CASE REPORT

An atypical presentation of colonic malignancy: *Clostridium septicum* aortitis

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SUMMARY

Clostridium septicum (CS) is a rare organism that accounts for only 1.3% of all clostridial infections. However, its detection is of great clinical significance, as over 80% of cases are associated with malignancy, often occult; the most common primary sites are the ascending colon and caecum, and the most common cause is haematological malignancy. We report a case of a 79-year-old woman, admitted with shortness of breath and left-sided chest pain, who, following subsequent investigations, was found to have CS aortitis. She was further evaluated with CT of the abdomen followed by colonoscopy and biopsy, which revealed adenocarcinoma of the caecum with liver metastasis. The CS aortitis has a reported mortality of 100% if left untreated. Therefore prompt intervention and surgical debridement is recommended. Despite these recommendations, our patient had some delays in her treatment and did not undergo surgical debridement due to frailty. We believe that it is highly unusual for a patient such as ours to have survived both the aortitis and the colonic malignancy, after undergoing endovascular radiological intervention and antibiotic therapy, without surgical debridement.

BACKGROUND

Clostridium septicum is a rare organism that accounts for only 1.3% of all clostridial infections. However, its detection is of great clinical significance, as over 80% of cases are associated with malignancy, often occult. The most common primary sites are the ascending colon and caecum (34%), and the most common cause is haematological malignancy (40%).¹ This infection has a very high reported mortality of 100% in 6 months, if left untreated. Its importance should not be overlooked, as a favourable outcome can be achieved with appropriate management.

CASE PRESENTATION

A 79-year-old woman who had undergone an uncomplicated left shoulder replacement 13 days prior to admission presented to our Medical Admissions Unit with a 1-day history of shortness of breath and left-sided chest pain that was worse on inspiration and radiated into the inter-scapular region. Her medical history included hypercholesterolaemia, recurrent urinary tract infections and arthritis. She was on treatment with trimethoprim and simvastatin. Prior to admission, she had been living with her husband and independently mobile.

General physical examination revealed a low-grade fever of 37.8°C, heart rate 90/min, blood

pressure 124/70 mm Hg, respiratory rate 19 breaths/min and oxygen saturations of 91% on room air. Systemic examination proved to be unremarkable.

INVESTIGATIONS

The patient's ECG showed no evidence of ischaemia, and an X-ray of the chest showed no active lung lesion. Preliminary biochemistry analysis revealed raised inflammatory markers, with a white cell count of $13.7 \times 10^9/L$ (neutrophilia $11.7 \times 10^9/L$) and C reactive protein of 275 mg/L. The patient's liver function tests were minimally deranged with alkaline phosphatase of 341 IU/L, alanine aminotransferase of 143 u/L and bilirubin of 21 $\mu\text{mol/L}$, and troponin T level was <0.03 ng/mL. Given the history of recent surgery coupled with the low oxygen saturations and positive D-dimer, a CT pulmonary angiogram (CTPA) was performed to rule out the possibility of a pulmonary embolus. Imaging of the thorax did not reveal evidence of pulmonary embolism but did reveal a mycotic aneurysm within the aortic arch inferiorly. The aneurysm contained internal gas loculations tracking within the wall of the ascending aorta and a small pseudoaneurysm arising from the inferior surface of the aortic arch, as shown in figures 1 and 2.

The case was discussed with a consultant cardiologist, who recommended an echocardiogram, as aortitis/mycotic aneurysm is usually seen in the context of infective endocarditis; the cardiologist also suggested that the systolic blood pressure be maintained below 120 mm Hg. Urgent transthoracic Echo showed no evidence of endocarditis. *C. septicum* was grown from two separate

Figure 1 CT pulmonary angiogram showing aortic arch intramural gas loculations (white arrows). A, ascending aorta; D, descending aorta.

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Figure 2 CT pulmonary angiogram showing initial size of aneurysm (white arrows).

peripheral blood cultures taken at the time of admission. *C. septicum* is a Gram-positive, spore-forming bacillus. *C. septicum* bacteraemia is often associated with a colonic malignancy, and with lesions of the caecum and ascending colon in particular. Consequently CT of the abdomen and pelvis was requested, which showed localised thickening of the ascending colon at the ileocaecal valve and several hypodense hepatic lesions highly suspicious of metastatic malignancy, as shown in figures 3 and 4. Colonoscopy and biopsy confirmed the diagnosis of moderately differentiated adenocarcinoma of the intestine. The biopsy revealed extensive necrosis within the tumour.

TREATMENT

Intravenous co-amoxiclav 1.2 g three times a day was started on the day of admission. The inflammatory markers continued to rise, with C reactive protein (CRP) peaking at 375 mg/L. The case was discussed with a microbiologist who, on the basis of sensitivity, recommended intravenous meropenem 1 g three times a day and metronidazole 500 mg three times a day.

Figure 3 CT of the abdomen showing thickening of ascending colon (white arrow) at ileocaecal valve.

