

A case of mycotic infrarenal abdominal aortic aneurysm after bacillus Calmette-Guérin immunotherapy for bladder cancer and a review of the literature

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ABSTRACT

A 69-year-old patient presented with a 9-month history of constitutional symptoms and a 3-week history of increasing abdominal and back pain. He had a history of bacillus Calmette-Guérin immunotherapy for bladder cancer 9 months earlier. An infrarenal mycotic aneurysm was detected by positron emission tomography-computed tomography. His abdominal aorta was reconstructed using a tube graft tailored from a bovine pericardium sheet. We chose this graft because of its acellular nature and reduced risk of postoperative infection. The culture from the aortic wall yielded acid fast bacilli, and he was treated with antituberculosis medication. His postoperative recovery was uneventful, except for chylous ascites. (J Vasc Surg Cases Innov Tech 2023;9:101213.)

Keywords: BCG vaccine; Bladder cancer; Mycotic aneurysm

Since its introduction in 1976, bacillus Calmette-Guérin (BCG) immunotherapy with a live attenuated form of *Mycobacterium bovis* has been used to treat high-risk superficial transitional cell carcinoma of the bladder. It has become one of the most accepted modalities of treatment owing to effectiveness and low complications rates. Nevertheless, the number of BCG treatment-related iatrogenic *M. bovis* infections with vascular involvement seems to be increasing. The patient provided written informed consent for the report of his case details and imaging studies.

CASE REPORT

A 69-year-old man presented to our unit with a 3-week history of increasing abdominal and back pain. He was already receiving medical investigations for a 9-month history of night sweats, a poor appetite, and weight loss.

His medical history included intravesical BCG immunotherapy between 2015 and 2017 for bladder cancer. He reported that he had developed a high fever after his last therapy session. At that

stage, one of his three urine samples cultured *M. bovis*, but this was treated conservatively.

The most recent investigations by the respiratory team confirmed normal chest radiograph findings, three negative urine samples, a normal full blood count, and normal liver function test, renal function test, and prostate-specific antigen test results. Only two nonspecific abnormalities were noted on the blood tests: an elevated alkaline phosphatase level (240 IU/L) and vitamin D deficiency. He was referred to the hematology department for consideration of an investigation for lymphoma. He underwent positron emission tomography, which detected an inflammatory aortic aneurysm, for which he was referred to our service initially as an outpatient.

Because of his history of back pain and the possibility of a mycotic aneurysm, we advised the patient to present to our unit for assessment. On admission, he was afebrile with normal vital signs; however, his aneurysm was tender. His blood test panel showed a white blood cell count of $6.8 \times 10^3/\text{dL}$, erythrocyte sedimentation rate of 6 mm/h, and a C-reactive protein level of 25 mg/L. His computed tomography angiogram suggested a 5.8-cm inflammatory aneurysm suitable for endovascular aneurysm repair (EVAR; Fig 1).

Overnight, the patient had one temperature spike to 38.2°C, which subsequently settled. Although the working diagnosis was an inflammatory aneurysm, we could not safely rule out the possibility of a mycotic aneurysm. Thus, we decided to treat the aneurysm as a mycotic aneurysm until proved otherwise. Because of his fitness and the possible ongoing infection, we opted for open repair. Intraoperatively, the patient had a large retromesenteric hematoma, an invasive inflammatory mass involving the infrarenal abdominal aorta with aortic wall disintegration, but no evidence of active aortoenteric fistula formation (Fig 2).

Teicoplanin and gentamicin were administered preoperatively, the inflammatory mass was debrided, and the abdominal aorta was reconstructed using a tube graft tailored from a bovine pericardium sheet (Fig 3). The bovine pericardium sheet was rolled

