Aortoenteric fistula after endovascular mycotic aortic aneurysm exclusion: lessons learned during the COVID-19 era

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SUMMARY

We report a case of aortoenteric fistula 2 years following endovascular aortic aneurysm repair (EVAR) for mycotic aneurysm presenting as upper gastrointestinal bleeding. Initial CT angiogram did not reveal the bleeding or connection to bowel, but endoscopy was suspicious of endograft in the duodenum. Management required a multidisciplinary approach. To stabilise the patient and to control bleeding, a 'bridging' endograft extension was performed. This was followed by open surgical removal of the EVAR endograft and lower limb in situ revascularisation. During postoperative recovery, the patient developed atypical, staged multisystemic symptoms (cardiac, pulmonary and neurological). With increasing awareness of the COVID-19 pandemic, the patient was found SARS-CoV-2-positive, which explained the progression of his symptoms. This was also reflected on other case reports in literature later.

BACKGROUND

Primary mycotic aortic aneurysm (PMAA) is a rare condition with a relative incidence of 1%–3% of all aortic aneurysms.[1 2] Endovascular aortic aneurysm repair (EVAR) for infected aortic aneurysm treatment was first reported in 1998 by Semba and collegues.[3] Aortoenteric fistula (AEF) is one of the rare complications following EVAR. High index of suspicion is essential in making the diagnosis. Management of these cases are challenging, especially in the context of an unstable patient with a bleeding fistula which might require combined approach (endovascular followed by open surgical intervention).

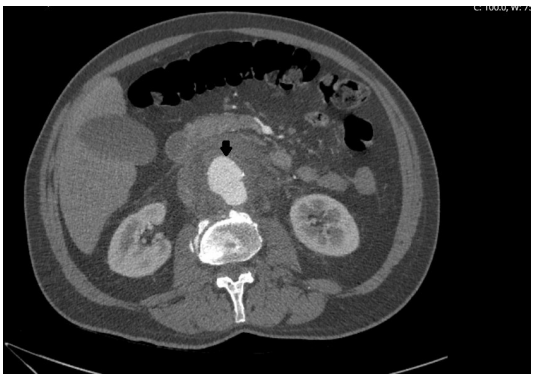

Figure 1 CT angiogram demonstrating aortic mycotic saccular aneurysm initial presentation (black arrow).

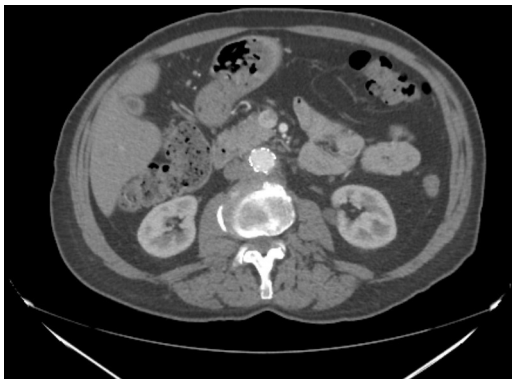

Figure 2 CT angiogram 1 year post endovascular aortic aneurysm repair.

CASE PRESENTATION

We report a case of 65-year-old man with a background of diet-controlled diabetes, stable ischaemic heart disease and alcohol-related liver cirrhosis. He was admitted in October 2017 to his local hospital with a 3-day history of lower abdominal, right flank pain, rigours and sweating. The patient reported no bowel or bladder symptoms. Initially, a diagnosis of pyelonephritis was made, and treatment commenced. The patient made no clinical improvement and blood cultures grew *Staphylococcus aureus*; so, a CT of the abdomen and pelvis was preformed 3 days later. A diagnosis of a 6.2 cm saccular, infrarenal abdominal aortic aneurysm, with retroperitoneal stranding and reactive lymph nodes (figure 1), was made, suspicious of a mycotic aneurysm.

