CASE REPORT

Non-lethal *Clostridium sordellii* bacteraemia in an immunocompromised patient with pleomorphic sarcoma

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SUMMARY

Clostridium sordellii is a spore-forming anaerobic Gram-positive rod that has rarely been reported to cause disease in humans. Resultant mortality from infection is estimated at nearly 70% and is most often correlated with gynaecological procedures, intravenous drug abuse or trauma. *C. sordellii* infection often presents similarly to toxic shock syndrome (TSS); notable features of infection include refractory hypotension, haemoconcentration and marked leucocytosis. Although clinically similar to TSS, a notable difference is *C. sordellii* infections rarely involve fever. The organism's major toxins include haemorrhagic (Tcsh) and lethal factor (Tcsl), which function to disrupt cytoskeletal integrity. Current literature suggests treating *C. sordellii* infection with a broad-spectrum penicillin, metronidazole and clindamycin. We present a case of *C. sordellii* bacteraemia and septic shock in an immunocompromised patient who was recently diagnosed with pleomorphic gluteal sarcoma. Despite presenting in critical condition, the patient improved after aggressive hemodynamic resuscitation, source control and intravenous antibiotic therapy.

BACKGROUND

Clostridium sordellii infection, first reported in 1922,¹ often presents clinically similar to toxic shock syndrome (TSS) and results in a 70% mortality rate.² Morphologically, *C. sordellii* is a spore-forming anaerobic Gram-positive rod, commonly found in soil samples. Despite being a common organism, it is a rare pathogen. The spectrum of reported infection is broad, with most cases involving healthy women undergoing gynaecological procedures (specifically medical abortion), intravenous drug abuse and musculoskeletal allografts.³ Several case reports have described the development of gas gangrene, myonecrosis and necrotising fasciitis secondary to *C. sordellii* infection.^{4 5}

CASE PRESENTATION

A 67-year-old woman, with recently diagnosed pleomorphic sarcoma of the right posterior thigh, presented to her primary care provider reporting of sudden onset fatigue and lethargy. On examination the patient was found to be febrile to 39.3°C, tachycardic to 160 bpm, tachypneic and grossly ill. One month prior to admission she had been diagnosed with a 23 cm×23 cm high-grade pleomorphic sarcoma of the right gluteal region. Her first chemotherapy cycle was completed without complication

2 days prior to admission and included cyclophosphamide, doxorubicin and dacarbazine.

On presentation, her right gluteal region appeared grossly erythematous and infected around the area of the sarcoma (figure 1), raising concern for a complicated skin and soft tissue infection with associated abscess. A CT scan of the pelvis revealed multiple air loculations in the right posterior thigh, in addition to increased size of the sarcoma (figure 2). A chest X-ray revealed no abnormalities. Pertinent initial laboratory findings included a white cell count of 1000/mm³, absolute neutrophil count (ANC) of 700/mm³, haemoglobin

Figure 1 Gross appearance of right gluteal sarcoma.

Figure 2 CT scan of pelvis displaying loculated free air within right gluteal sarcoma.

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of 9.1 g/dL, lactic acid of 1.8 mmol/L (normal range 0.5–2.2 mmol/L) and urinalysis remarkable for nitrates and trace bacteria.

Owing to persistent hypotension with a mean arterial pressure of 50 mm Hg despite aggressive fluid resuscitation, norepinephrine infusion was initiated for treatment of septic shock. Vasopressin was also initiated to help maintain blood pressure and reduce norepinephrine dose requirement.

