Primary *Clostridium septicum* aortitis: A rare cause of necrotizing suprarenal aortic infection

A case report and review of the literature

David M. Sailors, MD, John F. Eidt, MD, Paul J. Gagne, MD, Robert W. Barnes, MD, Gary W. Barone, MD, and David R. McFarland, MD, Little Rock, Ark.

A 74-year-old woman sought medical attention for general symptoms of nausea, vomiting, and back pain. A computed tomographic scan showed gas in the wall of the descending thoracic and suprarenal aortas. Emergency thoracoabdominal exploration revealed a necrotizing infection of the thoracic aorta extending to the origin of the celiac axis. After surgery *Clostridium septicum* was identified in tissue culture. Surgical management consisted of in-situ graft replacement of the thoracoabdominal aorta. Three months later, a pseudoaneurysm developed at the distal anastomosis. The patient refused further surgery and died 3 days later. The cause of death was presumed to be a ruptured mycotic aneurysm as a result of recurrent *C. septicum* infection. The relationship of *C. septicum* with occult gastrointestinal and hematologic malignancy has been documented. This patient represents the 10th reported case of *C. septicum* arteritis. Including the nine previous case reports of *C. septicum* arteritis, the mortality rate is 70%. When evaluating a patient with a mycotic aneurysm or arteritis, *C. septicum* should be considered. If it is found, a search should be carried out for an associated gastrointestinal or hematologic malignancy. Surgical repair should include extraanatomic revascularization and wide debridement of the infected field. Consideration should be given to lifelong antimicrobial therapy for this potentially fatal infection. (J VASC SURG 1996;23:714-8.)

*Clostridium septicum* arteritis is a rare life-threatening arterial infection that is often associated with an occult malignancy. The reported mortality rate from *C. septicum* infection is approximately 70%. We report the 10th documented case of *C. septicum* arteritis and pseudoaneurysm formation and review the literature with recommendations for management of this potentially fatal infection.

**CASE REPORT**

A previously healthy 74-year-old female nonsmoker was admitted to another hospital with a brief history of nausea, vomiting, and flank and upper-abdominal pain. Her history was remarkable for compression fractures of the thoracic spine, but no evidence of occlusive or aneurysmal aortic disease was present. Her vital signs at admission included a blood pressure of 128/70, a pulse of 90 beats per minute, and a temperature of 97.7°F. Physical examination was remarkable for minimal tenderness in the right upper quadrant and flank. Laboratory data revealed a white blood cell count of 19,000/mm³, a hemoglobin level of 10 gm/dl, and a hematocrit level of 31%. The patient was also noted to have iron-deficiency anemia with an iron level of 7 μg/dl (normal range, 65-165). A bone scan revealed no fractures, and results of a renal ultrasound scan were normal.

A computed tomographic (CT) scan identified a thoracoabdominal aneurysm with gas apparent in the soft tissue adjacent to the aneurysm. The proximal and distal aorta appeared to be relatively normal and had no signs of significant vascular disease. The patient was subsequently transferred to our institution for further treatment. Emergency thoracoabdominal exploration revealed a necrotizing infection of the lower thoracic aorta extending to the origin of the celiac axis. The aorta adjacent to the aneurysm was mildly affected by atherosclerotic disease, which manifested...
primarily as fatty streaks and thickening of the intima. An intraoperative gram-stain revealed white blood cells without organisms. No other intraabdominal or thoracic disease was identified. Surgical management consisted of in-situ replacement of the thoracoabdominal aorta with a Dacron graft and 12 weeks of antibiotic treatment after surgery. Antimicrobial treatment initially consisted of vancomycin and ampicillin/sulbactam (Unasyn; Pfizer Roerig, New York) for 5 days, followed by penicillin G when tissue cultures from the aortic bed grew *C. septicum*.