The patient underwent an uneventful emergency EVAR of the mycotic aneurysm using Endurant II (Medtronic, Dublin) aortouni-iliac endograft, right iliac embolisation and left-to-right fem-femoral crossover bypass using Impra PTFE graft (BRAD Peripheral Vascular, New Jersey, USA).

Parenteral antibiotic treatment guided by blood cultures was given for 4 days preintervention and continued for 6 weeks postintervention. He was discharged 18 days postoperatively with no evidence of endoleak or lower limb ischaemia. The patient's white cell count normalised within 6 weeks and C Reactive Protein (CRP) remained mildly elevated. The 6-week follow-up CT angiogram (CTA) showed significant improvement with minimal periaortic change, and the patient was kept on long-term antibiotics.

Unfortunately, the antibiotics were stopped 3 months following the procedure. This has triggered

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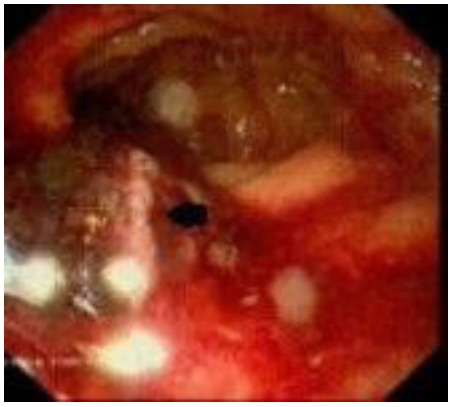

Figure 3 Oesophago-Gastro-Duodenoscopy (OGD) with blood clot and possible exposed endograft mesh (black arrow).

recurrence of the symptoms of lower back pain and fever. A repeat CTA suggested persistent inflammation but no aneurysm dilatation or leak with patent bypass grafts. A 6-week course of parenteral antibiotics was administrated followed by a step-down to oral antibiotics.

The patient was lost to follow-up but re-presented 1 year later with symptoms of intermittent claudication and gluteal pain initially thought secondary to right internal iliac embolisation. Spinal MRI excluded spinal pathology and CT at 1-year surveillance confirmed satisfactory appearance of the EVAR and bypass grafts with complete resolution of inflammatory changes (figure 2). The patient continued long-term antibiotic prophylaxis (ciprofloxacillin 500 mg two times per day and rifampicin 300 mg two times per day) and was advised to continue exercise to develop collateral circulation.

In 2019 and 2 years after emergency EVAR, the patient was admitted to his local hospital with a massive per-rectal bleed and a significant drop in haemoglobin levels. Comorbidities on this admission included type 2 diabetes mellitus, moderate aortic stenosis, alcohol-related liver cirrhosis and stable ischaemic heart disease. Upper gastrointestinal (GI) endoscopy suggested an active ulcer in the third part of the duodenum, D3, and possible visualisation of aortic graft material at the base of the ulcer (figure 3). CTA did not demonstrate any active GI bleeding or new changes around the duodenum; the EVAR stent was reported to be distant to the duodenal segment, with no soft tissue component around the stent in general. Clopidogrel was stopped and the patient was discharged with a simple GI ulcer.

Within days, the patient re-presented to the local emergency department with another episode of massive GI bleed. On this occasion, the patient was discussed with the vascular unit and was transferred to the arterial centre.

TREATMENT

In hybrid theatre, initial diagnostic angiogram did not demonstrate any active bleeding, but team decision was made to reline the aortouni-iliac graft with further iliac extension using Endurant II (Medtronic) as a temporary measure to help stabilise the patient and allow optimisation of his general condition. Parenteral antibiotics and nutritional support were commenced for 2 weeks before proceeding to surgical explanation of the graft, aortic replacement and duodenal repair.