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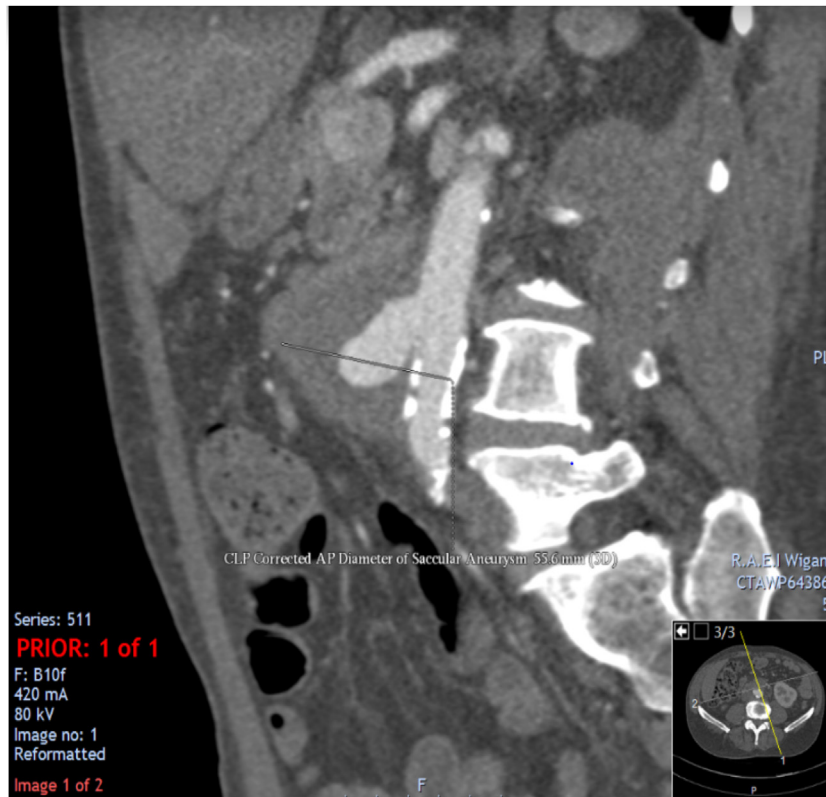


Fig 1. Computed tomography angiogram showing aneurysm of infrarenal aorta.

into a tube with the lumen adjusted to the size of the aorta. The extra material was excised, and the ends of the sheet were sutured in two layers using nonabsorbable monofilament sutures to one half the length of the graft. The proximal end was anastomosed, and clamps were applied to the proximal “neo-aorta.” The length was then adjusted to ensure a tension-free distal anastomosis, and the repair was completed using the same nonabsorbable monofilament sutures. We performed a rifampicin washout, and omental wrapping was used around the repaired aorta. Peritoneal fluid, para-aortic lymph nodes, and aortic tissue were sent for culture, including an urgent acid-fast bacilli assessment.

We chose bovine pericardium for biologic xenograft repair to avoid the use of synthetic material in an infected field. We believed that its acellular nature would be advantageous if the infection proved to be due to *M. bovis* owing to the intracellular nature of mycobacterium infection and spread.

His initial postoperative recovery was uneventful. Histologic examination of the para-aortic lymph nodes showed sterile noncaseating granuloma. Fluid from the abdominal cavity and the mesenteric hematoma were negative; however, the aortic wall hematoma tested positive for acid-fast bacilli. Subsequent culture and sensitivity tests yielded a BCG-vaccine strain of mycobacterium typically resistant to pyrazinamide. The patient developed transient deafness 24 hours after gentamicin treatment, which was stopped immediately, with good recovery.

The patient spent 4 days in the high dependency unit and 20 days in the ward and was finally discharged with

antituberculosis medication on advice from the hematology and respiratory teams. However, the patient was readmitted 5 weeks later to a satellite hospital with tense abdominal ascites, which proved to be chylous on abdominal paracentesis. The chylous was successfully treated with drainage, parenteral feeding, and octreotide for a 2-week period. The most likely cause of the chylous ascites was secondary to injury to the peri-aortic lymphatics and/or lower cisterna chyli that had not been recognized intraoperatively. The patient underwent regular clinical follow-up visits for 3 years with annual ultrasound surveillance. His last ultrasound scan confirmed an intact repair with no evidence of reaction or collection and no pathologic dilatation. He will continue long-term clinical follow-up and annual ultrasound surveillance.

DISCUSSION

BCG has been used since 1921 for prophylaxis of tuberculous infection.¹ It has been used in the treatment of bladder cancer for the last few decades. Intravesical instillation of BCG is recommended by the European Association of Urology guidelines to treat intermediate- and high-grade tumors.² It has been associated with serious side effects in <5% of the patients. BCG-related infection has been reported in <1% of the patients.³ Our case is one of the rare cases of mycotic aneurysm with BCG strain mycobacterium and aortic