The patient's postoperative course was complicated by hyperamylasemia, leg weakness, a neurogenic bladder, and incontinence from presumed spinal cord ischemia. In addition, she had acalculous cholecystitis that required cholecystectomy. Intraoperative cultures were negative for *C. septicum*. Results of a complete gastrointestinal examination (gastrointestinal endoscopy and contrast studies) was normal. Four weeks after surgery, a repeat CT scan of the abdomen for hyperamylasemia revealed an intact distal anastomosis. At exploration for cholecystectomy no evidence was found of aneurysmal changes of the distal anastomosis. Eight weeks after surgery the patient was transferred to a rehabilitation facility. On discharge from the rehabilitation hospital, she was noted to be ambulating with the aid of a walker and to have normal bladder function, although she remained incontinent of stool. She did well for 5 weeks before again seeking medical attention for a new fever and flank pain. A repeat CT scan showed a large pseudoaneurysm at the distal anastomosis. The patient refused further treatment and died 3 days later, presumably resulting from sepsis or rupture of the pseudoaneurysm.

**DISCUSSION**

*C. septicum* is a gram-positive obligate anaerobe. It is believed to cause only 1.3% of all clostridial infections.6,10 *C. septicum* is known to proliferate in tissues that have a low pH level, an elevated lactate level, and a low oxygen level. *C. septicum* has been associated with gastrointestinal or hematologic malignancy in as many as 85% of cases.7 *C. septicum* at one time was thought to be a normal inhabitant of the gastrointestinal tract.8 More recent reports on the bacterial flora of the gastrointestinal tract in 229 healthy adults did not reveal *C. septicum*.9,12

The mechanism for *C. septicum* infection is unknown. Malmgren and Flanagan13 showed that clostridial spores require necrotic tissue in which to germinate. Their experiments with tumor-bearing mice and normal control mice have shown that clostridial spores germinate in areas of tumor where tissue necrosis has occurred. The spores did not germinate in normal control mice. Thiele et al.14 showed that clostridial organisms will proliferate in nontumor necrotic tissue, as is seen with mucosal ischemia. This may explain why *C. septicum* infections occur in patients with ischemic bowel and necrotic colonic tumors. Patients with a hematologic malignancy may have gastrointestinal manifestations of their disease, such as pseudomembranous colitis, granulocytic colitis, ischemic colitis, or necrotizing colitis. The inflamed and necrotic bowel wall loses its mucosal integrity and serves as a portal of entry for infection. This translocation of bacteria can lead to bacteremia and metastatic foci of infection. The arterial infections are able to perpetuate unchecked because of the neutropenia and thrombocytopenia that are manifestations of these hematologic diseases. A final mechanism for this infection may be that the thrombocytopenia alters the ability of the endothelium to maintain normal integrity.15

Including our report, 10 cases of *C. septicum* arteritis with aneurysm formation have been reported.16-24 Five were men and five were women. All patients were in the seventh or eighth decade of life. The features of the patients with *C. septicum* infection are outlined in Table I. Primary *C. septicum* arteritis (with no primary focus) has been identified in two patients; the patient described in this report and one other patient with *C. septicum* infection of the infrarenal aorta presenting as a contained retroperitoneal rupture.

Secondary *C. septicum* arteritis (in which the primary focus is identified) was diagnosed in the other eight patients. Six patients (75%) with secondary *C. septicum* arteritis had either a gastrointestinal or hematologic malignancy. One patient had proven ischemia as the probable event leading to infection. Another patient had a perinephric abscess with contiguous development of aortitis and pseudoaneurysm formation. She was presumed to have an associated malignancy, although this malignancy was never documented. Five of the six patients with malignancies related to *C. septicum* arteritis had colon carcinoma proximal to the splenic flexure, which emphasized the need for colonoscopy rather than sigmoidoscopy in the evaluation for associated gastrointestinal malignancy. The remaining patient had a hematologic malignancy.