INVESTIGATIONS

While CT scan of the pelvis revealed multiple right posterior thigh air loculations, no evidence of perirectal infection or inflammation was noted. Blood cultures were obtained on presentation (prior to antibiotic administration) and were positive for β -lactamase and negative for *C. sordellii* in two of two anaerobic cultures at 7 hours and 24 min. Coagulase-negative *Staphylococcus* was identified in one of two aerobic cultures at 34 hours and 19 min. Appropriate repeat blood cultures were unfortunately not obtained until hospital day 7 and resulted in no growth. Given her low ANC, and recent chemotherapy administration, fungal blood cultures and acid-fast bacilli smears were ordered and resulted negative. Other viral aetiologies including a hepatitis panel (hepatitis A/B/C serologies) and herpes simplex virus type 1 and 2 serologies were negative. Wound cultures obtained intraoperatively were positive for *Pseudomonas aeruginosa* and *Escherichia coli*; however, attempted anaerobic wound cultures were of poor quality.

DIFFERENTIAL DIAGNOSIS

The patient, with neutropenia secondary to recent chemotherapy, presented with septic shock, potentially secondary to opportunistic pathogen. The infectious appearing gluteal sarcoma was clinically concerning as the source of the resultant septic shock. The area depicted in figure 1 raises concern for conditions such as necrotising fasciitis, gas gangrene, malignancy, myonecrosis or abscess. While bacterial infection seemed most likely, fungal and viral aetiologies were also considered given her immunocompromised status.

TREATMENT

The patient required aggressive resuscitation and hemodynamic support for septic shock in the medical intensive care unit, with vasopressors being fully weaned by hospital admission day 3. Intravenous vancomycin, piperacillin–tazobactam and clindamycin were initially given for the treatment of septic shock with likely soft tissue infection. Antibiotic therapy was narrowed to piperacillin–tazobactam on hospital day 2 once *C. sordellii* was identified via two positive blood cultures. Piperacillin–tazobactam was continued for 14 days from the first negative blood culture set obtained on hospital day 7. While only admission blood cultures grew *C. sordellii*, repeat cultures were unfortunately not obtained appropriately until hospital day 7. Source control was achieved by performing surgical incision and drainage (I&D) of the right gluteal fluid collection and pleomorphic neoplasm on hospital day 2 and again on hospital day 5. She was transferred out of the intensive care unit on hospital day 7.

OUTCOME AND FOLLOW-UP

On day 18 of hospitalisation the patient was deemed clinically stable for discharge to home with a peripherally inserted central catheter for prolonged antibiotics. Antibiotic therapy with piperacillin–tazobactam was continued for 2 weeks after repeat blood cultures were found to be negative on hospital day 7.

DISCUSSION

Commonly found in soil and in animal gastrointestinal flora, *Clostridium sordellii* infection is primarily associated with childbirth, medical abortion and intravenous drug use.³ A case review by Aldape *et al*³ revealed an overall mortality of 69% in a group of 45 *C. sordellii* infections. Furthermore, 100% of these cases involving childbirth, medical abortion or spontaneous abortion resulted in death. The typical clinical course involved a rapidly progressive infection, with 80% of fatal cases resulting in death only 2–6 days after initial presentation. Classic symptoms of *C. sordellii* infection include leukemoid reaction, hypotension, haemoconcentration, tachycardia and the absence of fever. While the lack of fever in *C. sordellii* infections is not clearly understood, current research suggests this may be due specific cytokine dysregulation.^{6 7}

While the majority of *C. sordellii* infections are fatal, pathogenicity largely relies on the presence of the organism's two major toxins—haemorrhagic toxin (TcsH) and lethal toxin (TcsL).⁶ Both TcsH and TcsL share similarities to *Clostridium difficile*'s A and B toxins, resulting in compromised cytoskeletal structure. This direct toxin effect results in impaired cell-cell adherence, ultimately leading to massive intravascular fluid loss and subsequent peripheral oedema. Clinically, intravascular depletion is responsible for the TSS-like presentation of many *C. sordellii* infections.⁷ Despite a high mortality rate, a French case series identified 15 non-lethal *C. sordellii* foot infections with all *C. sordellii* isolates lacking the TcsL gene.⁸ Seven of these patients had isolated bacteraemia. The lack of TcsL likely explains the positive outcome and absence of TSS-like presentation in these cases. Further support that the presence of the TcsL gene results in increased pathogenicity was the documented survival of a patient with bacteraemia with cholangitis in a case report of a TcsL gene negative *C. sordellii* infection.⁹

