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CASE REPORT

Vascular Complications in *Coxiella burnetii* Infection: A Report of Two Cases

Victoria A.L. Kanowski [a,*], **Sherab G. Bhutia** [b]

[a] Department of Surgery, Cairns Hospital, Cairns, Queensland, Australia
[b] Department of Vascular Surgery, Cairns Hospital, Cairns, Queensland, Australia

Introduction: First described in 1937, Q fever remains a relatively new disease, with much to be learned about its presentation and diagnosis. Due to its role in the development of aortic aneurysms and vascular graft infections, its implications in the vascular domain have become increasingly reported. This is a report of two cases of vascular complications associated with *C*oxiella burnetii infection, and the challenges in managing their unique presentations.

Reports: Case 1: A 70 year old man with a prosthetic aortobiiliac graft and past Q fever infection presented with acute sepsis. Abdominal computed tomography (CT) showed soft tissue thickening and stranding around the graft, and locules of gas within the vessel. Pelvic magnetic resonance imaging (MRI) revealed a chain of abscesses within the right gluteal region, of which aspirate grew *Prevotella oris* and *Escherichia coli*. Open explanation of the aortic graft and replacement by superficial femoral vein was performed. Tissue culture confirmed a polymicrobial infection, and PCR of the aortic wall and pre-aortic lymph node was positive for Q fever. He was treated for recrudescent Q fever infection with a good outcome and recovery. Case 2: A 73 year old man had an incidental abdominal aortic aneurysm (AAA) identified at the time of Q fever diagnosis. Following an incomplete course of doxycycline and hydroxychloroquine, the aneurysm rapidly progressed, leading to presentation with right flank pain. Fluorodeoxyglucose (FDG) positron emission tomography (PET) showed multiple foci of uptake within the aneurysm wall. Open AAA repair with a polyester graft was performed, with AAA tissue positive for Q fever on PCR. The operation was successful, with the patient continuing clearance therapy at time of writing.

Discussion: Q fever infection poses serious implications for patients with vascular grafts and AAAs, and thus, should be considered in the differential diagnosis of mycotic aortic aneurysms and in aortic graft infections.

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INTRODUCTION

Q fever is a zoonotic disease caused by *Coxiella burnetii*. The bacterium resides in animals such as cattle and can be transmitted via inhalation of aerosolised bacteria. The disease is found worldwide, sparing only New Zealand.[1]

Both acute and chronic manifestations of Q fever are seen. In the acute phase, the patient commonly displays flu like symptoms, including fever, myalgias, and headache. Some patients develop pneumonia and hepatitis. Chronic Q fever may arise months or years after the initial illness in the form of endocarditis, bone and joint infection, or endovascular infection.[1,2] Due to the non-specific nature of the infection, clinicians must actively suspect and screen for the disease. As will be demonstrated, diagnosis is not always straightforward, and treatment and surveillance can be challenging.

This report presents two cases of vascular complications in the setting of *Coxiella burnetii* infection.

REPORT

Case 1

Case 1 involves a 70 year old man with a background of open abdominal aortic aneurysm (AAA) repair with polyester aortobiiliac graft. Nine years after the repair, he presented with right sided abdominal pain, fatigue and weight loss without fever. Abdominal computed tomography (CT) showed fat stranding and a thick rind of soft tissue surrounding the aneurysm sac, consistent with prosthetic graft infection. He returned negative blood cultures and negative serology for *Brucella*, *Salmonella typhi*, *Bartonella*, *Treponema pallidum*, *Legionella*, and *Mycoplasma pneumoniae*. Inflammatory markers and white cell count (WCC) were unremarkable. The only positive finding on infective screen was persistently elevated Q fever phase 2 antibodies, but

* Corresponding author.
E-mail address: victoria.kanowski@gmail.com (Victoria A.L. Kanowski).

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with values never meeting the diagnostic criteria for chronic Q fever.

The patient received six weeks of piperacillin-tazobactam and one week of doxycycline. Subsequent CTs and labelled white blood cell scan were reassuring for resolution. Due to patient preference, further antibiotics were ceased. The patient was followed up for two years and discharged.

Less than a year later, he re-presented with right hip pain, fevers, and a painful right heel lesion, with a preceding six month history of weight loss and malaise.

