

# NECROTIZING FASCIITIS OF THE RETROPERITONEUM: AN UNUSUAL PRESENTATION OF GROUP A *STREPTOCOCCUS* INFECTION

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A 14-year-old girl presented with symptoms resembling acute appendicitis. Five days after appendectomy and continued fever and severe abdominal pain, blood cultures were found positive for *Streptococcus pyogenes*. Two days later a diagnosis of group A streptococcal peritonitis with necrotizing retroperitoneal fasciitis was confirmed by retroperitoneal cultures obtained at laparotomy. Although multiple organ systems showed impaired functioning, including hepatic, renal and respiratory changes, she did not meet the criteria for streptococcal toxic shock syndrome. She was treated with a combination of high-dose parenteral penicillin and clindamycin, followed by prolonged treatment with clindamycin orally. Recovery was complicated by persistent hydronephrosis, which was slow to resolve.

Une jeune fille de 14 ans s'est présentée avec des symptômes qui ressemblaient à ceux de l'appendicite aiguë. Cinq jours après l'appendicectomie et comme la fièvre et une grave douleur abdominale persistaient, on a procédé à des hémocultures qui ont révélé la présence de *Streptococcus pyogenes*. Deux jours plus tard, un diagnostic de péritonite à streptocoque du groupe A conjugué à une fasciite rétropéritonéale nécrosante a été confirmé à la suite de cultures rétropéritonéales prélevées par laparotomie. Même si de multiples systèmes organiques présentaient une déficience du fonctionnement, y compris des changements au foie, aux reins et à l'appareil respiratoire, la patiente ne satisfaisait pas aux critères du syndrome de choc toxique à streptocoque. Elle a été traitée au moyen d'une combinaison de pénicilline et de clindamycine à fortes doses administrées par voie parentérale, suivie d'un traitement prolongé à la clindamycine administrée par voie orale. Une hydronéphrose persistante, qui a pris du temps à se résorber, a compliqué le rétablissement.

**N**ecrotizing fasciitis, due to invasive group A *Streptococcus* (GAS) infection, referred to by the lay press as "flesh eating disease," has recently received considerable attention. However, there have been no literature reports of cases of necrotizing fasciitis involving only the peritoneum. In this report, we describe the investigation and management of a 14-year-old girl with necrotizing fasciitis of the peritoneum.

## CASE REPORT

A previously healthy 14-year-old army cadet was referred to the emergency department with a 3-day history of malaise and fever, and 12 hours of worsening right lower quadrant (RLQ) pain. She denied having ever been sexually active and had completed a normal menstrual period 6 days earlier. At the time of presentation she was completing a 1-month

summer field course at a cadet camp in Ontario. There had been a recent outbreak of exudative pharyngitis and fever at this cadet camp, coincident with her time there.

On examination, the patient appeared ill; she had a temperature of 38.6 °C and marked RLQ tenderness with signs of RLQ peritoneal irritation. She refused rectal and pelvic examinations. Bowel sounds were present. The remainder of the physical

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examination was unremarkable, except for an excoriated rash involving both legs, which had been attributed to poison ivy. The rash had been present for several days. Although some of the excoriations were erythematous, none appeared frankly infected. She denied any symptoms of pharyngitis. Initial blood work was within normal limits, including a leukocyte count of  $8.8 \times 10^9/L$  (only machine differential was provided and it was also within normal limits). Abdominal ultrasonography was suggestive of appendicitis.

At appendectomy through a small McBurney incision, the appendix appeared normal, and a small amount of serous fluid was noted in the abdomen. The local portions of cecum, colon and small bowel were examined in detail and found to be normal. There was no evidence of severe mesenteric inflammation or fibrinous plaque formation, as was identified later. The diagnosis was revised to mesenteric adenitis.

Postoperatively, the patient re-

mained febrile, with fevers spiking temperatures above  $40^\circ C$ . She continued to complain of severe abdominal pain that had become diffuse and was associated with generalized rebound tenderness. She had a persistent low grade leukocytosis ( $13$  to  $15 \times 10^9/L$ ), with an increasing left shift over the ensuing postoperative days. There was also evidence of renal impairment, with elevation of the serum creatinine to over  $200$   $\mu mol/L$ . Aspartate aminotransferase and alanine aminotransferase levels were also elevated to more than twice normal values. Although the patient's chest radiograph appeared essentially normal, her respiratory rate increased to  $30$  to  $36$  respirations/min. and remained elevated until the 10th hospital day. Oxygen saturation remained greater than  $92\%$  on room air, but supplemental oxygen therapy was supplied through a nasal cannula. The patient's coagulation parameters remained normal throughout her stay, as did her platelet count and blood pressure.

