Two Cases of Group A Streptococcal Toxic Shock-like Syndrome with Diffuse Peritonitis

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Abstract
Streptococcal toxic shock-like syndrome (TSLS) is characterized by rapidly progressive shock and organ damage caused by infection with Group A Streptococcus pyogenes (GAS). Reportedly, most of the infected sites are soft tissues, such as the fascia, although a few previous reports of primary peritonitis have been made. Here, we report two cases of TSLS with primary peritonitis.

Case 1 was a 49-year-old woman who was transported to hospital because of sudden abdominal pain. An emergency operation was performed because the patient was in shock upon arrival and showed signs of peritoneal irritation. Intraoperative findings showed no perforation or necrosis, and lavage and drainage were performed. Postoperative disseminated intravascular coagulation and renal dysfunction required intensive treatment. Streptococcus pyogenes was detected in the ascites culture 3 days after surgery, and the patient was diagnosed as having TSLS. The patient's general condition gradually improved, and she was discharged 21 days after the operation.

Case 2 was a 53-year-old woman who was admitted to hospital with a chief complaint of abdominal pain and was diagnosed as having infectious gastroenteritis. Streptococcus pyogenes was detected in a blood culture obtained on the 3rd day of hospitalization. The patient continued to take antibiotics. However, on the 5th day, her consciousness deteriorated, and she developed shock; therefore, an emergency operation was performed based on a diagnosis of primary peritonitis and TSLS. No signs of perforation or necrosis were found intraoperatively, and lavage and drainage were performed to complete the surgery. The patient exhibited an immediate postoperative improvement in hemodynamics and was discharged 7 days after the surgery. In both cases, the patient's condition was improved by lavage and drainage, and early surgical intervention was important.

Key words: Group A streptococcal/toxic shock-like syndrome, peritonitis, septic shock

Introduction
Streptococcal toxic shock-like syndrome (TSLS) is an infection caused by Group A Streptococcus pyogenes (GAS) that progresses from local infections, such as pharyngitis, to systemic infections, such as pneumonia and fasciitis, resulting in rapid progression to septic shock and organ damage. The mortality rate is approximately 30%, and the prognosis is very poor. TSLS was first reported by Cone et al. in 1987 and later by Shimizu et al. in Japan in 1992. Several cases of soft tissue infections, such as necrotizing fasciitis, have been reported, but only about 1% of people diagnosed as having TSLS exhibit primary peritonitis. The diagnostic criteria presented by the Centers for Disease Control and Prevention in 1993 define TSLS by (1) the detection of Streptococcus, (2) a reduced blood pressure, and (3) the failure of at least two organs. Primary peritonitis is diagnosed using blood and ascites cultures because there are no characteristic blood examination or imaging findings. A definitive diagnosis is almost always made using intraoperative ascites cultures. Here, we report two patients with TSLS.
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Case report

Case 1: A 49-year-old woman had abdominal pain and watery diarrhea for a month. During the same period, the patient was scheduled to undergo a gynecologic examination because of irregular genital bleeding. The abdominal pain worsened sharply, and the patient was brought to our hospital in an ambulance the following day. She was admitted to our hospital following a diagnosis of diffuse peritonitis and a suspected perforation of the digestive tract. Her medical history was unremarkable. Although the patient was fully conscious, she was in shock: her body temperature was 38.5°C, her blood pressure was 78/50 mmHg, her pulse was 122 beats/min, and her respiratory rate was 28 breaths/min. Abdominal findings showed full swelling, tenderness, and muscular defense. Blood tests revealed the following findings: a white blood cell (WBC) count of 26,640/μL, an increased inflammatory response with a C-reactive protein (CRP) level of 31.21 mg/dL, and renal dysfunction with a creatinine (Cr) level of 2.82 mg/dL. A computed tomography (CT) scan showed no evidence of suspected free air or intestinal necrosis, but an increase in the mesenteric fat tissue concentration and ascites retention was confirmed (Fig.1). An emergency surgery was performed with a diagnosis of diffuse peritonitis of unknown cause. The intraoperative findings showed purulent ascites in the abdominal cavity and redness and thickening of the mesentery and greater omentum, but gastrointestinal perforation or intestinal necrosis was not confirmed (Fig.2). The inside of the abdominal cavity was washed with 10,000 mL of hot saline, and a multi-channel drainage tube was placed under the diaphragm and in the pouch of Douglas. Postoperatively, the patient developed disseminated intravascular coagulation (DIC), and thrombomodulin and γ globulin were administered. The patient was also treated with the antibacterial drug doripenem (2 g/day). To promote circulation, noradrenaline (NAD) was used. Streptococcus pyogenes was detected in an ascites culture on the third postoperative day, leading to a diagnosis of TSLS. The patient’s pharmacological treatment was switched to levofloxacin and vancomycin, based on drug sensitivity results. NAD was discontinued on the seventh postoperative day. The patient was discharged from the intensive care unit (ICU) on postoperative day 14 and was discharged from hospital on postoperative day 21 (Fig.3).