On examination, he was unable to weight bear, displaying exquisite tenderness over the right gluteal region. WCC (16.4×10^9/L) and CRP (141 mg/L) were elevated.

CT abdomen and pelvis revealed soft tissue thickening and stranding around the aortic graft, with locules of gas seen within the vessel (Fig. 1A and B). Pelvic magnetic resonance imaging (MRI) showed a chain of abscesses within the right gluteal region (Fig. 1C and D).

The heel lesion was biopsied, showing necro-inflammatory histology, with gram negative cocco-bacilli, and scant gram positive bacilli. *Streptococcus anginosus* was cultured. In addition to the *Streptococcus*, right gluteal abscess aspirate grew *Prevotella oris* and *Escherichia coli*.

Over the next 24 hours, the patient deteriorated and was commenced on piperacillin-tazobactam and vancomycin. Blood culture grew *Streptococcus anginosus*.

A week later, the patient underwent laparotomy, explantation of the aortic graft, and synchronous replacement with reversed right superficial femoral vein. A layer of slime was observed over the old aortic graft, and the duodenum was densely adhered to the aorta, seemingly consistent with impending aortoduodenal fistula.

Aortic wall, graft, and pre-aortic lymph nodes were collected. A polymicrobial infection was confirmed, with tissue culturing *Streptococcus anginosus*, *Escherichia coli*, and *Propionibacterium acnes*. PCR of the graft and aortic lymph node was positive for Q fever.

The post-operative course was complicated by development and drainage of a para-aortic gas and fluid containing collection. The patient completed two years of hydroxychloroquine and doxycycline for the treatment of Q fever aortic graft infection. Six monthly follow up occurred for three years, with annual CT angiogram. He has now been discharged to his general practitioner (GP).

Case 2

Case 2 involves a 73 year old man referred with a 52 mm infrarenal AAA on ultrasound. This was an incidental finding during work up for a two week history of fatigue, lethargy, and subjective chills. An infective blood screen revealed probable chronic Q fever (Q fever PCR negative, and Phase 1 IgG elevated >1 280). The erythrocyte sedimentation rate (ESR) was mildly elevated (20 mm/h), and WCC was normal.

Doxycycline and hydroxychloroquine were commenced, and the patient underwent CT angiography and fluorodeoxyglucose positron emission tomography (FDG PET) CT to assess for aortitis. An inflammatory rind was identified on CT, but there was no evidence of underlying inflammation on PET. Given the patient's aneurysm remained asymptomatic, and the lesion did not meet size criteria for intervention (54 mm on CT), it was decided to continue surveillance until the AAA was >55 mm.