This was continued for 6 weeks, then changed to oral co-amoxiclav 625 mg three times a day, as inflammatory markers improved significantly. The patient became unwell 2 days later with fever and raised CRP, and the case was re-discussed with the microbiology consultant, who suggested re-starting meropenem and metronidazole, which were continued for 2 weeks followed by oral co-amoxiclav 625 mg three times a day long term (dates for antibiotics and surgery shown in table 1).

The patient was also started on antihypertensive medications to maintain the recommended systolic blood pressure of <120 mm Hg: amlodipine followed by an ACE inhibitor and bisoprolol.

Initially, the patient was considered unsuitable for surgical intervention due to her frailty. A repeat CT scan after 6 weeks of appropriate intravenous antibiotic therapy demonstrated that the aneurysm had dramatically increased in size to 5×5.5 cm. In addition, it was causing dysphagia and hoarseness of voice due to local compression of the oesophagus and recurrent laryngeal nerve, respectively, as shown in figure 5. The patient was still deemed unfit for full aortic arch graft replacement. Therefore, a covered endoluminal stent was inserted into the aortic arch radiologically (as shown in figure 6) to allow blood flow without further expansion of the aneurysm.

As a consequence of the stent occlusion of the left common carotid and left subclavian arteries, the patient also required a pre-emptive carotid–carotid bypass graft to maintain blood flow to the left side of the circle of Willis. She recovered well from surgery but developed left subclavian vein thrombosis and was started on warfarin to treat this. She was discharged with regular follow-up, including 3–6 monthly surveillance CT scans.

OUTCOME AND FOLLOW-UP

The case was discussed in the hepatobiliary and colorectal multi-disciplinary team; it was thought that the patient would not survive colectomy and concern was expressed that the aneurysm was a greater threat. Initially, the patient was not keen to consider potentially curative colorectal surgery, however, after 12 months of the patient being stable post-thoracic surgery, a decision was made to perform two-stage curative surgery, in part due to concern that the caecal tumour could become obstructive. Therefore, 18 months after her initial presentation, the patient underwent laparoscopic right hemi-colectomy (T4,

Figure 4 CT of the abdomen showing liver metastasis (white arrows).

Table 1 Dates of antibiotics and surgery

Dates	Antibiotics	Surgery
21/07/2010 to 23/07/2010	Intravenous co-amoxiclav 1.2 g TDS	
24/07/2010 to 02/09/2010	Intravenous meropenem 1 g TDS and Intravenous metronidazole 500 mg TDS	
08/09/2010 to 10/09/2010	Oral co-amoxiclav 625 mg TDS	
10/09/2010 to 20/09/2010	Intravenous meropenem 1 g TDS and Intravenous metronidazole 500 mg TDS	TEVAR, right carotid–carotid and left carotid subclavian bypass
21/09/2010 to date	Oral co-amoxiclav 625 mg TDS	
11/01/2012		Laparoscopic right hemicolectomy for ascending colon cancer
12/05/2012		Metastatic liver resection

TDS, three times a day; TEVAR, thoracic endovascular aortic repair.

N0, Dukes B adenocarcinoma) and 4 months later she had a resection of two segments (three and five) of the liver. She did not have adjuvant chemotherapy prior to surgical intervention. She had an excellent postoperative recovery from both surgical interventions despite some delays.

Her subsequent follow-up CT scans did not show any evidence of recurrence of her malignancy, and her aortic stent remains patent with no progression of the aneurysm. She is currently on a colonoscopy surveillance programme and managing well at home with her husband.

DISCUSSION

Our patient's clinical features were initially thought to be due to pulmonary embolism.

In retrospect, the inter-scapular nature of her pain was consistent with an aortic origin. Subsequent investigation showed an infra-arch aortic aneurysm due to aortitis caused by *C.*

Figure 5 Follow-up CT scan at 6 weeks showing expansion of aneurysm (black arrows).

Figure 6 Fluoroscopic image showing endoluminal stent insertion and successful exclusion of contrast from the aneurysm.

septicum. Positive findings included raised inflammatory markers, positive blood cultures for *C. septicum* bacilli and an aortic arch aneurysm on radiological imaging. Because of its strong association with occult colonic malignancy, our patient was further evaluated with CT of the abdomen followed by colonoscopy and biopsy, which revealed adenocarcinoma of the caecum with liver metastasis.