Case 2: A 53-year-old woman was admitted to our hospital after experiencing fever, malaise, and
abdominal pain for several days. She was diagnosed as having infectious enteritis and was treated with meropenem. *Streptococcus pyogenes* was detected in a blood culture on the third day of hospitalization, and the administered antibiotics were changed to sulbactam/ampicillin and clindamycin. On the fifth day of hospitalization, she developed a consciousness disorder and type 2 respiratory failure with abdominal distention. Furthermore, the patient was transferred to our department because she was in shock. Her consciousness was E4V4M6, her body temperature was 37.4 °C, her blood pressure was 80/50 mmHg, her pulse rate was 135 beats/min, and her respiratory rate was 36 breaths/min. Her abdomen was swollen and tender throughout, but no signs of peritoneal irritation were present. A blood test revealed a WBC count of 7,180/μL, an increased inflammatory response (CRP, 28.14 mg/dL), and renal dysfunction (Cr, 2.19 mg/dL). A blood gas analysis showed respiratory acidosis (pH 7.281; PaO₂, 78.8 mmHg; and PaCO₂, 75.8 mmHg). CT images showed no evidence of free air or intestinal necrosis. Elevated mesenteric fat tissue levels and ascites retention were observed. The intestinal tract was fully dilated, with evidence of paralytic ileus (Fig. 4). Although there were a few signs of peritoneal irritation, the patient was diagnosed as having TSLS with diffuse peritonitis based on the findings of ascites retention, intestinal dilatation, and paralytic intestinal obstruction. An emergency surgery was performed. The intraoperative findings showed purulent ascites in the abdominal cavity and redness
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Fig. 5 Intraoperative findings. Purulent ascites had accumulated in the abdominal cavity, and the mesentery was red and thickened.

The left vertical line: mean arterial pressure, The right vertical line: pulse rate, The horizontal line: hospitalization day
NAD: noradrenaline, MEPM: Meropenem, SBT/ABPC: Sulbacillin, CLDM: Clindamycin

Fig. 6 Progress during hospitalization.

and thickening of the mesentery. We searched the abdominal cavity and found no evidence of infection, such as necrosis or perforation (Fig.5). After washing with 10,000 mL of hot saline, a multi-channel drain was placed in the pouch of Douglas. The patient’s hemodynamics stabilized after the operation, and the administration of catecholamine was discontinued on postoperative day 1. The patient showed good progress and was discharged on postoperative day 7 (Fig.6).

Discussion
TSLS is a condition that suddenly develops and rapidly progresses to septic shock and multiple organ failure, with a high mortality rate of 30%. According to an announcement made by the Ministry of Health, Labour and Welfare, the number of cases in Japan was around 100 per year before 2010 but has subsequently increased to around 200 per year. Soft tissues, such as fascia, are the most common sites of infection, and only around 1 % of people diagnosed
with TSLS are found to have primary peritonitis\(^\text{46}\). A search for cases of TSLS with primary peritonitis in Japan using the keywords “peritonitis” and “TSLS” in the Japan Medical Abstracts retrieved a total of 21 cases reported since 2000, including the 2 presently reported cases (Table1). There were 3 male patients and 18 female patients, with an average age of 51 years.

Females under the age of 60 years accounted for 76.2% of the total number of TSLS cases, which tended to be more common among middle-aged females.

Various routes of infection are possible, such as percutaneous, transmucosal, and unknown. In the case of females, many females may develop infection via the vaginal mucosa.

The number of deaths among the retrieved results was 3 (14%), which was lower than the 30% overall mortality rate that has been reported for TSLS.

Adverse events associated with TSLS included organ failure caused by acute kidney injury (AKI) (59%), DIC (59%), and acute respiratory distress syndrome (ARDS). AKI and DIC are considered to occur relatively frequently in TSLS, similar to that observed in the present study.