An initial laparotomy confirmed aortoduodenal fistulation. The duodenum was mobilised, revealing a bile-stained EVAR stent (figure 4). The proximal aorta above the fistula was too thin to allow safe suturing; the suprarenal fixation component

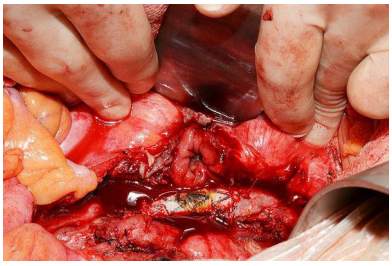

Figure 4 Intraoperative endograft bile staining.

was set in the Superior Mesenteric Artery (SMA) origin, and the tissues were too friable to allow full explanation. The graft was then divided below the proximal two rings of the stent, leaving a 'synthetic aortic neck' to re-enforce the aortic wall and allow repair. This was felt to be the safest option, despite dissecting the aorta up to SMA origin to enable clamping, we preferred to use an intraluminal balloon occlusion to avoid clamping friable aortic tissue. The rest of the stent graft and the right iliac occluder system were removed and all necrotic tissue was debrided. The duodenum was repaired primarily while a bovine pericardium patch (XenoSure Biologic Patch, LeMaitre Vascular, Massachusetts) was being fashioned to form a biological tube graft, used to restore in-line flow to the left iliac system (figure 5).

OUTCOME AND FOLLOW-UP

The cultures from intraoperative tissue samples grew GI flora, *Escherichia coli*, actinomyces, lactobacillus plantarum and *Candida*, in comparison to the *S. aureus* culture from the initial mycotic aneurysm cultures. The patient had inotropic support, antibiotics and Total Parenteral Nutriotion(TPN) in critical care unit (CCU). Three days later, he stepped down to normal ward. A gastrograffin swallow showed no leak and the patient was gradually started on enteral feeding (figure 6).

Three days following CCU discharge, the patient unexpectedly developed two generalised tonic clonic seizures associated with transient homonymous hemianopia, initially treated as posterior reversible encephalopathy syndrome as per radiological and clinical findings and started on antiepileptics. Follow-up demonstrated no residual neurological deficits.

One week later, the patient suddenly dropped oxygen saturation (SpO_2) and developed fast atrial fibrillation and acute kidney injury. He was readmitted to the CCU and had an echocardiogram that suggested sudden deterioration of left ventricular function with an ejection fraction of 35%. He was initially treated for pulmonary oedema. With an increasing number of cases related to COVID-19 infection, PCR swab was sent and came back as positive. Subsequent serial chest radiographs (CXRs) confirmed changes consistent with COVID-19 chest infection (figures 7 and 8).

The patient received supportive Continuous Postitive Airway Pressure (CPAP), diuretics, dual antiplatelet therapy and

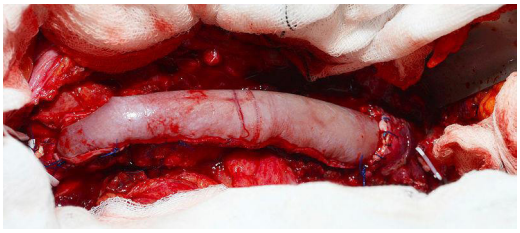

Figure 5 Bovine in situ graft revascularisation.

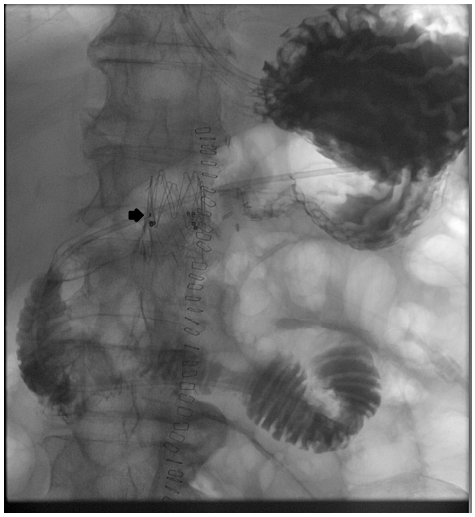

Figure 6 Gastrografin swallow with no evidence of contrast extravasation. Proximal cuff on previous endograft is visible (black arrow).

continued antibiotic treatment. He was stepped down to ward level 2 days later and was discharged after 43 days in the hospital on long-term oral antibiotics. Sixty days after discharge, patient was recovering well and gaining weight and was asymptomatic.