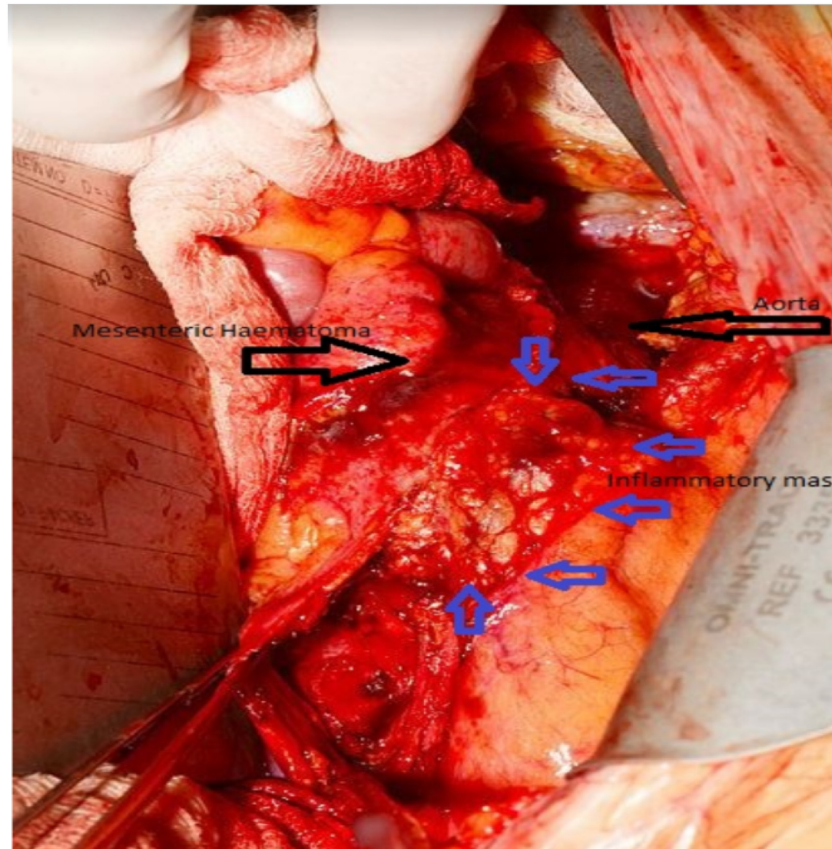


Fig 2. Intraoperative image showing inflammatory mass and aneurysm.

reconstruction using bovine pericardium in the context of BCG infection with long-term follow-up.

We found 37 reported cases of primary infrarenal abdominal aortic mycotic aneurysms after BCG intravesical treatment of bladder cancer, including our case⁴⁻³⁷ (Table). The mean age at presentation was 72.38 years (range, 57-94 years). In addition, all the patients were men. Although the latter could have been because bladder cancer is more common among men, the finding of no female patients at all is difficult to explain. The aortic wall can be infected by invasion of the degenerated lymph nodes, invasion of the vasa vasorum into the media or adventitia, or direct invasion from adjacent structures.³⁸ In our patient, both the peritoneal fluid cultures and lymph node tests were negative, and only the aortic wall hematoma tested positive, providing more support to the theory of spread via the vasa vasorum. The reports provided insufficient data to discern any patterns regarding the dose, duration of therapy, cancer stage, and symptoms after BCG treatment. However, a pattern was noted of patients reporting a fever soon after or during BCG therapy. Of the nine patients with fever reported, five had developed fever during or soon after treatment, two of whom were treated for septic shock.

Mycotic aneurysm formation is usually a late presentation of BCG bladder treatment with a latent period of 17 months after intravesical injection.³⁹ Our patient presented 9 months after his last intravesical treatment. Back pain and low-grade fever are the most common presenting symptoms. The diagnosis of a tuberculosis aneurysm depends on the clinical presentation and mycobacterial culture results. Culture of mycobacterium will take 6 to 8 weeks and requires 10,000 organisms per 1 g of tissue.¹⁹ Thus, the culture yield for this organism is usually low. However, in the primary infrarenal aorta, 29 of the 37 cases (78%) yielded positive cultures.

The basic principle of infected aortic aneurysm management is excision and debridement of all infected tissue and restoration of perfusion to lower limbs with arterial reconstruction using either extra-anatomic bypass or in situ reconstruction. With extra-anatomic bypass, the concerns are aortic stump blow out and the durability of the bypass. The patency rate for the axilofemoral graft is 64% to 75% at 5 years and the reported life-threatening bleeding rate with stump blow out is $\leq 27\%$.⁴⁰ Aortic reconstruction can be performed using antibiotic-impregnated prosthetic grafts, cryopreserved allografts, or neo-aortic reconstruction with vein or

