Acute Pancreatitis Associated with Streptococcal Toxic Shock Syndrome

Group A β-hemolytic streptococci may cause a variety of illnesses ranging from very common, usually clinically mild conditions (such as pharyngitis and impetigo) to less common severe infections (including bacteremia and toxic shock syndrome). We recently cared for a patient with acute pancreatitis and clinically and microbiologically proven streptococcal toxic shock syndrome. To our knowledge, this is the first case report indicating that acute pancreatitis may be associated with streptococcal toxic shock syndrome.

An 18-year-old girl presented with a 6-day history of intermittent fever and abdominal pain. At the time of admission, she had severe epigastric tenderness. A hemogram revealed a leukocyte count of 10.9 × 10⁹/L (68% neutrophils, 16% lymphocytes, 13% monocytes, and 3% band forms), a hemoglobin concentration of 13.2 g/dL, and a platelet count of 165 × 10⁹/L. The biochemical findings are not specific for M. tuberculosis infection and may be associated with other mycobacterial infections [5, 6]. In vitro resistance of M. xenopi to antituberculous drugs (notably ethambutol and rifampin) is not uncommon but is not predictive of an in vivo response [1]. The duration and the type of antibiotic therapy for atypical mycobacterial infections are not yet clearly defined; these infections may require treatment with new antitymococcal agents, such as clarithromycin [1, 9].

Despite our patient’s extensive spinal infection with epidural and subcutaneous abscesses, we found that surgical management is not systematically required, as reported in the two previously published cases [5, 6]. Long-term follow-up is required because relapse may occur after a long delay (e.g., 3 years in the case reported by Prosser [5]).

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References
Figure 1. Abdominal CT of a patient with acute pancreatitis associated with streptococcal toxic shock syndrome; this scan demonstrates a swollen pancreas (arrow).

examination of the abdomen showed increased echogenicity of the pancreas. A CT demonstrated a swollen pancreas without focal abnormalities (figure 1). The patient initially received supportive treatment only.

Two days later the abdominal pain worsened, and physical examination revealed peritoneal signs. She became disoriented and tachypneic. Her blood pressure dropped to 69/47 mm Hg, and her pulse rate was 144. A follow-up hemogram demonstrated a leukocyte count of 18.5 × 10^9/L (61% band forms, 34% neutrophils, and 5% lymphocytes), a hemoglobin concentration of 10.5 g/dL, and a platelet count of 220 × 10^9/L. The biochemical data were abnormal, with the following values: serum total bilirubin, 7.0 mg/dL; direct bilirubin, 4.1 mg/dL; aspartate aminotransferase, 68 U/L; amylase, 128 U/L; lipase, 937 U/L; and albumin, 2.5 g/dL. The calcium and glucose concentrations were normal. There was no coagulopathy. A repeated ultrasound examination showed a moderate amount of serous fluid in the abdominal cavity.

Acute pancreatitis complicated with peritonitis was suspected, and the patient underwent laparotomy as soon as her hemodynamic status was stabilized. About 300 mL of serous fluid was drained. There was no internal bleeding. Culture of blood taken at the time of admission subsequently yielded group A β-hemolytic streptococci. These isolates were further characterized by PCR analysis and were shown to harbor the speB gene. Culture of the serous fluid was sterile. The patient was given therapy with ampicillin and ceftriaxone. Her condition stabilized within 48 hours when she no longer required blood pressure and respiratory support. No skin rash or desquamation was observed throughout her clinical course. She ultimately made a full recovery after receiving a 10-day course of antimicrobial therapy.

Acute pancreatitis is usually a sterile inflammatory process caused by chemical autodigestion of the pancreas. Mostly, it is associated with alcoholism, trauma, and biliary diseases [1]. Viral agents, including mumps virus and coxsackievirus, are sometimes involved. Acute pancreatitis has been rarely associated with bacterial infections [1]. Mycobacterium species have previously been reported to cause this disease [1]. The precise mechanism by which bacterial infections may cause pancreatitis is still unknown. Previous studies [2, 3] have tried to establish a causal relation between pancreatitis and bacterial sepsis; these studies indicated that endotoxemia resulting from the release of components of gram-negative bacteria from the gut is common in patients with acute pancreatitis. Data from a opossum model of pancreatitis also pointed out that bacterial translocation from the gut lumen to mesenteric lymph nodes with subsequent hematogenous dissemination could be a possible mechanism of the development of acute pancreatitis [4].

Whereas the exact subsequent pathogenesis of bacterial translocation is unknown, there is only a potential pathway—namely, an inflammatory response of the pancreas that is induced by the cytokines (including at least interleukin 6 and tumor necrosis factor [TNF] α) [5, 6]. Direct evidence supporting this implication has been obtained from a study of transgenic mice [7]; this study found that the expression of TNF-α in the pancreatic islets may induce an inflammatory response that is restricted to the islets of Langerhans and progresses to insulitis but not to diabetes. On the basis of this information, we presume that in our case the superantigens (i.e., the streptococcal pyrogenic exotoxins) mediated a non-antigen-specific binding between the T cell receptor and the major histocompatibility complex class II molecules on antigen-presenting cells; consequently, the mononuclear cells were activated to produce large amounts of the cytokines, which were in fact directly responsible for the development of the inflammatory phenomena of the pancreas. In patients such as ours, the cardiovascular system is another target organ of the cytokines, as shown by the dilatation and altered permeability of the blood vessels that lead to the development of shock, hypoalbuminemia, and ascites.

