Phlegmonous Gastritis Associated with Group A Streptococcal Toxic Shock Syndrome

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Abstract

Phlegmonous gastritis (PG) is a rare, acute, severe infectious disease of the gastric wall that is often fatal due to *Streptococcus* spp. A 77-year-old man with diabetes and a gastric ulcer was urgently admitted due to prolonged nausea and vomiting. Computed tomography revealed widespread diffuse thickening of the gastric wall, and PG was suspected. The patient expired less than 9 hours after admission despite intensive treatments. Later, an analysis of the blood and gastric juice revealed group A *streptococcus* (GAS) and virulence factors associated with toxic shock syndrome (TSS). We herein diagnosed a patient with an extremely aggressive course of PG caused by GAS TSS.

Key words: phlegmonous gastritis, group A *streptococcus*, toxic shock syndrome, gastric juice culture

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Introduction

Phlegmonous gastritis (PG) is a severe bacterial infection of the gastric wall, particularly caused by Gram-positive cocci. This extremely rare and rapidly evolving disease leads to fatal systemic infection within hours without proper treatment, with a mortality rate of approximately 40% (1, 2). PG may affect a focal point in the gastric wall and most cases belong to the diffuse type where the entire stomach is infected. Risk factors for PG include alcohol consumption, chronic gastritis, malignancy, mucosal injury, diabetes, and immunosuppression (1-7). An early diagnosis of PG is difficult due to the nonspecific nature of the clinical manifestations, including epigastric pain, nausea, and vomiting (1, 2). In general, PG can be diagnosed by a combination of various modalities, such as computed tomography (CT) scans, upper gastrointestinal (GI) endoscopy, endoscopic ultrasound (EUS), and gastric juice culture (1-3, 8, 9). We herein describe a fatal case of diffuse PG associated with toxic shock

syndrome (TSS) caused by group A *streptococcus* (GAS).

Case Report

A 77-year-old man visited a primary care physician six hours after complaining of nausea and vomiting. He had a history of type 2 diabetes and hypertension which were controlled by oral medications. The level of glycated HbA1c was 6.4%. The patient also had a history of gastric ulcers and was taking oral famotidine to raise his gastric pH. The patient had no history of upper GI endoscopy for at least one year. He received a diagnosis of viral gastroenteritis and was discharged.

Because his symptoms worsened rapidly 24 hours after the initial visit, the patient was transferred to the emergency department (ED) of our hospital by ambulance. At the time of admission, the patient had moderate tenderness to the abdomen but no pharyngitis, tonsillitis, or arthralgia. In addition, there were no signs of cellulitis, erythema, or blisters. A medical examination showed that he had not eaten raw

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Table. Laboratory Data on Admission

Complete Blood Count		Chemistry	
White Blood Cells	21,400/ μ L	Creatine	2.15mg/dL
Neutrophil	58.0%	BUN	46.1mg/dL
Lymphocyte	8.0%	Sodium	131mEq/L
Monocyte	2.0%	Potassium	4.1mEq/L
Eosinophil	1.0%	Chloride	92mEq/L
Basophil	0.0%	AST	28IU/L
Metamyelocyte	11.0%	ALT	13IU/L
Myelocyte	20.0%	γ -GTP	16IU/L
Red Blood Cells	542 $\times 10^4$ / μ L	T-Bil	2.1mg/dL
Hemoglobin	17.8g/dL	LDH	320IU/L
Hematocrit	49.0%	Total Protein	6.9g/dL
Platelet count	17.6 $\times 10^4$ / μ L	CRP	39.5mg/dL
		Glucose	205mg/dL
		Endotoxin	<3pg/mL
		Procalcitonin	>100

fish before the onset. When he arrived at the ED, his vital signs were the following: blood pressure, 94/66 mmHg; heart rate, 120 beats/min; and body temperature, 37.1°C. In addition, his laboratory results revealed a high-grade inflammatory status (white blood cell count: 21,400/ μ L; CRP: 39.5 mg/dL) and renal impairment (creatinine: 2.15 mg/dL) (Table). These findings were suggestive of septic shock. Simple CT revealed widespread thickening of the gastric wall, consistent with PG (Figure).

Immediately after admission, we conducted massive fluid replacement and administered a single dose of ceftriaxone (1 g). Within 1 hour after the admission, the patient developed a high fever and severe hypotension (69/45 mmHg), and a blood sample was collected for a culture analysis. In the interim, his blood pressure remained low despite fluid resuscitation. We started the patient on catecholamines and he was transferred to the intensive care unit (ICU). During the transfer, we initiated continuous hemodiafiltration combined with direct hemoperfusion using a polymyxin-B immobilized fiber column. In addition, the patient was administered meropenem (1 g) intravenously. Unfortunately, these intensive treatments did not improve his blood pressure and the renal impairment worsened. Furthermore, he developed mental confusion in the ICU. His extremely poor condition did not allow for upper GI endoscopy. Because this clinical course supported the diagnosis of PG, gastric juice was collected for the culture analysis using a nasogastric tube. His status deteriorated rapidly into circulatory failure, and he expired in the ICU less than 9 hours after admission. We did not receive permission to perform an autopsy on this patient.