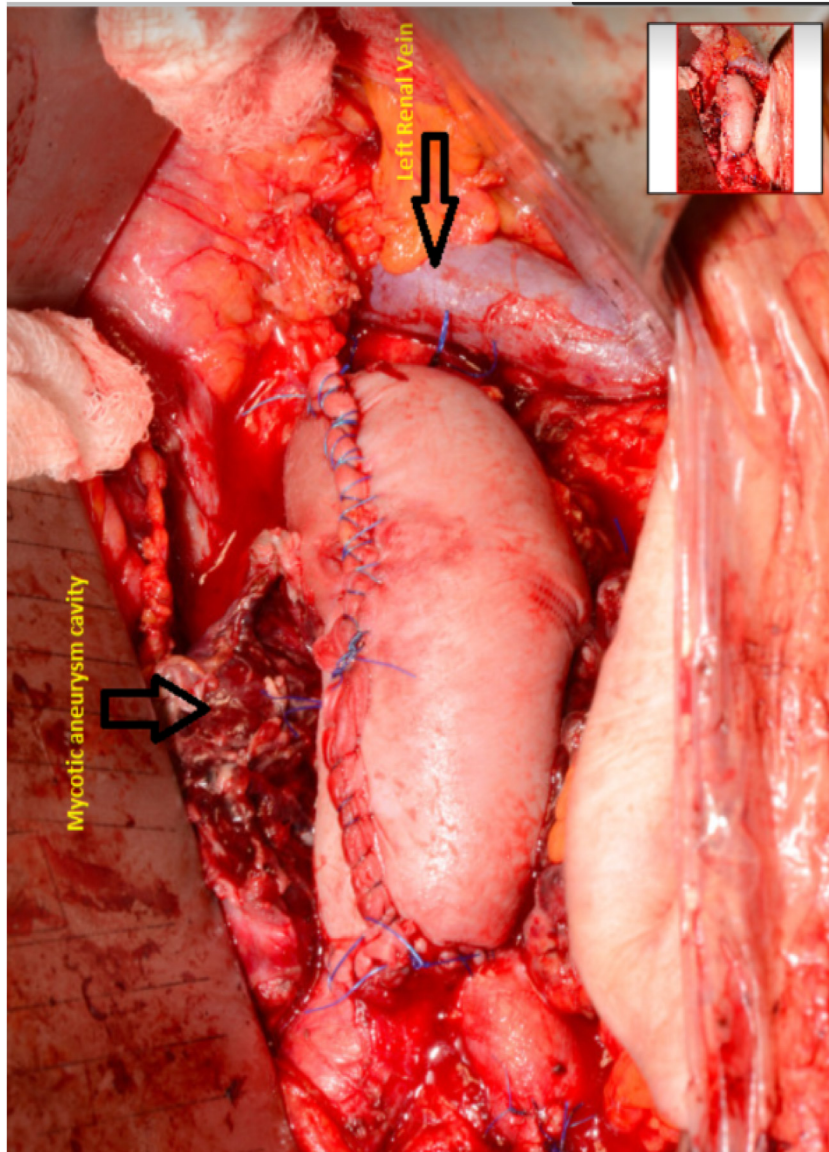


Fig 3. Postoperative view of reconstructed aorta with biologic graft.

biologic grafts. Prosthetic reconstruction can be performed relatively more quickly compared with other methods but has high reinfection rates. In our review, 29 of the 37 patients (78%) had undergone prosthetic graft reconstruction (16 aortic grafts, 3 axillofemoral grafts, and 10 EVAR stents). Four more patients had undergone surgery; however, the type of surgical repair was not specified. Only three patients had undergone “biologic” graft repair but with three different materials.

A secondary aortoenteric fistula was reported only in two cases. However, because the follow-up periods were short, later complications were likely less often reported. A cryopreserved allograft has the risk of late aneurysmal formation.⁴¹ Neo-aorta iliac reconstruction with a vein graft has less risk of infection but is a complex

surgery with higher rates of complications and significant morbidity.^{42,43}

Notably, the gold standard of autologous vein reconstruction was used in only one patient (2.7%), a reflection of the general unfitness of these patients at presentation to tolerate such an extensive surgery. Another patient underwent cryopreserved allograft reconstruction but only survived 9 months. In addition, our patient underwent reconstruction with a bovine pericardium graft. The patient treated conservatively did not survive.