Although there is no definite proof that our patient’s pancreatitis was attributed to the streptococcal infection and although more patients with these two conditions would provide a more convincing argument that there is an association, the absence of other possible causes, the concomitant bacterial infection, and the clinical improvement following antibiotic therapy indeed suggest a possible causal relation. This report indicates that streptococcal toxic shock syndrome should be considered as another possible cause of acute pancreatitis.

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References
Symptomatic Vulvovaginitis Due to Fluconazole-Resistant Candida albicans in a Female Who Was Not Infected with Human Immunodeficiency Virus

Azoles that are active against mycoses are an important advance in the management of serious fungal infections. Recent reports of clinical resistance and failure associated with triazole therapy have been of considerable concern [1-8]. Candida albicans isolates with high-level resistance to azoles (including fluconazole) have been identified, particularly in patients with advanced HIV infection; detection of these isolates usually occurs after administration of long-term systemic azole regimens, which often include low doses of maintenance fluconazole therapy [1-3, 6, 7]. To date, fluconazole-resistant C. albicans is rare in persons who are not infected with HIV, and reports of nosocomial infection caused by resistant C. albicans are infrequent [4, 5]. Resistance to fluconazole has not been reported in immunocompetent individuals who were not hospitalized. We describe a healthy female who had azole-resistant C. albicans vaginitis that responded to therapy with boric acid.

A 38-year-old female with a 3-month history of continuous yeast vaginal infection was referred to the Vaginitis Clinic at Wayne State University (Detroit) on 3 March 1995. Before the referral, the patient had experienced only occasional episodes of candidal vaginitis. Symptoms at presentation included pruritus, vulvovaginal burning, and dyspareunia. During the 3 months before presentation, the patient had received over-the-counter topical antimycotic agents as well as prescribed terconazole and fluconazole (150 mg orally daily) for 1 month.

The patient returned to the clinic 10 days later, at which time she was still uncomfortable and had persistent clinical signs of vulvovaginitis; microscopic examination of vaginal secretions in 10% KOH revealed yeast, and culture of a vaginal specimen again yielded C. albicans. While susceptibility tests were being performed, she was treated with clotrimazole vaginal suppositories (100 mg daily for 7 days).

The patient returned to the clinic 10 days later, at which time she was still uncomfortable and had persistent clinical signs of vulvovaginitis; microscopic examination of vaginal secretions in 10% KOH revealed yeast, and culture of a vaginal specimen again yielded C. albicans. There was no question of lack of compliance with her medications. The patient received therapy with boric acid (600-mg vaginal capsule twice daily for 2 weeks). She returned to the clinic after 17 days; at that time she was asymptomatic and a pelvic examination did not reveal any abnormalities. The results of all laboratory studies (including cultures) were negative, and follow-up examination 6 weeks later revealed that she was clinically and mycologically cured.

In vitro susceptibility tests performed according to NCCLS (National Committee for Clinical Laboratory Standards) methodology [9] revealed that the vaginal C. albicans isolates were susceptible to amphotericin B (MIC, 0.01 µg/mL), miconazole (MIC, 0.05 µg/mL), and fluconazole (MIC, 0.63 µg/mL) and that they were resistant to fluconazole (MIC, > 40 µg/mL), itraconazole (MIC, 6.25 µg/mL), and ketoconazole (MIC, 3.12 µg/mL). The C. albicans isolates had intermediate susceptibility to clotrimazole (MIC, 0.39 µg/mL). All three isolates were compared with use of CHEF (contour-clamped homogeneous electric field) typing (data not shown) and found to be an identical C. albicans clone.

To our knowledge, azole-resistant C. albicans has not been previously reported as a cause of vulvovaginitis. We recently reported the results of susceptibility testing of over 500 vaginal yeast isolates, including 300 isolates of C. albicans, obtained from patients in our clinic; no evidence of azole resistance was observed [10]. Our patient’s case demonstrated high-level resistance to fluconazole as well as cross-resistance to ketocanazole and itraconazole, drugs that she had not received. She had received a prolonged course of daily fluconazole for 1 month.

We believe that our case is an example of fluconazole resistance that was associated with the development of cross-resistance to other azoles in a vaginal strain of C. albicans in an immunocompetent patient who was not exposed sexually or otherwise to a reservoir that might have selected for resistance in C. albicans. Unfortunately, the specimen of C. albicans isolated before the course of fluconazole was administered was not available to determine preexposure susceptibility; thus, it is unclear at which stage resistance to fluconazole developed. Since superinfection with a resistant isolate is unlikely, it is possible that our patient was initially infected with a fluconazole-resistant strain or that resistance developed during topical azole therapy or under the selective pressure of vulvovaginitis; microscopic examination of vaginal secretions in 10% KOH revealed yeast, and culture of a vaginal specimen again yielded C. albicans.