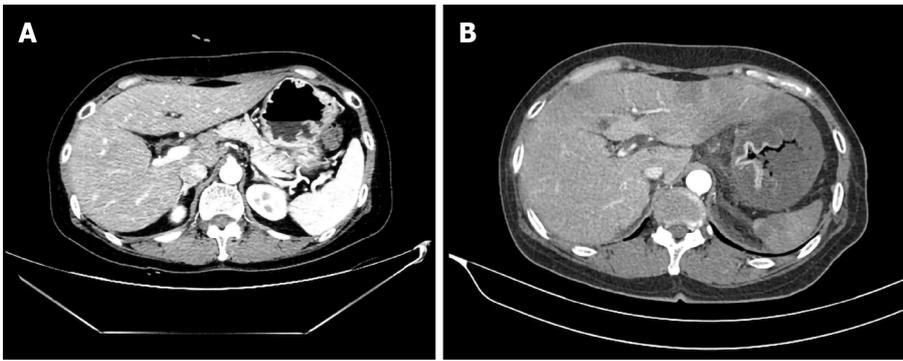


Figure 1 Computed tomography of the patients. A: Before treatment; and B: At the time of visiting the emergency room. No abnormality of stomach was observed before the treatment, while gastric wall is enhancing and air space is shown after the treatment.

Physical examination

At the time of the emergency room visit, her blood pressure was normal with a systolic blood pressure of 130 mmHg and a diastolic blood pressure of 80 mmHg. She had a mild fever (37.6 °C) and tachycardia (heart rate of 110 beats/min). She also had tachypnea at 30 breaths per minute. She had abdominal tenderness in the epigastric to the left upper quadrant area. Her abdomen was a little hard. However, no rebound tenderness was observed.

Laboratory examinations

During the outpatient treatment period, her counts of white blood cells, red blood cells, and platelets were all normal. However, at the time of the emergency room visit, her counts of white blood cells and platelets were reduced to 700/ μ L and 61000/ μ L, respectively. Since her neutrophil level was decreased to 5% and C-reactive protein level was elevated to 14.35 mg/dL, systemic infection was strongly suspected. Test results for liver enzymes were: aspartate aminotransferase, 347 U/L; ALT, 52 U/L; and gamma glutamyl transferase, 458 U/L. Her prothrombin time international normalized ratio was 1.2.

Imaging examinations

Contrast-enhanced abdominal CT revealed a huge stomach with layered wall thickening in the fundus and upper body (Figure 1B), which was not found before she received treatment (Figure 1A). Air in the stomach wall was observed in some areas. Decrease of mucosal enhancement was also detected.

FINAL DIAGNOSIS

We diagnosed the patient with necrotizing gastritis accompanying septic shock.

TREATMENT

Her blood pressure was normal at the time of admission to the emergency room. However, at 30 min after the emergency room visit, her blood pressure decreased (systolic blood pressure was less than 80 mmHg). The patient was immediately transferred to the intensive care unit and intravenous hydration and antibiotic treatment were started immediately. At two hours after admission to the intensive care unit, her blood pressure was increased (systolic blood pressure at 127 mmHg and diastolic blood pressure at 95 mmHg) while receiving inotropics (norepinephrine) and fluid treatment.

OUTCOME AND FOLLOW-UP

Her heart rate suddenly started to slow from three hours after entering the intensive care unit. Bedside echocardiography was performed and severe stress-induced

cardiomyopathy with ejection fraction of less than 10% was observed. Thus, extracorporeal membrane oxygenation was prepared. During preparation for the procedure, sudden cardiac arrest with pulseless electrical activity started. Accordingly, cardiopulmonary resuscitation was performed for more than 30 min. extracorporeal membrane oxygenation was also applied. However, the patient died of cardiac arrest.

DISCUSSION

Treatment for autoimmune hepatitis is determined based on the severity of symptoms, elevation of serum ALT and gamma globulin, histological findings, and various other side effects of treatment[10,11]. The recommended starting point of treatment varies slightly for each guideline. If levels of ALT and gamma globulin are normal or not deviating significantly from normal and if hepatitis is not severe on liver biopsy, treatment is not recommended because significant liver damage is not likely to progress in these cases.

However, if ALT level is elevated more than 5 times or gamma globulin levels are high as in our patient, immunosuppressive treatment is recommended. Since both steroids and azathioprine have side effects, regular liver function tests, blood sugar, and complete blood count test are crucial after treatment initiation[12-14]. In most cases, follow up laboratory test is recommended every week, especially for first month after treatment initiation. In our case, although physical examinations and blood tests were performed every week, we could not predict the occurrence of sudden necrotizing gastritis.