DISCUSSION

PMAA is a rare condition with a relative incidence of 1%–3% of all aortic aneurysms.[1 2] Usually, it tends to occur in patients with severe comorbidities, particularly those with immunodeficiency.[4] Despite advances in antibiotic, purely medical management for PMAA is often inadequate because of the possibilities of persistent infection, subsequent aneurysm rupture and death. Open surgical intervention, on the other hand, is associated with significant morbidity and mortality.[5]

EVAR for infected aortic aneurysm treatment was first reported in 1998 by Semba and collegues.[3] The main advantages of endovascular repair are the avoidance of large incision, aortic cross clamping, interference with respiratory function, revascularisation and significant blood loss.

Although the classical triad of features, fever, abdominal/back or chest pain, and leucocytosis, is usually present in majority of cases,[6] the diagnosis can be difficult, as the clinical presentation can be non-specific and confused with other intra-abdominal septic conditions like pyelonephritis in our case.

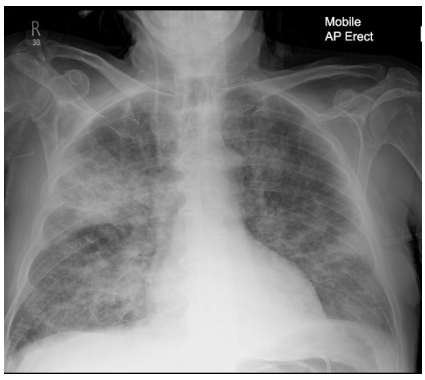

Figure 7 Anteroposterior Chest Xray Day 9 postoperation with non-specific bilateral patchy increased densities suggestive of COVID-19.

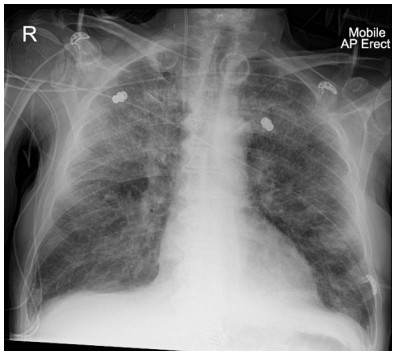

Figure 8 Day 11 postoperation, bilateral non-specific lung infiltrate suggestive of COVID-19.

Antibiotic therapy should be initially broad spectrum then guided by blood culture results.[4] Twenty to forty per cent of PMAA blood or tissue cultures are negative.[7] *S. aureus* is the main reported causative pathogen for an infected aortic aneurysm in Western countries, with *Salmonella* being the major reported causative agent in Asia.[6] *Salmonella*-infected aneurysms usually exhibit rapid disease progression with a risk of early rupture with a good response to antibiotic and acceptable long-term outcomes. In contrast, non-*Salmonella*-positive blood cultures develop serious late complications.[4 8] In this case, the initial blood cultures revealed *S. aureus* growth.

Kan *et al* suggest that patient age 65 years or older, ruptured aneurysm (including fistulation), fever at the time of operation and use of preoperative antibiotics less than 1 week are predictors of persistent infection, which is associated with a 12-month survival rate of only 39%.[9] The authors suggested a benefit form a week of preoperative parenteral antibiotics[2] or to delay procedure until negative blood cultures result.[7]

Although PMAA is excluded by EVAR grafts, the inside of the infected aneurysmal sac may lead to sepsis.[10] To reduce the organism and infection load, some authors suggested surgical debridement or percutaneous drainage.[11] In our case, CT scan suggested stranding around the aneurysm and adjacent reactive lymph nodes rather than severe infection or drainable collection. Furthermore, 30-day follow-up CT scan suggested significant improvement and minimal residual inflammation.