C. septicum is a Gram-positive, spore-forming anaerobic bacillus. It was originally thought to be a normal inhabitant of the gut flora, but stool studies of healthy adults do not support this.² *C. septicum* is known to proliferate in conditions of low pH, low oxygen and high lactate or areas of poor vascular supply. Malmgren and Flanigan³ described this in their experiments on tumour bearing mice, which showed clostridial spores required necrotic tissue to germinate. This may explain the proliferation of clostridial spores in our patient, who had extensive necrosis in her caecal tumour, histologically. Thiele *et al*,⁴ showed that clostridial organisms would proliferate in non-tumour necrotic tissue, such as that seen in mucosal ischaemia, which can occur in patients with ischaemic bowel. In addition, mucosal ulceration within the tumour likely allows *C. septicum* to disseminate.⁵ There is also an association with haematological malignancy. The mechanism of spread may be due to the gastrointestinal manifestation of the disease or its treatment, leading to disruption of bowel mucosal integrity due to colitis, which would then serve as a portal of entry to infection, causing bacteraemia and foci of infection at distant sites.⁶

The organism has the ability to metastasise and invade tissues facilitated by its flagella and the production of toxins including haemolysin α toxin, DNase β toxin, hyaluronidase γ toxin and the thioactivated/septocolysin δ toxin.^{7,8} α Toxin is considered responsible for the virulence of clostridial infections causing intravascular haemolysis and tissue necrosis.⁹

Although *C. septicum* comprises only 1.3% of all clostridial infections, its detection is of great clinical significance because of its association with underlying occult malignancy, which may be haematological as well as colonic. Alpern and Dowell¹⁰ reported that over 85% of patients with this particular *Clostridium* infection had an underlying malignancy. In 1989,

Kornbluth *et al*¹ reviewed 162 patients with *C. septicum* infection, of whom 81% had associated malignancy.

Clinical manifestations

Patients with *C. septicum* infection usually present in their seventh and eighth decade of life. *C. septicum* can affect any part of the aorta, from aortic root to the iliac arteries, including the aorta's branches. The clinical spectrum of signs and symptoms depends on the location of infection, its severity and its complications (aortitis, aneurysm, dissection and rupture). This includes pain, fever, nausea, vomiting, a pulsatile mass, a new murmur, or septic or hypovolaemic shock. CT may show soft tissue prominence and increased contrast enhancement, and a periaortic fluid collection or intramural gas, which is a characteristic feature of clostridial infection and other gas forming organisms.

Treatment

C. septicum aortitis is a rare but life-threatening infection that needs immediate recognition and appropriate surgical as well as medical treatment.

The main aim of treatment is to eradicate the source of infection, as it can be a continuous focus of infection with metastatic potential. Although surgical repair is the mainstay of treatment, antimicrobial treatment also plays a crucial role. Once infection with *C. septicum* is suspected or confirmed, broad-spectrum intravenous antibiotics should be started; initial treatment may be with penicillin G. Other alternatives for patients who are allergic to penicillin are third-generation or fourth-generation cephalosporins, metronidazole, imipenem or vancomycin, all of which have been shown to be effective against the organism.⁵ These agents may be combined with a second agent to provide coverage for mixed organisms. The choice of antimicrobial should be directed by antibiotic sensitivity testing. The duration of treatment depends on identification of the primary source of infection. A minimum of 6 weeks of intravenous antibiotics is recommended for patients in whom a source of clostridial infection has been identified and prompt surgical intervention has taken place.

The definitive treatment of *C. septicum* aortitis is surgery. Mortality rates of surgically managed cases are in the order of 64% at 6 months. Without surgery, mortality rates approach 100%. Once *C. septicum* infection is documented, screening for aortic aneurysm with CT of the abdomen is recommended. There are no reports of eradication of infection without surgical intervention. Surgical options include resection, wide debridement, extra-anatomic bypass and in situ graft repair with either prosthetic or autologous tissue.¹¹

As *C. septicum* infection is frequently associated with occult bowel or haematological malignancy, a prompt search for underlying malignancy is recommended. Treatment of any underlying malignancy follows the same principles as those without *C. septicum* infection.

In our patient, the primary source of infection was a caecal carcinoma, and she completed her curative surgery with colectomy and metastatic resection 22 months after her initial presentation. Her antibiotics were continued long term. Her aortic arch aneurysm was treated initially with a stent followed by a carotid-carotid subclavian bypass graft due to stent occlusion.

Conclusion

We present a case of *C. septicum* aortitis associated with an underlying occult malignancy. This infection has a very high reported mortality of 100% in 6 months if left untreated. All patients with *C. septicum* aortitis warrant prompt surgical intervention as well as thorough evaluation for haematological and gastrointestinal malignancy, particularly adenocarcinoma of the colon. Although prompt intervention is recommended, our patient did well despite some delays. We believe it is highly unusual for a patient such as ours to survive the aortitis as well as the colonic malignancy, after undergoing endovascular radiological intervention and antibiotic therapy, without surgical debridement.

Learning points

- ▶ *Clostridium septicum* aortitis is associated with malignancy in over 80% of cases.
- ▶ *C. septicum* aortitis has a very high reported mortality of 100% in 6 months if left untreated.
- ▶ All patients with *C. septicum* aortitis warrant prompt surgical intervention as well as thorough evaluation for haematological and gastrointestinal malignancy, particularly adenocarcinoma of the colon.
- ▶ Favourable outcome can be achieved with appropriate management.

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Competing interests None declared.

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