For our case, immunosuppressants might have acted as risk factors for necrotizing gastritis. Of the two drugs (steroid and azathioprine) used for our case, azathioprine was more likely to be the cause. Common gastrointestinal side effects of azathioprine are known as nausea, vomiting, abdominal pain, and increased stomach irritation. In addition, both leukopenia and infection observed in this patient are side effects reported for azathioprine users[15]. Considering that steroids were tapered for the patient, azathioprine was more likely to be the cause. According to Teich *et al*[16], azathioprine side effects are more common in patients taking oral steroids. Thus, steroid might act as a secondary exacerbation factor.

Since necrotizing gastritis is a disease with a very low incidence, we could not find any other case of necrotizing gastritis in patients with autoimmune hepatitis. Instead, we searched for reports of necrotizing gastritis in patients without autoimmune hepatitis (Table 1)[17-26]. In most cases, treatment included total gastrectomy or the use of antibiotics[27,28]. In our case, initial treatment was also the use of intravenous antibiotics. However, the patient deteriorated despite rapid antibiotic administration and fluid treatment. Thus, anaerobic bacteria were highly likely to be the cause of sepsis. This was hypothetical because no bacteria were identified in blood cultures reported after the patient's death. Mortality rates of necrotizing gastritis in previous reports were lower than 50%. However, such finding cannot be generalized because of a small number of studies. Most of previous reported cases of necrotizing gastritis were accompanied by sepsis with elevation of white blood cell counts. However, our case showed a decrease of leukocytes. It could be interpreted as another manifestation of sepsis.

There are no separate guidelines for necrotizing gastritis. However, taking the previous cases and our case together so far, we think that the best diagnostic method is abdominal CT. Endoscopy may also be considered. However, it has a risk of worsening symptoms and perforation[29]. Since necrotizing gastritis is often accompanied by sepsis, gastroscopy is a contraindication if vital sign is unstable. Thus, we do not recommend gastroscopy as a first diagnostic option for necrotizing gastritis. Exploratory laparotomy could be done for diagnosis purpose. Exploratory laparotomy plus gastrectomy might also be considered when diagnosis and treatment are required at the same time.

Necrotizing gastritis has a low incidence. It is a field that has not been well studied yet. This is the first study to report a case of necrotizing gastritis in a patient with autoimmune hepatitis. Clinicians should be aware that such rare side effect can occur. Such possibility should be suspected if a patient with autoimmune hepatitis has complaint of gastrointestinal symptoms such as abdominal pain when taking immunosuppressants.

Table 1 Literature review of necrotizing gastritis

Ref.	Diagnosis	Risk factors	Clinical course
Tejas <i>et al</i> [17], 2017	CT	None	Exploratory laparotomy and discharge
Perigela <i>et al</i> [18], 2014	CT	None	Exploratory laparotomy and discharge
Dharap <i>et al</i> [19], 2003	CT	None	Exploratory laparotomy and discharge
Hsing <i>et al</i> [20], 2019	CT	None	Intensive unit care and intravenous antibiotics then, discharge
Le Scanff <i>et al</i> [21], 2006	CT	Acute myeloblastic leukemia with chemotherapy	Intensive unit care and discharge
Iwakiri <i>et al</i> [22], 1999	CT	None	Intensive unit care and discharge
King <i>et al</i> [23], 2012	CT	Acute myeloid leukemia with chemotherapy	Intravenous antibiotics, granulocyte colony stimulating factors use, then discharge
Nasser <i>et al</i> [24], 2019	CT	Deep vein thrombosis, pulmonary embolism, hypertension, diabetes mellitus, atrial fibrillation, heart failure, chronic obstructive pulmonary disease	Intensive unit care and intravenous antibiotics then, discharge
Al-Jundi <i>et al</i> [25], 2008	CT	Non-small cell lung cancer	Intensive unit care and discharge
Loi <i>et al</i> [26], 2007	CT	Chronic hepatitis B, hepatocellular carcinoma	Intensive unit care and discharge
Kobus <i>et al</i> [28], 2020	CT	Proton pump inhibitor	Total gastrectomy and death

CT: Computed tomography.

CONCLUSION

This is the first case report of a fatal necrotizing gastritis in a patient with autoimmune hepatitis receiving azathioprine and steroid. Clinicians should be aware of such rare side effect and make close observations during immunosuppressant treatment.

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