Postinterventional antibiotics is of paramount importance. However, the available literature for parenteral antibiotic use shows a significant variation in intervals. In the early postoperative period, parenteral antibiotics are recommended for 10 days or until the patient remains afebrile for 72 hours.[6] Other reports adopted a longer period of 6–8 weeks.[2 4 11] In our case, the patient was on parenteral antibiotics for 6 weeks.

Late infection-related complications do occur, often lethal and usually triggered by antibiotic discontinuation. Long-term or lifelong oral antibiotics are recommended by many scholars, but patient compliance is critical to achieving a good outcome.[6 11] In a series of 14 patients, 1 patient discontinued the antibiotic therapy after discharge and died of haematemesis 2 months later due to infection-related aortoduodenal fistula.[4] Similar findings were also reported by a larger-scale review of 123 patients, with 9 patients suffering a fatal recurrent infection-related event after discontinuation of antibiotics. Most recurrent infections occurred within the first year, predominately within the first 6 months. As such, they recommend long-term antimicrobial therapy for at least 6–12 months and possibly lifelong treatment.[8]

In our case, the patient did stop his oral antibiotics briefly 4 months post EVAR. This led to recurrence of back pain and fever.

Although his blood cultures were negative on this occasion, he received a short course of parenteral antibiotics and restarted oral antibiotics once symptoms settled. This event strongly supports the need for lifelong antibiotic prophylaxis especially as potential septic source (mycotic aneurysm sac) was not eliminated. Notably, the follow-up CT 1 year later showed complete radiological resolution and normal inflammatory markers.

High index of suspicion is essential in making the diagnosis in cases of massive GI bleeding with a medical history of EVAR intervention. Our patient presented with massive GI bleeding 26 months after emergency EVAR, and although endoscopy suspected a graft erosion in D3, CTA and diagnostic angiogram both failed to demonstrate active bleeding or direct link to bowel.

The Multicenter Study on Aortoenteric Fistulization After Stent Grafting of the Abdominal Aorta (MAEFISTO) study group reported only 32 AEFs in 3932 patients who underwent EVAR. The study group reported a list of risk factors associated with this catastrophic complication, including local infection (mycotic aneurysm) and mechanical factors (graft pressure necrosis, migration, kinking or disruption of graft material, increased endotension, sac morphology and massive coil embolisation of the aneurysmal sac).[12]

The classic CT features suggestive of AEF include air bubbles surrounding the stent graft, periprosthetic fluid collection, thickening of the duodenal wall, and absence of interval tissue between the graft and bowel. Interestingly, all CT scans of the reported AEF in the MAEFISTO study did not detect contrast extravasation into the bowel. Endoscopy failed to diagnose AEF in 25% of the cases; however, Fluorodeoxyglucose -Positron emission tomography (FDG-PET) showed 100% sensitivity in detecting stent graft infection in all the 10 patients it was used for.[12] Our described case was no exception from the MAEFISTO study, and no contrast extravasation into bowel was found on CTA.

The complex management of AEF aims to control the haemorrhage, control sepsis and maintain the perfusion to the lower limbs.[13] Suprarenal and even supracoeliac aortic clamping is usually required to allow removal of infected prosthesis. This was reported in 82% of the patients in the MAEFISTO study.[12] To avoid placing vascular grafts in a contaminated area, an extra-anatomical bypass has been advocated. However, poor long-term patency of the axillobifemoral bypass grafts or bleeding from the aortic stump, 'blow out', is a major disadvantage. In situ graft repair has been reported to be a feasible technique in cases where there is an absence of grossly local infection or pus.[6] A combination of techniques is usually required, and the intervention is individually tailored.