The impact of pathogenicity with the presence of TcsL gene in *C. sordellii* was further investigated in animal models after infection with TcsL-negative *C. sordellii*; TcsL-negative infected rodents resulted in no mortality.⁹ The pathogenicity resultant of TcsL was demonstrated in another study showing significantly decreased mortality in toxigenic *C. sordellii* infection when injected with anti-TcsL immunoglobulin.¹⁰ While additional research is needed on the clinical implications of *C. sordellii* toxin expression, it does appear that TcsL is closely correlated with mortality and results in a clinical presentation similar to TSS.

Although the majority of reported *C. sordellii* infections were correlated with childbirth, medical abortion and intravenous drug use, these are not the sole causes of infection. Notable cases included a hospital-wide laboratory contamination,¹¹ infection associated with colorectal carcinoma² and infectious pericarditis.¹² While it was not clear what the source of *C. sordellii* was in our patient, her neutropenia secondary to recent myelosuppressive chemotherapy was a likely risk factor.

Beyond the presence of TcsL, several factors play an important role in overall prognosis, specifically, the site and nature of infection, immunocompromised state and antimicrobial resistance. Although historically gynaecological infections were believed to carry the highest mortality rate, a review of the current literature indicates intravenous drug abuse-related infections have similar data.³ In non-lethal infections with TcsL-positive *C. sordellii*, early treatment with culture-sensitive antimicrobials seems to be a major factor contributing to improved outcomes.⁷ Antibiotic resistance studies to date suggest that the many *C. sordellii* species are sensitive to penicillins, metronidazole and clindamycin.^{2 6} Treatment should include aggressive therapy for septic shock with volume

resuscitation, hemodynamic support with vasopressors if required and early initiation of broad-spectrum antibiotics.

Unfortunately the TcsL assay was not available at our facility for complete pathological assessment; however, other means of identification were not sought after consideration of incurring both patient and medical cost for identification; the information was felt unlikely to alter medical management. Although the patient's initial presentation with septic shock is suspicious for the presence of TcsL, this is confounded by the possibility of polymicrobial infection with urine cultures growing *P. aeruginosa*, one of the two blood cultures growing coagulase-negative *Staphylococcus*, and intraoperative wound culture growing *E. coli* and *P. aeruginosa*. Unfortunately, intraoperative anaerobic cultures were not obtained appropriately. The presence of loculated gas within the sarcoma, correlated with the positive blood culture of *C. sordellii* is concerning for the infectious source. An alternative possibility is that the patient could have had TcsL-negative *C. sordellii* bacteraemia in the setting of a superinfection by the aforementioned pathogens. Pseudomonal sepsis is possible given that the species was found in her tumour culture and urine culture; however, this failed to grow on multiple blood cultures and thus was felt to be less of a pathogenic culprit. The isolated culture of coagulase-negative *Staphylococcus* likely represents a contaminant, supported by

the 48 hours needed for growth. Early aggressive treatment of septic shock with fluid resuscitation, hemodynamic support with vasopressors and broad-spectrum antibiotics likely improved the patients overall chance of survival. Unfortunately, a quality repeat blood culture specimen was not collected until 6 days after the initial positive blood cultures, which extended the antibiotic therapy to ensure complete treatment.

In conclusion, *C. sordellii* infection is rare and highly fatal in most cases. Of the documented non-lethal cases, the majority of species were found to lack TcsL. With <30% of patients surviving *C. sordellii* bacteraemia, further research is needed to improve therapy and quickly identify the infection. An updated meta-analysis of non-lethal *C. sordellii* infections could also improve further efforts in preventing, recognising and treating the infection.