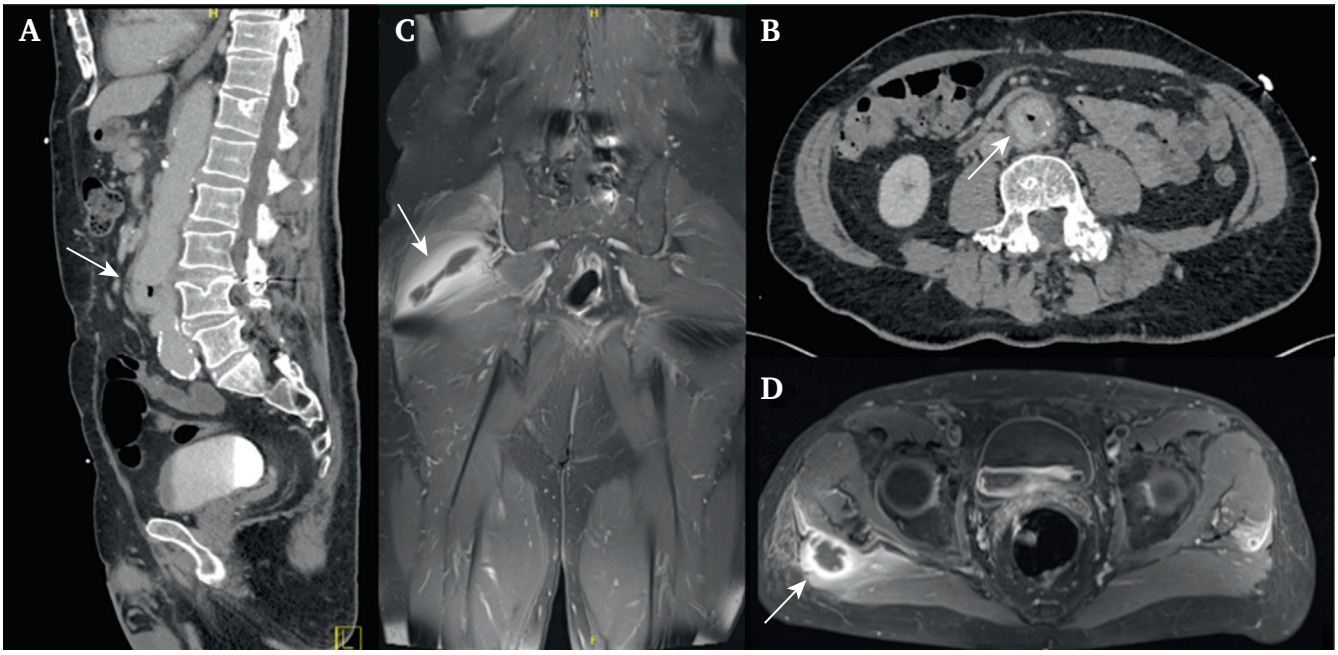

Fig. 1. (A) Computed tomography (CT) angiogram of the abdomen and pelvis (sagittal view) demonstrating abdominal aortic graft peri-luminal soft tissue density thickening with slight stranding, and a small focus of gas centrally. (B) Axial view of the CT angiogram. (C) Magnetic resonance imaging (MRI) showing a chain of abscesses within the right gluteal region, in particular, the interface between the right gluteus medius and maximus. There is intense associated inflammatory oedema and enhancement. (D) Axial view of the MRI.