On the fourth postoperative day (POD), abdominopelvic computed tomography (CT) revealed a moderate amount of free fluid in the paracolic gutters and in the pelvis, as well as diffuse enhancing inflammatory changes in the mesenteric fat (Fig. 1). Considerable inflammatory and phlegmonous changes were noted in the pelvis, with thickening of the rectal and bladder walls, but without any evidence of localized abscess formation. Bilateral hydronephrosis was also noted. Despite the patient's denial of any sexual contact, a diagnosis of acute pelvic inflammatory disease (PID) was entertained and the patient was started on ampicillin, gentamicin and metronidazole intravenously.

The following day, the laboratory reported 2 blood cultures as positive for *Streptococcus pyogenes*. The patient's antimicrobial regimen was modified to clindamycin, gentamicin and high-dose penicillin.

The patient failed to show any significant improvement despite continued intensive antimicrobial therapy. Her leukocyte count increased to  $25.7 \times 10^9/L$  with a marked leftward shift ( $32\%$  band forms, with  $2\%$  to  $3\%$  metamyelocytes). She was returned to the operating room on POD 7 for definitive diagnosis and any required surgical intervention. The working diagnosis remained tubo-ovarian disease. Laparoscopic access was initially difficult, but good visualization was eventually obtained.

At laparoscopy, there was edema of the pelvic peritoneum with patchy areas of whitish discoloration, which were consistent with fibrinous exudate, around areas of more normal-looking peritoneum. There was some generalized inflammation surrounding the ovaries, fallopian tubes and uterus, but no evidence of acute PID was seen. Because of the nondiagnostic findings, an open laparotomy was



FIG. 1. Abdominopelvic computed tomography scan shows areas of irregularly increased fatty tissue density in the bowel mesentery (arrows).

carried out.

Upon entering the peritoneal cavity, we noted a moderate amount of serosanguineous fluid without obvious pus. On close inspection, the large and small bowel appeared normal. However, there was a whitish discoloration of almost the entire retroperitoneum with predominant involvement of the base of the mesentery, in sharp contrast to the rest of the mesentery (Fig. 2). The retroperitoneum was opened and revealed vascular thrombosis and hyperemia of the lymph nodes. A portion of the abnormal tissue and 2 retroperitoneal lymph nodes were excised and sent for pathological and microbiologic examination. Histologic examination showed intense polymorphonuclear cell infiltration with diffuse connective-tissue necrosis, compatible with necrotizing fasciitis. Cultures of the same tissue were later found to be positive for GAS, type M12, type T12, serum opacity factor negative and *Streptococcus pyrogenes* toxin B (SpeB) positive.

The peritoneal cavity was thoroughly irrigated with a solution of saline and bacitracin and the abdominal wound closed; the skin and subcutaneous tissue layers were left open. After surgery, the patient showed very slow but progressive improvement from a clinical and a laboratory perspective. She completed 14 days of parenteral penicillin and clindamycin. Her postoperative course was mainly



FIG. 2. Operative view showing whitish discoloration of the base of the mesentery compared with the rest of the mesentery.

complicated by a prolonged ileus and persistent hydronephrosis.

She was discharged with a plan for 4 weeks of clindamycin taken orally. Follow-up 11 weeks after discharge revealed that she had required 8 weeks of clindamycin therapy (as a result of a persistently elevated erythrocyte sedimentation rate), but she continued her gradual recovery. The left hydronephrosis had resolved, with persistence on the right, as seen by repeat ultrasonography. Susceptible family members were given prophylaxis with cephalexin. The cadet corps had already disbanded and adequate follow-up could not be achieved.

## DISCUSSION

Necrotizing fasciitis is a rare illness that causes extensive destruction of the fascia and subcutaneous tissue. One of the etiologic agents is GAS, which is a common cause of pharyngitis and mild cutaneous infections in children and young adults, as well as being a colonizer of the respiratory tracts of approximately 15% of healthy children.