To the best of our knowledge, the present case is the first case of a tuberculosis mycotic aneurysm treated with biologic graft neo-aorta reconstruction using a bovine pericardial sheet. This method is relatively quicker compared with vein reconstruction, and the risk of

Table. Summary of literature review

Investigator	Age, years	Sex	Time from BCG treatment, months	Symptoms	Location	Procedure	Culture results	Status at last follow-up
Deresiewicz et al ⁴	67	Male	14	Loss of weight	Infrarenal aorta and iliac arteries	Axillofemoral bypass	Negative	Died
Wolf et al ⁵	80	Male	24	Back pain, malaise, night sweats	Infrarenal aorta	Prosthesis complicated by aortoenteric fistula; required axillofemoral bypass	Positive	Aortoenteric fistula after 20 months
Hellinger et al ⁶	71	Male	25	NS	Infrarenal aorta	Prosthesis	NS	Survived (NS)
Rozenblit et al ⁷	76	Male	69	Back pain, weight loss	Infrarenal aorta	Stenting	Positive	Died after 15 months of myocardial infarction
Damm et al ⁸	71	Male	4	Back pain, fever	Infrarenal aorta	Prosthesis	Positive	Survived (NS)
Seelig et al ⁹	58	Male	30	Back pain, low-grade fever, weight loss	Infrarenal aorta	Prosthesis	Positive	Survived (11 years)
Seelig et al ⁹	71	Male	53	Low-grade fever	Infrarenal aorta and popliteal artery	Prosthesis	Positive	Survived (4 years)
Wada et al ¹⁰	75	Male	32	NS	Infrarenal aorta and femoral artery	Prosthesis	NS	Survived (NS)
Dahl et al ¹¹	69	Male	18	Back pain, radiculopathy	Infrarenal aorta	Prosthesis	Positive	Survived (NS)
Harding et al ¹²	80	Male	24	Fever, malaise, weight loss	Juxtarenal aorta	Prosthesis	Positive	Survived (15 months)
Safdar et al ¹³	79	Male	11	Intermittent fever, night sweats, chills, fatigue	Infrarenal aorta	Axillofemoral bypass	Positive	Survived (3 months)
Costiniuk et al ¹⁴	75	Male	24	Abdominal and back pain	Infrarenal aorta and femoral artery	Prosthesis	Positive	Survived (9 months)
Khandelwal et al ¹⁵	68	Male	36	Fever, back pain, night sweats	Infrarenal aorta	Axillofemoral bypass	Positive	Survived (NS)
Psoinos et al ¹⁶	69	Male	4	Abdominal pain, fever, malaise, weight loss	Infrarenal aorta	Cryopreserved allograft	Positive	Survived (9 months)
Samadian et al ¹⁷	94	Male	23	Back pain, malaise, functional impairment	Infrarenal aorta	NS	Positive	NS
Roylance et al ¹⁸	77	Male	18	Aortoenteric fistula	Infrarenal aorta	Prosthesis	Negative	Died
Floros et al ¹⁹	57	Male	14	Abdominal pain	Infrarenal aorta	Stenting	NS	Left against medical advice 4 days after surgery

(Continued on next page)

Table. Continued.