We adopted in situ revascularisation with omental covering of the graft, which was suggested previously.[2 12] Although the use of cryopreserved allografts or venous graft 'femoropopliteal neoaortoiliac systems' is associated with longer operative time (>500 min), they have a better 5-year survival compared with prosthetic replacements.[14]

Unfortunately, the prolonged hospital stays expected in such a complex case coincided with the development of the COVID-19 pandemic across the region. Our initial management of the patient's desaturation focused on common causes of heart failure, acute kidney injury and ruling out pulmonary embolism. The initial CXR suggested bilateral atypical features. Subsequently, the patient tested positive for COVID-19, and serial CXRs showed what we later learnt to be a typical COVID-19 pattern. CXRs have a 69% sensitivity; CT has a low rate of missed diagnosis of COVID-19 of 3.9% and was suggested as a standard method for the rapid diagnosis of COVID-19.[15] Reverse transcription RT-PCR remains the gold standard with observed 91% sensitivity.[16]

Five days prior to COVID-19 diagnosis, the patient developed a seizure and homonymous hemianopia unexpectedly. At that time, his brain CT scan did not show evidence of stroke but was suggestive of encephalopathy syndrome (posterior reversible). Subsequent reports published later suggested that encephalitis with meningeal irritation symptoms and loss of consciousness can be a manifestation of the novel virus,[17] which seem a more plausible diagnosis in retrospect.

In a large multicentre review of 3011 COVID-19 infected patients, 2% non-ischaemic cardiac complications, including myocarditis and heart failure, were reported among 349 patients who developed cardiac complications,[18] and one patient developed severe left ventricular failure (LVEF 30%). We observed a similar result in the case reported with an LVEF of 35%.

Dysfunctional coagulation cascade and subsequent formation of intra-alveolar or systemic fibrin clots have been reported in coronavirus infections.[19] Thrombocytopenia and elevated D-dimer was reported in 36.2% and 46.4% of infected patients, respectively, which can contribute to bleeding complications. Similarly, fibrinogen levels and prothrombin time can be prolonged and might develop disseminated intravascular coagulopathy picture secondary to consumption, which carries a bad prognosis. In the case reported, fibrinogen, platelet count and coagulation profile remained within normal values during the COVID-19 infection period. D-dimer was expected to be elevated in the context of inflammatory response following major surgery and hence was not tested routinely. Different pathogenic mechanisms, including endothelial inflammation and coagulation activation, can explain multisystem presentations in patients with COVID-19, including our case (pulmonary, cardiac and neurological). Further medical research could explain multisystem involvement in patients infected with this novel virus.

COVIDSURG collaborative has shown a SARS-CoV-2 infection rate in the preoperative period in 294 out of 1128 (26.1%) patients. Thirty-day mortality was 23.8% (268 of 1128). Pulmonary complications occurred in 577 (51.2%).[20] Our patient was discharged from CCU 3 days following admission and was

Learning points

- During the current pandemic, COVID-19 should be excluded in unexplained presentations and atypical manifestations following surgical intervention.
- Open surgical management of primary mycotic aortic aneurysm should be considered if the patient is clinically stable and fit for surgery to allow vascular repair and removal of the infected aneurysm sac.
- Long-term antibiotics (or even lifelong) is required if mycotic aortic aneurysm is treated with endovascular aortic aneurysm repair (EVAR) as the septic sac is not eliminated.
- Aortoenteric fistula (AEF) should be considered as the potential aetiology of upper gastrointestinal bleeding, not only after open Abdominal Aortic Aneurysm (AAA) repair but also after EVAR, especially with high false-negative endoscopy and CT angiogram results observed.
- EVAR can be considered as a temporary 'bridging' measure in the treatment of bleeding AEF to stabilise the patient and to arrest bleeding and prepare for definitive surgical intervention if the patient is fit for surgery.

discharged 6 months ago with no further complication reported in his follow-up.

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