Serious and often lethal GAS infections were common in the early part of this century but waned in frequency and severity until recently. The initial reduction was attributed to improvements in sanitation and antimicrobial therapy, but current theories suggest that natural changes in virulence patterns may be more responsible for the decline of GAS infection severity.<sup>1</sup> However, since 1985, there has been an apparent increase in the number of cases of bacteremia and severe infections due to GAS.<sup>2</sup>

Necrotizing fasciitis was first described in France in 1783; at that time, the disease was seen in military hospitals in times of war when there was cohabitation. There was a marked decrease in the incidence of the dis-

ease during the 1940s, with a worldwide re-emergence in the 1980s. In Canada, surveillance for GAS began in 1991 in Ontario. Based on these data, 2 to 3 people per million suffer serious GAS infections annually. Most of these serious infections occur during the autumn and winter months.<sup>2</sup>

GAS can be characterized by serotyping (M and T types, with over 80 M types identified) and by detection of pyrogenic exotoxins (5 Spe types identified). Reported cases in both bacteremic and severe invasive disease worldwide have been found to be more frequently associated with types M1 and M3 and with elaboration of SpeA and SpeB. The M12 type identified in this case is a more common pharyngeal pathogen and is relatively uncommon in pyoderma and skin lesions<sup>3</sup> but has been associated with invasive disease with some frequency.<sup>4</sup> The reported correlation between the presence of Spe A or B (or both) and serious disease has been as high as 80% to 93% worldwide. Demers and associates<sup>5</sup> found more variation in the M and T typing with time, even within a similar geographic area. They also found the presence of SpeA in patients with severe disease was not as high. In their report of 33 isolates of GAS, M1T1 was isolated in 8, M12T12 in 10 and M3T3 in 1. SpeA was associated with 36% (12 of 33) of isolates, SpeC in 48% and SpeB in all isolates.

The site of entry of the GAS is thought to be through the skin or mucous membranes, although a definite portal cannot be ascertained in at least 45% of cases.<sup>1,6</sup>

Rarely, the organism has been acquired through person-to-person contact with an index case, as in cases of infection of some health care personnel.<sup>7</sup> Most commonly, the GAS infection begins at a site of minor local trauma that may not even result in a

break in the skin.<sup>1</sup> In this case report, the leg excoriations were presumed to be the portal of entry, but this could not be proven. In the series of Demers and associates,<sup>5</sup> a primary focus of infection was identified in 76% of the cases, with soft tissue being the site involved most frequently. The site of the initial infection was usually the extremities.

The accepted treatment of GAS necrotizing fasciitis involves débridement of infected and necrotic tissue as well as high-dose antibiotic therapy. Penicillin can be relatively ineffective in eradicating streptococci from the tissues if the bacteria are present in very high concentrations, a situation known as the "Eagle effect."<sup>8</sup> This is thought to be related to the slow rate of multiplication of the bacteria. Based on animal studies, clindamycin, a protein synthesis inhibitor, is not subject to the Eagle effect seen with penicillin and offers synergistic effects when combined with the wall action of penicillin.<sup>12,9</sup> Experimentally, treatment with IgG has been advocated, but there is no evidence of its efficacy in necrotizing fasciitis.<sup>2</sup>

Although most cases of invasive streptococcal infection have been described in the extremities, anecdotal cases of infection occurring in the retroperitoneal space have been published. The case reported by Llibre and associates<sup>10</sup> described a silent retroperitoneal abscess caused by GAS. Crepps, Welch and Orlando<sup>11</sup> also reported a case of psoas muscle myositis. Woodburne and colleagues,<sup>12</sup> in a review of 19 patients with necrotizing fasciitis, found a subgroup of 5 patients with a retroperitoneal spread of the infection; all infections originated in or around the anus (Fournier's gangrene), were polymicrobial and were associated with some cutaneous manifestations. The outcomes were uniformly fatal. We know of no case of isolated GAS necro-

tizing fasciitis of the retroperitoneum such as we have described here.

Spontaneous peritonitis, often involving GAS, is well known in pediatrics, though there has been a marked decrease in incidence and lethality over the past 30 years.<sup>13</sup> Golden and Shaw<sup>13</sup> described 2 cases of spontaneous peritonitis which showed very similar clinical pictures to our case; in both children, normal appendices were noted at operation, as well as increased accumulation of free abdominal serous fluid.

A few characteristics of this case are worthy of further review. First, the disease occurred at a military camp, where the increased person-to-person spread of GAS is well known. Furthermore, the patient had a skin break in the form of multiple poison ivy plaques, many with excoriation, allowing a possible portal of entry. At this point we theorize that the infection localized itself in the retroperitoneum via either hematogenous or lymphatic spread.