Eight of the 10 patients had intramural gas involving the arterial wall. Seven of the eight (88%) died as a result of the arterial infection. Two of the ten patients also had radiographic evidence of mediastinal enlargement and pneumomediastinum with subsequent proven aortic arch aneurysms. Of the eight patients with aortitis, four had aortas that ruptured or had dissections. Three of these four patients died. The one survivor had a contained retroperitoneal rupture of the infrarenal aorta. Another patient died with a
Table I. Literature review of patients with *C. septicum* arteritis

<table>
<thead>
<tr>
<th>Ref. no.</th>
<th>Age (yr)</th>
<th>Clinical presentation</th>
<th>Procedure</th>
<th>Antibiotics</th>
<th>Cause</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>68</td>
<td>Pain, fever, leukocytosis, mass/shock</td>
<td>Aortic debridement and oversewn axillofemoral-bifemoral bypass</td>
<td>Erythro- mycin 7 mo</td>
<td>0</td>
<td>Survived (rupture)</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>Pain, fever, nausea, diarrhea, leukocytosis; later gas aortic wall rupture</td>
<td>Operative death</td>
<td>0</td>
<td>Gangrenous ileum</td>
<td>Death (rupture)</td>
</tr>
<tr>
<td>3</td>
<td>67</td>
<td>Fever, pain, leukocytosis, pulsatile mass; gas aortic wall</td>
<td>Axillofemoral-bifemoral bypass followed by aortic debridement and oversewn</td>
<td>6 wk</td>
<td>5-cm pedunculated polyp w/ atypia</td>
<td>Survival</td>
</tr>
<tr>
<td>4</td>
<td>62</td>
<td>Diarrhea, fever, pain, leukocytosis, thrombocytopenia, anemia, gas wall aorta</td>
<td>None</td>
<td>Penicillin</td>
<td>Waldenstrom macroglobulinemia (long-term chemotherapy); prednisone, alkylating agents</td>
<td>Death in radiology suite</td>
</tr>
<tr>
<td>5</td>
<td>85</td>
<td>Fever, nausea, vomiting, murmur, leukocytosis; later backache and intramural gas aortic knob</td>
<td>None—1st admit</td>
<td>Penicillin G 3 wk; Vancomycin 7 days</td>
<td>Adenocarcinoma cecum</td>
<td>Death before surgery (ascending aortic dissection)</td>
</tr>
<tr>
<td>6</td>
<td>70</td>
<td>Substernal chest pain, fever, malaise, epigastric pain—later pericardial effusion &amp; pericarditis</td>
<td>None—1st admit</td>
<td>Penicillin G 5 wk followed by oral penicillin long term</td>
<td>Right colon adenocarcinoma</td>
<td></td>
</tr>
<tr>
<td>Readmit</td>
<td>19 days later</td>
<td>Fever, sepsis, new onset systolic murmur</td>
<td>Resection arch aneurysm and pulmonary artery fistula w/in-situ Dacron graft</td>
<td></td>
<td></td>
<td>Survival</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>Cool, mottled right leg, leukocytosis, hyperglycemia, gas soft tissues in right leg; later aneurysm transverse aorta</td>
<td>Above-knee amputation-guillotine transverse colectomy</td>
<td></td>
<td>Transverse colon carcinoma</td>
<td>Death (rupture arch aneurysm)</td>
</tr>
<tr>
<td>8</td>
<td>80</td>
<td>Septicemia, 3 mo later leukocytosis fever, right lower quadrant abdominal pain</td>
<td>Exploratory laparotomy, right colectomy</td>
<td></td>
<td>Cecal carcinoma</td>
<td></td>
</tr>
<tr>
<td>Returned</td>
<td>2 wk after surgery</td>
<td>Leukocytosis, fever, air wall aneurysm</td>
<td>Excision iliac aneurysm, right common iliac stump closed, femoral-femoral bypass</td>
<td></td>
<td></td>
<td>Death at 10 mo</td>
</tr>
<tr>
<td>9</td>
<td>74</td>
<td>Malaise, fever, confusion, melena, sacral cellulitis/gangrene</td>
<td>Ultrasound-guided drainage, retroperitoneal fluid collection, excision of necrotic sacral skin</td>
<td>No</td>
<td>Suspected colonic neoplasm; Perinephric abscess</td>
<td>Death at 3 wk</td>
</tr>
<tr>
<td>10</td>
<td>74</td>
<td>Right flank pain, nausea, vomiting</td>
<td>Thoracoabdominal exploration, debridement of thoracoabdominal aorta, in-situ graft repair</td>
<td></td>
<td></td>
<td>Death at 3 mo</td>
</tr>
</tbody>
</table>

Documented 11-cm aneurysm with gas collection around the aorta; however, the exact cause of death is not written in this report. In patients with aortitis, the involved aortic site and surgical management is outlined in Fig. 1. Two patients had peripheral arteritis. One died of the arterial infection; the other died from a separate disease process.