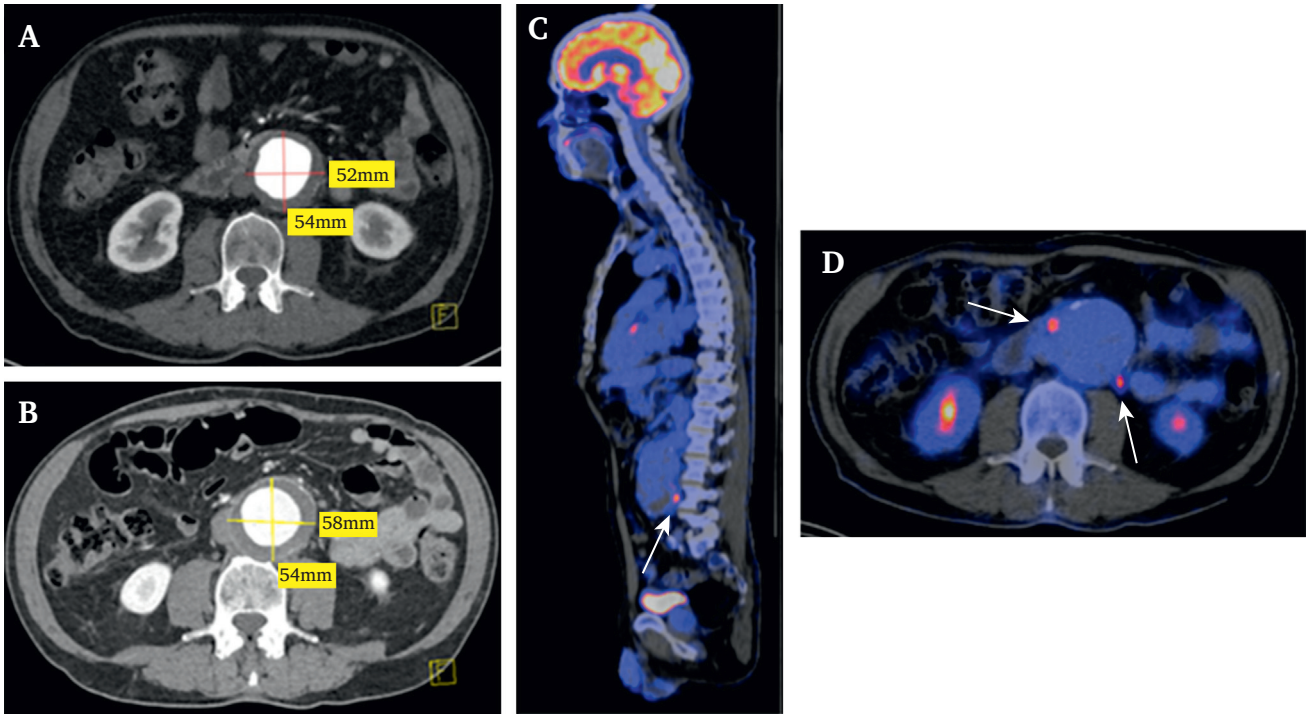

Fig. 2. (A) Computed tomography (CT) angiogram of the abdomen (axial view) showing the abdominal aortic aneurysm with a maximum diameter of 54 mm. (B) CT angiogram of the abdomen (axial view) demonstrating a 58 mm diameter abdominal aortic aneurysm following a five month interval. (C) Fluorodeoxyglucose (FDG) positron emission tomography (PET) CT showing abnormal FDG uptake within the aneurysmal wall. Note: Moderately prominent radiotracer uptake in the left ventricular myocardium probably represents physiological tracer uptake related to the dietary preparation for the study and is not thought to represent endocarditis. (D) Axial view of the FDG PET CT.

After six weeks, the patient self ceased the medications due to intolerance. Three months later, he re-presented, with a now symptomatic aneurysm. He reported right flank pain radiating to the lower back with nausea, but no fever. CT angiogram revealed a 58 mm AAA (Fig. 2A and B). Due to the size increase over such a short timeframe, the decision was taken to perform open AAA repair. A pre-operative FDG PET CT was performed, now revealing multiple foci of FDG avidity with the aneurysmal wall, suspicious of an active inflammatory or infective process (Fig. 2C and D).

Open AAA repair was performed, and a bifurcated polyester graft was placed inside the aneurysm sac. AAA tissue was Q fever PCR positive, and culture of the aortic wall showed no growth.

Post-operatively, the patient recommenced hydroxychloroquine and doxycycline. There have been ongoing challenges with clearance therapy due to medication intolerance, with ciprofloxacin trialled, and finally the patient continuing with trimethoprim-sulfamethoxazole. He has ongoing follow up with Infectious Diseases to manage the antimicrobials and is planned for annual reviews and CT angiogram with the Vascular clinic.

DISCUSSION

Two presentations of *C. burnetii* infection have been described: the first case involved a patient who contracted Q fever and developed subsequent prosthetic graft infection requiring explantation of graft material and *in situ* reconstruction (ISR) with autologous vein; the second case involved a patient with mycotic aneurysm requiring repair with a polyester graft.

Vascular graft infection of any aetiology occurs at a rate of approximately 1—5% in the abdominal and thoracic cavities.[3] In patients with acute Q fever, the presence of a graft is a known predisposing factor for progression to a chronic phase.[4]

Although graft infection with *C. burnetii* was suspected in Case 1, diagnosis of a chronic Q fever process proved to be particularly challenging. Chronic Q fever is present if Q fever phase 1 IgG is $\geq$1:1 024 by immunofluorescence assay, alongside an identifiable persistent focus of infection.[2] Interestingly, the patient's peak titre during surveillance only came to 1:320, and blood PCR and culture were persistently negative. Definitive diagnosis for chronic Q fever was only made once the aortic graft was explanted, on the basis of positive graft and aortic lymph node PCR.

Prior to presentation with sepsis, the patient had been monitored for two years to assess for recurrent aortitis. CT angiogram was the surveillance modality used and is the first line imaging technique recommended by the European Society for Vascular Surgery (ESVS).[3]

Had there been clinical indication of endograft infection, FDG PET CT would have been performed. This modality is suggested where there is clinical suspicion of endograft infection but non-convincing CT.[3] FDG PET CT is superior in