Contributors AKB is the primary author of the manuscript and resident who cared for the patient on service. SEES is the Pulmonary and Critical Care Medicine fellow and was involved in the caring for the patient, and assisted in the preparation of the manuscript. PJM was the attending physician caring for patient and assisted in the preparation of the manuscript.

Competing interests None declared.

Patient consent Obtained.

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Learning points

- ▶ *Clostridium sordellii* is a rare Gram-positive anaerobic rod that traditionally causes a toxic shock syndrome-like syndrome. Most commonly these infections occur in the setting of gynaecological procedures and intravenous drug abuse; however, a wide variety of presentations have been documented. A key finding is the lack of fever in many cases.
- ▶ Haemorrhagic (TcsH) and lethal factor (TcsL) are the major pathogenic toxins in *C. sordellii* species. Both proteins function to disrupt cell-cell adherence by cytoskeletal deregulation, resulting in severe vascular permeability.
- ▶ Nearly 70% of reported *C. sordellii* infections were fatal. The published literature suggests that the vast majority of non-fatal cases involve species lacking TcsH and TcsL.
- ▶ Recommended treatment for *C. sordellii* bacteraemia includes aggressive supportive care, adequate source control and broad-spectrum antibiotics such as penicillin, metronidazole and clindamycin.
- ▶ Patients with bacteraemia should receive daily repeat blood cultures until they result in no growth, as this can have a significant impact on treatment duration.

REFERENCES

- 1 Sordellii A. Un anaerobie agent de gangrene gazeuse. *C R Seances Soc Biol* 1922;87:838–48.
- 2 Matten J, Buechner V, Schwarz R. A rare case of *Clostridium sordellii* bacteremia in an immunocompromised patient. *Infection* 2009;37:368–9.
- 3 Aldape MJ, Bryant AE, Stevens DL. *Clostridium sordellii* infection: epidemiology, clinical findings, and current perspectives on diagnosis and treatment. *Clin Infect Dis* 2006;43:1436–46.
- 4 Kimura AC, Higa JJ, Levin RM, et al. Outbreak of necrotizing fasciitis due to *Clostridium sordellii* among black-tar heroin users. *Clin Infect Dis* 2004;38:e87–91.
- 5 Tsokos M, Schalinski S, Paulsen F, et al. Pathology of fatal traumatic and nontraumatic clostridial gas gangrene: a histopathological, immunohistochemical, and ultrastructural study of six autopsy cases. *Int J Legal Med* 2008;122:35–41.
- 6 Vidor C, Awad M, Lyras D. Antibiotic resistance, virulence factors and genetics of *Clostridium sordellii*. *Res Microbiol* 2015;166:368–74.
- 7 Aronoff DM. *Clostridium novyi*, *sordellii*, and tetani: mechanisms of disease. *Anaerobe* 2013;24:98–101.
- 8 Bouvet P, Sautereau J, Le coustumier A, et al. Foot infection by *Clostridium sordellii*: case report and review of 15 cases in France. *J Clin Microbiol* 2015;53:1423–7.
- 9 Walk ST, Jain R, Trivedi I, et al. Non-toxigenic *Clostridium sordellii*: clinical and microbiological features of a case of cholangitis-associated bacteremia. *Anaerobe* 2011;17:252–6.
- 10 Hao Y, Senn T, Opp JS, et al. Lethal toxin is a critical determinant of rapid mortality in rodent models of *Clostridium sordellii* endometritis. *Anaerobe* 2010;16:155–60.
- 11 Aronoff DM, Thelen T, Walk ST, et al. Pseudo-outbreak of *Clostridium sordellii* infection following probable cross-contamination in a hospital clinical microbiology laboratory. *Infect Control Hosp Epidemiol* 2010;31:640–2.
- 12 Chaudhry R, Verma N, Bahadur T, et al. *Clostridium sordellii* as a cause of constrictive pericarditis with pyopericardium and tamponade. *J Clin Microbiol* 2011;49:3700–2.

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