Investigator	Age, years	Sex	Time from BCG treatment, months	Symptoms	Location	Procedure	Culture results	Status at last follow-up
Leo et al ²⁰	81	Male	36	Acute periumbilical pain, 10-month history of low-grade fever, lower back pain, weight loss	Infrarenal aorta	Primary stent developed psoas abscess after 2 months; required open drainage	Positive	Died after 10 months of acute cerebral hemorrhage
Leo et al ²⁰	70	Male	24	Back pain, low-grade fever	Infrarenal aorta	Prosthesis	Positive	Survived (3 months)
Smith ²¹	68	Male	NS	Night sweats	Infrarenal aorta	Stenting	NS	Survived (NS)
Kusakabe et al ²²	76	Male	12	Back pain, malaise, loss of appetite	Infrarenal aorta	Prosthesis	NS	Survived (3 months)
Berchiolli et al ²³	70	Male	3	Back pain	Infrarenal aorta	Primary stent complicated by aortoenteric fistula; required graft explantation and axillobifemoral bypass	Specific antituberculosis culture not requested	Died
Lareyre et al ²⁴	75	Male	36	Back pain, weight loss	Infrarenal aorta	Prosthesis	Positive	Survived; at 1 year developed graft infection
Yildiz et al ²⁵	78	Male	5	Fever, night sweats	Infrarenal aorta	Surgery (NS)	Positive	NS
Coddington et al ²⁶	72	Male	8	Malaise, fever	Infrarenal aorta	Prosthesis	Positive	Survived (1 month)
Tehrani et al ²⁷	73	Male	NS	Abdominal pain, low-grade fever	Infrarenal aortic pseudoaneurysm	Stenting	Positive	Survived (3 months)
Nam et al ²⁸	70	Male	1	Low back pain, cyanotic toes	Infrarenal aorta and iliac arteries	Prosthesis	Positive	Survived (18 months)
Nishizawa et al ²⁹	72	Male	4	Fatigue, poor appetite, weight loss	Infrarenal aorta	Stenting followed by abscess; required open surgery with prosthesis	Positive	Survived (11 months)
Flynn et al ³⁰	72	Male	8	Fever, night sweats, abdominal pain	Infrarenal aorta	Stenting	Positive	Survived (8 months)
Wadhwani et al ³¹	67	Male	4	Weight loss, night sweats	Infrarenal aorta	Autologous vein graft	Positive	Survived (6 months)
Darriet et al ³²	66	Male	24	Weight loss, low-grade fever	Infrarenal aorta	Surgery (NS)	FISH positive	Survived (9 months)
Okon et al ³³	76	Male	NS	Low-grade fever, weakness, night sweats, weight loss	Infrarenal aorta	Conservative; unfit for surgery	Positive	Died
Simar et al ³⁴	78	Male	5	Fever, weight loss, malaise	Infrarenal aorta	Surgery (NS)	Positive	Survived (2 years)
Holmes et al ³⁵	64	Male	5	Back pain	Suprarenal aorta	Prosthesis	Positive	Survived (10 months)

Table. Continued.

Investigator	Age, years	Sex	Time from BCG treatment, months	Symptoms	Location	Procedure	Culture results	Status at last follow-up
Mizoguchi et al ³⁶	81	Male	24	Incidental	Infrarenal aorta	Stent infected; required extra-anatomic bypass	Positive	NS
van Moorselaar et al ³⁷	60	Male	1	Malaise, back pain	Infrarenal aorta (AAA present before BCG, which rapidly enlarged and ruptured after BCG)	Stenting after graft infection managed with CT-guided drainage	Positive	Survived (12 months)
Present patient	69	Male	9	Loss of appetite, weight loss, back pain	Infrarenal aorta	Bovine pericardium sheet	Positive	Survived

AAA, Abdominal aortic aneurysm; BCG, bacillus Calmette-Guérin; CT, computed tomography; FISH, fluorescence in situ hybridization; NS, not specified.

reinfection is less. Commercially available patches are processed to be acellular, preventing transplanta-tion of bovine proteins or DNA into the host.⁴⁴

Glutaraldehyde is a typical processing agent, crosslinking –NH₂ groups of lysine, hydroxylysine, or the N-terminus of amino acids, to form amine linkages with the elimination of water. These amine linkages form covalent bonds between adjacent proteins that are stable at physiologic temperatures and pH. The resultant cross-linking process increases the tissue strength to inhibit biodegradation and reduces antigenicity to sterilize the tissue.⁴⁵

Stenting can be a bridging therapy for patients with a bleeding aneurysm in an aortoenteric fistula or pseudoaneurysm. Once stabilized, the patient will require definitive treatment. Of the 37 treated patients, 10 had received EVAR stenting, which could have been related to the perceived patient fitness at the time. One patient did not survive, and six patients had documented follow-up data available. The mean survival for the latter was 9.8 months (range, 3-15 months), likely related to persistent infection and poor baseline function. There are even a few reported cases of tuberculosis infection occurring in existing grafts and previous stents.⁴⁶ Conservative treatment with long-term antibiotics is preserved for patients deemed to be unfit for any surgery, most of whom die within the first 2 years.²³

After 3 years of follow-up, our patient did not have any complications related to surgery. The 2020 European Society of Vascular Surgery clinical practice guidelines on the management of vascular graft and endograft infections recommends cryopreserved allografts as the first choice for the conduit. However, the use of a bovine pericardial sheet requires further evidence.⁴² Interest is increasing in the use of this technique, and the

medium-term results at least are very encouraging.⁴⁷ We have used this option in our unit to treat infected grafts with various organisms during the past 4 years with good medium- to long-term outcomes.

CONCLUSIONS

We believe reconstruction with a bovine pericardial sheet can be considered for patients with an infected aneurysm because of the relatively quicker surgery compared with other graft materials and the lower risk of reinfection and late aneurysmal degeneration. More patients and additional studies are needed to support its widespread use and confirm the long-term durability of such an approach.

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