The infection clinically mimicked acute appendicitis, supported by ultrasonographic findings. In retrospect, the ultrasonographic lesion, which looked like an inflamed appendix, was likely a collection of inflamed lymph nodes. As mentioned, early ultrasound findings did not show extensive inflammatory changes or a large accumulation of fluid. It was only at repeat laparotomy that fibrinous exudate was noted in the retroperitoneum and mesenteric base, but not in the bowel proper. With this in mind, it is questionable, though worth considering, whether a paramedian incision or more extensive exploration would have yielded a definitive diagnosis at the time of initial surgery; additional clues could possibly have been obtained.

Our patient's leukocyte count remained near normal for the first 10 days of the infection; in fact, it only showed a marked elevation once appropriate an-

tibiotic therapy had been instituted. In spite of the minimal elevation, a steadily increasing left shift was noted: with over 30% bands as well as metamyelocytes at one point. This relative neutropenia, as well as associated lymphopenia has been noted in other studies of invasive GAS infection.<sup>4</sup> This relative lack of leukocytosis may be related to the rapid progression of the infection, with overwhelming of the host immune defence. Streptococcal infection is also closely associated with a form of toxic shock syndrome (TSS).<sup>1</sup> A set of criteria have been proposed to define TSS.<sup>14</sup> Along with proven streptococcal infection, the criteria include: a drop in systolic blood pressure to less than 90 mm Hg in adults or below the 5th percentile for children, and 2 or more of renal impairment, coagulopathy, liver involvement, adult respiratory distress syndrome, generalized erythematous rash (with or without desquamation) and soft-tissue necrosis. This patient showed evidence of renal and hepatic involvement along with the necrotizing fasciitis. Also, she showed borderline evidence of respiratory involvement, with decreased oxygen saturation and increased respiratory rate. At no time during her hospitalization did this patient exhibit hypotension, therefore by definition she did not have TSS. We theorize that her preservation of cardiac function may be related to her young age and premorbid fitness level. Other than supplemental oxygen and intravenous fluid support (with fluid rates of up to 150 mL/h), no other specific supportive care was required. Specifically, in this case, there was no requirement for intubation, dialysis or inotropic support.

Laparoscopy to evaluate the tubo-ovarian structures was also inconclusive, and the diagnosis was eventually only confirmed by laparotomy and biopsy. The M12T12 SpeB genotype of this infection culture is not unusual for GAS in Ontario. It appears that



the hydronephrosis is likely secondary to generalized retroperitoneal inflammation. The hydronephrosis gradually improved but had not resolved 11 weeks after initiation of therapy, raising the possibility of retroperitoneal fibrosis as a postinfectious cause of morbidity.

The determining factor in the cure of this patient was the institution of the proper antibiotic regimen; improvement was only noted after the addition of clindamycin. Despite aggressive treatment, this young patient did not show improvement for an extended period of time. Not surprisingly, she had a prolonged ileus secondary to the retroperitoneal infection and laparotomy. It should be noted that débridement was effectively impossible in this case, since the infection and inflammation involved essentially the entire retroperitoneum and mesentery. Although débridement is usually critical to successful outcomes, other cases have been reported in which outcomes were good despite the lack of débridement, but in those cases as well as in ours, there was no evidence of fascial tracking of infection or of cutaneous manifestations.<sup>10,15</sup>

In more localized disease, particularly with abscess formation, débridement would be more feasible. As with other cases of necrotizing fasciitis, extensive aggressive débridement would be indicated, likely requiring bowel resection and possible nephrectomy or hysterectomy (or both). If CT suggests a localized retroperitoneal abscess, without definite intra-abdominal involvement, extraperitoneal approaches could be considered as has been done for some appendiceal abscesses, although in light of the initially unrecognized wide extent of the disease, a transperitoneal approach would also be reasonable.

In summary, invasive GAS infections of the abdomen and retroperitoneum can occur without overlying cutaneous manifestations, and their presentation can closely mimic surgical conditions such as appendicitis. This diagnosis should be considered in patients who appear seriously ill but who have unconvincing or inconsistent surgical findings such as normal appendices with increased free peritoneal fluid. The relative resistance of these serious infections to penicillin should also be kept in mind when instituting antibiotic therapy.

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