Regarding treatment methods, drainage was performed in 19 of the 21 cases; regarding the method of approach, drainage by open surgery was performed in 16 cases, while percutaneous drainage was performed in 2 cases and transvaginal drainage was performed in 1 case. Most patients who underwent open surgery opted for this procedure because secondary peritonitis could not be ruled out, even though there were no findings such as perforation or necrosis in the preoperative diagnosis. Furthermore, for cases in which percutaneous drainage was selected, CT images did not show evidence of secondary peritonitis, such as free gas. Percutaneous drainage was selected in these cases because it was thought that the surgical risk would be high due to DIC and septic shock\(^7\).\(^8\). Two patients were treated with conservative treatment only, and one of them died. The patient who died was treated based on a diagnosis of acute pancreatitis and was diagnosed as having TSLS upon autopsy. The authors stated the need for early culture and drainage\(^9\). On the other hand, Iwashita et al. reported a case that was successfully treated using conservative treatment alone\(^10\). The generally accepted indications for conservative treatment are mild organ damage and pe-

| Year | Author | Age | Sex | Drainage | Outcome | Culture | Organ failure |
|------|--------|-----|-----|----------|---------|---------|-------------|
| 2003 | Imamura | 54  | female | operation | survive | ascites | – |
| 2003 | Tsuruta  | 38  | female | operation | survive | ascites, blood, vagina | AKI, DIC |
| 2004 | Kanetake | 40  | female | operation | survive | ascites | AKI, DIC |
| 2004 | Horie   | 67  | female | operation | death | blood | AKI, DIC |
| 2010 | Matumura | 59  | female | percutaneous drainage | survive | ascites, stool, blood | DIC |
| 2010 | Hoshino | 50  | female | operation | survive | ascites | AKI, ARDS |
| 2013 | Tanaka  | 70  | male | No | death | blood, sputum, Pleural effusion | AKI, DIC |
| 2012 | Hisada  | 35  | female | percutaneous drainage | survive | ascites, vagina | DIC |
| 2014 | Ura     | 39  | female | operation | survive | ascites, blood, vagina | AKI, DIC, ARDS |
| 2015 | Ikegami | 30  | female | operation | survive | ascites | AKI, DIC |
| 2015 | Kawa    | 26  | female | operation | death | ascites | AKI, DIC |
| 2016 | Matuyoshi | 58  | female | operation | survive | ascites | AKI, DIC |
| 2016 | Yokoyama | 40  | female | operation | survive | ascites | ARDS |
| 2016 | Adachi  | 71  | male | operation | survive | ascites | – |
| 2016 | Nagashima | 56  | female | operation | survive | ascites | – |
| 2017 | Hasui   | 50  | female | operation | survive | ascites, blood, vagina | AKI, DIC |
| 2017 | Ootuka  | 67  | female | transvaginal drainage | survive | ascites | AKI |
| 2018 | Nakayama | 80  | male | operation | survive | ascites | AKI, DIC |
| 2019 | Iwashita | 39  | female | No | survive | blood culture | AKI, DIC |
| 2020 | Suzuki  | 49  | female | operation | survive | ascites | AKI, DIC |
| 2020 | Suzuki  | 53  | female | operation | survive | blood | AKI, DIC |
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Peripheral circulatory failure, but no clear criteria have been established. However, after admission to the ICU, noradrenaline and endotoxin adsorption therapy (PMX-DHP) immediately improved circulation, and the administration of noradrenaline was ceased within 24 hours. Conservative treatment may be an option in cases where circulation can be rapidly maintained. However, because there is typically no evidence of primary peritonitis, the exclusion of secondary peritonitis should always be kept in mind. In cases with primary peritonitis, findings such as free gas and necrosis are not seen using CT and other diagnostic imaging modalities. CT findings can include ascites and an increase in fatty tissue density, but these findings are not sufficiently definitive to indicate emergency surgery. This situation occurred in the presently reported cases as well, but the peritoneal irritation symptoms were subtle, making it difficult to decide whether emergency surgery was required. Even if this disease is suspected, several days are needed to obtain definitive culture results; therefore, open surgery for the diagnosis and treatment of diffuse peritonitis is considered appropriate. In the second of our reported cases, GAS was identified by blood culture and TSLS was diagnosed preoperatively, but a paralytic intestinal obstruction was present so abdominal irrigation was deemed necessary and a laparotomy was performed. If the circulation had been unstable, it may have been necessary to avoid surgery and to choose percutaneous drainage instead. Surgery for an immediate and reliable reduction of bacteria is appropriate only if the patient can withstand general anesthesia. In recent years, the number of cases in which laparoscopic surgery has been performed for the treatment of acute abdomen has increased, but only a few reports have described the use of laparoscopic surgery in patients with TSLS\textsuperscript{11,12}. Furthermore, both of these studies were from Europe and the United States. In Japan, the use of laparoscopic surgery in cases with peritonitis caused by Group A hemolytic streptococcus has only been reported for patients without septic shock, and TSLS-related information is not available for these cases. The main symptom of TSLS is septic shock. The influence of the pneumoperitoneum on circulation is thus a concern, and the application of laparoscopic surgery should be evaluated carefully while not overlooking the postoperative benefits of a less invasive procedure. The accumulation of further reports in Japan is expected to provide greater clarity on this issue. Irrigation and drainage are clearly the most effective treatment methods for TSLS with peritonitis to reduce the number of bacteria. Percutaneous drainage may be an option for that approach, but it may still be necessary to observe the abdominal cavity by surgery to achieve adequate irrigation and drainage and to rule out secondary peritonitis. Our findings suggest that although a diagnosis can be difficult, proper irrigation and drainage can be used to treat TSLS effectively.