Three days later, we isolated GAS from both the blood and gastric juice cultures. Our patient met the Japanese diagnostic criteria of GAS TSS (10). The results from the antibiotic susceptibility testing revealed that the GAS isolate was sensitive to most β -lactam antibiotics, ciprofloxacin, clindamycin (CLDM), and linezolid (LZD). The isolated GAS strain was further analyzed for virulence factors. Both cultures contained the MIT1 GAS strain (*emm1* type) ex-

Figure. Abdominal simple computed tomography at the time of admission showed a diffuse thick-walled stomach on horizontal (A) and coronal (B) sections.

pressing the streptococcal pyrogenic exotoxin (*spe*) genotype: *speA* (+), *speB* (+), and *speF* (+) (11, 12).

Discussion

PG is most commonly caused by *Streptococcus* spp., followed by *Enterobacter* spp., *Escherichia coli* (*E. coli*), and *Proteus* spp., in that order (1). The overall mortality rate of PG has been reported to be approximately 40%, with disease caused by *Streptococcus* spp. having a mortality rate of 53% with an extremely poor prognosis (1, 2). Although the exact etiology of PG is unknown, one type develops in a limited portion of the stomach (localized type) and another develops throughout the entire stomach (diffuse type). The localized type is associated with a lower mortality rate than the diffuse type (10% vs. 54%, respectively) (1). Thus, we considered that our patient's prognosis was extremely poor because GAS was the pathogenic bacterium and CT images showed the diffuse type. In addition, Kim et al. reported that among five patients with PG caused by GAS, four patients had the diffuse type and three patients died within a short period of time (1). Similar to the present case, we suspect the patients had PG associated with GAS TSS in some of these reported cases.

CT is non-invasive and useful for initial diagnosis. In cases with PG, CT images typically show localized or diffuse marked thickening of the gastric wall. However, confirmation requires a differential diagnosis between PG, adenocarcinoma, lymphoma, GI stromal tumor, and anisakiasis (1, 2, 13-15). Therefore, it is difficult to reach a definitive diagnosis with CT findings alone. Diagnosis using GI endoscopy, particularly EUS, is considered to be the best approach. EUS can accurately identify gastric wall thickening, degree of inflammation, and other conditions (8, 9). In addition, complex evaluations combining gastric juice cultures with a pathological examination of the biopsy samples obtained with the endoscope enable a definitive diagnosis to be made. In addition, collection of the gastric juice culture from patients with PG is important for the selection of antimicrobial agents (1, 3). Although we were unable to conduct an endoscopic examination in the present case, the combination of CT findings with the gastric juice culture was useful in making the definitive diagnosis of diffuse PG.

Alcohol consumption, chronic gastritis, and diabetes are major risk factors for morbidity of patients with PG (1-3). Many cases of PG have also been reported to develop following upper GI endoscopic treatment (4-7). In 2010, Paik et al. presented a rare case of PG complicated with GAS TSS after endoscopic treatment (6). A patient was also recently described to have PG complicated with acute leukemia during chemotherapy (16). A detailed medical interview revealed that our patient typically consumed light to moderate amounts of alcohol. Furthermore, he had a history of mild diabetic anamnesis with a gastric ulcer and was taking oral famotidine to reduce his gastric acidity. These findings support our hypothesis that our immunocompromised elderly patient was at an increased risk of developing PG by bacterial invasion of the damaged gastric mucosa under alkaline conditions.

PG is classified into three disease types: phlegmonous, emphysematous, and necrotizing. The phlegmonous type is considered to be the representative PG type (1). CT findings of the present case revealed no gas production, therefore ruling out the emphysematous type. Due to his poor condition and rapid clinical course, we could not perform contrast CT or an endoscopic examination. Thus, we were unable to rule out the necrotizing type, which has an extremely high mortality rate (1). In the past few decades, necrotizing PG was very rare and caused mainly by *E. coli* or other non-GAS *Streptococcus* spp. (17-20). Therefore, most cases of PG associated with GAS are probably of the phlegmonous type. Because our patient had no findings suggestive of gastric perforation or generalized peritonitis, we believe our patient had phlegmonous PG.

In recent years, following the remarkable advances in antimicrobial treatment, there have been many reports of PG patients being cured with medical therapy; however, the medical therapy alone showed a significantly higher mortality rate than the surgical treatment, according to the review by Kim et al. (1-6, 16, 21, 22). In addition, treatment with

gastrectomy may also be successful in some cases of emphysematous and necrotizing gastritis, suggesting the need for tailored therapy based on the disease type of PG (1, 17, 19). Conversely, as with our case, many patients with PG are in poor conditions, and gastrectomy is not an option for them; in such cases, early medical intervention using a broad-spectrum antimicrobial therapy is recommended (1-3). Iwakiri et al. reported that a patient with PG was successfully treated with early antimicrobial therapy alone (22). We speculate that our patient may not have rapidly progressed had antimicrobial therapy been quickly administered when PG was suspected. Moreover, surgical treatment and/or additional antibiotics, such as CLDM and LZD, should be also considered (1-3, 11). The ability of CLDM and LZD to suppress exotoxin production in GAS has been shown *in vitro* (23).

In conclusion, our immunocompromised elderly patient died of a rapidly invasive infection, which was later diagnosed as PG associated with GAS TSS. Although he was first suspected to have PG based on CT findings his nonspecific clinical appearance and rapidly fatal course made the definitive diagnosis difficult. Most PG cases are associated with acute life-threatening infections such as GAS TSS. Therefore, any patients suspected to have PG require both an early diagnosis using various modalities and aggressive management, such as a combination of antimicrobial therapy and surgical treatment.

The authors state that they have no Conflict of Interest (COI).

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