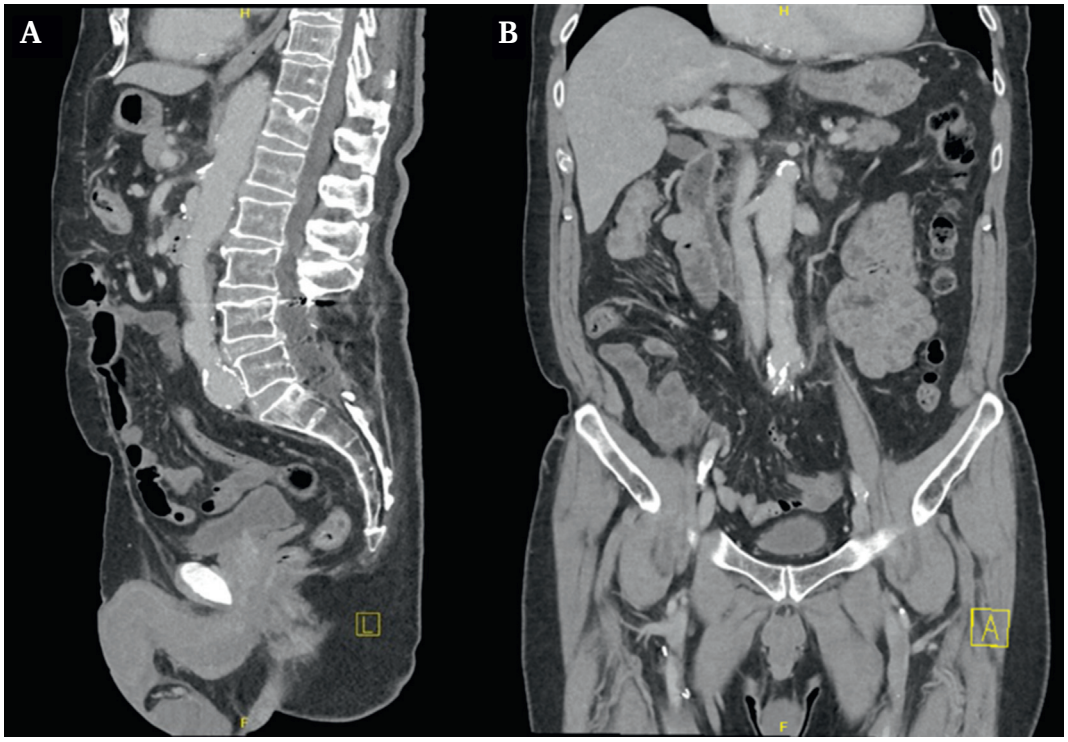

Fig. 3. (A) Computed tomography (CT) abdomen and pelvis showing appearance of the aorta post-repair with reversed right superficial femoral vein. The aorta is patent, although with a slightly thickened wall which is stable compared with previous post-operative imaging. (B) Coronal view of the same imaging.

detecting infected aortic aneurysms and is known to detect infective foci in individuals where Q fever serology has been inconclusive.[5,6]

Although not routinely recommended, a single Tc99m labelled white cell scan was performed at the beginning of surveillance, and whilst negative, it is speculated whether repeating it prior to discharge would have detected low grade infection that CT did not (sensitivity of 0.90 *vs.* 0.67, respectively).[7] Limitations, however, include access to this technique, as well as its time consuming nature.[7]

Definitive treatment of an infected vascular graft requires excision of infected graft material and tissue.[3] This was completed, and success of the procedure was evident in complete resolution of the infection on imaging and bloods after three years (Fig. 3).

Case 2 was a presentation of mycotic aneurysm and highlights a further manifestation of *C. burnetii* infection. Intra-operatively, appearances were in keeping with a standard degenerative AAA without evidence of gross infection. There was no slough, slime, or purulent material involving the aortic tissue and surrounds. As such, a decision was made to preserve the tissue and place the polyester graft within the aneurysm sac.

The ESVS guidelines recommend repair with deep femoral veins, cryopreserved allografts, silver grafts, or rifampicin impregnated grafts.[3] Despite this, a polyester graft was used. A rifampicin soaked graft was avoided due to evidence demonstrating its role in the development of systemic drug resistance.[8] Additionally, when compared with doxycycline, rifampicin is not as effective at treating *C. burnetii* infection.[9] As a result, the present authors' institutional pharmacy does not support its use, and it is unavailable at their facility. A silver graft was not used due to the benign macroscopic appearances of the AAA. Despite use of a simple prosthetic graft alone, the patient has progressed well post-repair, with no sign of recurrence after 11 months.

CONCLUSION

Coxiella burnetii infection presents insidiously and is not always thought of in the primary differential. A multidisciplinary approach is key in surveillance and management of these patients, and completion of the appropriate course of antibiotic therapy is crucial for disease clearance. The present authors recommend that Q fever be considered in the differential diagnosis of mycotic aortic aneurysms and aortic graft infections.

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None.

CONFLICT OF INTEREST

None.

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