Conflict of interest: None.

References

1) Stevens DL, Tanner MH, Winship J, et al: Severe Group A Streptococcal Infections Associated with a Toxic Shock-like Syndrome and Scarlet Fever Toxin A. N Engl J Med 321:1-7, 1989
2) Cone LA, Woodard DR, Schlievert PM, et al: Clinical and Bacteriologic Observations of a Toxic Shock-like Syndrome Due to Streptococcus pyogenes. N Engl J Med 317:146-149, 1987
3) Shimizu Y, Ohyama A, Kasama K, et al: Case Report of Toxic Shock-like Syndrome Due to Group A Streptococcal Infection. J Japanese Assoc Infect Dis 67:236-239, 1993
4) Monneuse O, Tissot E, Gruner L, et al: Diagnosis and Treatment of Spontaneous Group A Streptococcal Peritonitis. Br J Surg 97:104-108, 2009
5) Defining the Group A Streptococcal Toxic Shock Syndrome. Rationale and Consensus Definition. The Working Group on Severe Streptococcal Infections. JAMA 269:390-391, 1993
6) Hasui N, Shimizu A, Aso N, et al: Two Cases of Primary Peritonitis Due to Group A Streptococcus Pyogenes. Nihon Shokyu Geka Gakkai Zasshi (Journal Japan Surg Assoc) 78:1904-1910, 2017
7) Matsumura Y, Oda S, Sadahiro T, et al: A Case of Toxic Shock-like Syndrome Due to Spontaneous Bacterial Peritonitis Successfully Treated with Continuous Hemodiafiltration Involving Two Consoles Using a Polymethylmethacrylate Membrane Hemofilter (Double PMMA-CHDF). Nihon Shuchu Chiryo Igakukai zasshi 17:505-512, 2010
8) Hisada M, Kawakita H, Ishizaki T, et al: A Case Report of Sever Group A Streptococcal Infections Associated with a Toxic Shock-like Syndrome which Caused by Pelvic Peritonitis. Nihon Gekakei Rengo Gakkaishi (Journal Japanese Coll Surg) 37:869-875, 2012
9) Tanaka H, Shokyu Y, Ishii T, et al: A Case of Primary Peritonitis and Empyema Associated with Strepto-
coccal toxic shock-like syndrome. Nihon Kyukyu Igakukai Zasshi 24:357-362, 2013
10) Iwashita K, Kobayashi A, Takada A: Primary Streptococcal Peritonitis Treated Conservatively—A Case Report—. Nihon Rinsho Geka Gakkai Zasshi (Journal Japan Surg Assoc) 80:798-803, 2019

11) Legras A, LoDico R, Ferre R, et al: Primary peritonitis due to Streptococcus A: Laparoscopic treatment. J Visc Surg 148:e315-317, 2011
12) Abellán Morcillo I, González A, Selva Cabañero P, et al: Primary peritonitis by Streptococcus pyogenes. A condition as rare as it is aggressive. Rev Esp Enferm Dig 108:231-232, 2016