The options for surgical management of arteritis...
and aortitis generally include (1) ligation of the affected artery, wide local debridement, and extraanatomic revascularization; (2) debridement and in-situ grafting of the affected vessel with prosthetic material; or (3) debridement and in-situ repair with autogenous tissue.

Five patients had surgical resection of the infected aneurysm or pseudoaneurysm. Three of these five patients had extraanatomic bypass and resection of the aneurysm. Two underwent axillary bifemoral bypass and aortic debridement. One patient with an infected iliac aneurysm had the aneurysm resected and a femorofemoral bypass graft implanted. Two of the three patients with extraanatomic reconstruction were long-term survivors; the remaining patient died of metastatic colonic disease 10 months after surgery. Two patients underwent in-situ graft repair of their aneurysm. One had replacement of the transverse aortic arch and was reported as being well 36 months after surgery. Our patient died, presumably as a result of recurrent infection, although this assumption was not definitively proved. In this review the overall mortality rate of patients with *C. septicum* arteritis was 70% (7 of 10). The only death related to recurrent arterial infection in surgically treated patients is the patient described in this report. All five patients who did not have surgical resection of the infected aneurysm or pseudoaneurysm died as a result of either aneurysm rupture or infection.

Three of the four patients with *C. septicum* bacteremia had known malignancies before any surgical intervention. One patient had definitive treatment of the aneurysm before definitive treatment of the colonic lesion. This patient continued taking antibiotics for a long period of time with no further complications. Two patients had definitive treatment of their colon lesions before definitive treatment of their aneurysms. Both had recurrent bacteremia and documented enlargement of the aneurysm before it was repaired. Antibiotics were used for 7 and 56 days, respectively, which suggests that although patients with *C. septicum* bacteremia may have an infectious focus initiated in the gastrointestinal tract, if an aneurysm is present or develops, it can be a continuous potential metastatic focus of infection. Surgical intervention is necessary because the antibiotics alone do not appear to eradicate the infection.

After surgical repair, antimicrobial treatment also plays a crucial role. Based on the findings of sensitivity tests and patient studies, penicillin is the drug of choice. Chloramphenicol is effective but is used infrequently as an antimicrobial agent. Metronidazole and clindamycin also provide alternatives but are not as effective. The appropriate duration of antibiotic treatment in patients with clostridial vascular infections is not known. We believe that lifelong antimicrobial treatment is reasonable, especially in patients in whom the source of clostridial infection is not identified. In patients in whom a primary focus is identified and prompt surgical treatment is undertaken, lifelong antibiotic treatment may not be justified.
CONCLUSION

C. septicum arteritis has a reported mortality rate of 70%. Patients with C. septicum infections are frequently found to have gastrointestinal or hematologic malignancies. The most common gastrointestinal malignancy associated with C. septicum arteritis appears to be right colon carcinoma. All patients with C. septicum arteritis should have complete gastrointestinal and hematologic evaluation including gastrointestinal endoscopy. Given the ability of C. septicum spores to infect the arterial wall, all patients with C. septicum infections should be screened for aneurysmal disease (Fig. 1.) If an aneurysm is identified, prompt surgical intervention is required. We believe that surgical treatment, when feasible, should include resection of the aneurysm and extraanatomic bypass. The antimicrobial drug of choice is penicillin. Consideration should be given to lifelong antimicrobial therapy, especially in patients in whom a primary focus of infection is not identified.

REFERENCES


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