Distinguishing Sterile Inflammation from Graft Infection

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Case Report

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Abstract

Background:

It is often difficult to distinguish a noninfectious inflammatory response from infection in peri-graft fluid collection. The diagnosis of graft infection is usually based on clinical findings supported by the clinical course and radiological and microbiological investigations.

Case presentation:

We describe a 68-year-old man who underwent ascending aortic replacement and thoracic endovascular aortic repair. Four years later, the patient noticed right neck pain, and CT showed that the fluid in the mediastinum had expanded and extended to the neck. Echocardiography revealed progressive severity of aortic regurgitation and decreased ejection fraction. Given the progression of aortic regurgitation, decreased cardiac function, and rapidly expanding fluid collection causing neck pain, surgery was indicated. All microbiological tests, including polymerase chain reaction, were negative. The patient was being followed without antibiotics, and CT did not show peri-graft fluid 2 years postoperatively.

Conclusions:

We cannot exclude the infection completely, but we report the importance of medium selection, additional medium orders, extension of culture, genetic testing, and communication with microbiology laboratories when normal culture tests for general bacteria and fungi were all negative, which can successfully avoid increased drug-resistant bacteria count, elevated medical costs, and drug side effects due to the improper use of antibiotics through proper diagnosis.

Case Presentation

The patient was a 68-year-old man who underwent partial arch replacement with brachiocephalic artery reconstruction for Stanford type A dissection at our hospital 4 years ago. In the same month, zone 1 two-debranched thoracic endovascular aortic repair (2d-TEVAR) with an axillo-axillary and axillo-left common carotid bypass was performed for enlargement of the false lumen at the distal arch (50 mm).

One month prior, annual follow-up CT was conducted, and fluid collection was observed around the ascending aorta graft and 2d-TEVAR without any symptoms.

Two weeks before surgery, the patient noticed neck pain on the right side, and plain CT revealed that the fluid in the mediastinum had expanded and extended to the right neck side (Figure 1). The patient was hospitalised and developed a fever. After two sets of blood cultures were performed, antibiotics (ampicillin 3 g per 12 hours) were started, and the fever subsided. (18) F-fluorodeoxyglucose ((18)F-FDG) positron-emission tomography (PET) confirmed high accumulation (standardized uptake values max; SUV max) around the fluid (Figure 2 a, b). Graft infection was considered, given the improvement in fever after administration of antibiotics, improvement in blood test findings, and accumulation noted on PET.
CT-guided needle aspiration was conducted. Approximately 150 mL of yellow-white and highly viscous fluid was collected, showing an abundance of neutrophils, which was suggestive of infection upon microscopic examination, but the culture was negative. Echocardiography revealed progressive severity of aortic regurgitation and decreased ejection fraction. Given the progression of aortic regurgitation, decreased cardiac function, and rapidly expanding fluid retention causing neck pain, surgery was indicated.

Thorough a median re-sternotomy, avoiding the subclavian artery graft bypass, cardio-pulmonary bypass was established with the femoral artery and vein. Abscess-like fluid erupted in the mediastinum; this was cultured. The stent graft was exposed, and no native aortic wall was observed (Figure 3). Yellowish-white and highly viscous fluid was retained around the prosthetic and stent grafts. The proximal and distal anastomoses were highly adhered, and we could not remove the prosthetic and stent grafts. Although the aortic annulus was 25 mm, due to a felt strip inside the proximal anastomosis and the narrow sinotubular junction, we managed to put a 21-mm bioprosthetic valve in the supra-annular position. The aortotomy was closed in two layers. Haemostasis was confirmed in the pericardium, and the omentum was collected. The area around the grafts was washed with lavage fluid, and omental filling was conducted whereupon the surgery was completed. After consultation with the infectious disease department and microbiology laboratory, additional cultures from all preoperative and intraoperative fluid collections were performed in liquid medium for enrichment culture. Then, they showed all negative results confirmed using polymerase chain reaction (PCR) with 16S rRNA for bacteria and 18S rRNA for fungi. The preoperative blood cultures were extended for four weeks and were negative. Postoperative antibiotics were discontinued after PCR tests were negative. The patient was being followed without antibiotics, and CT did not show peri-graft fluid 2 years postoperatively.

**Discussion**

It is often difficult to distinguish noninfectious inflammatory responses from infections in peri-graft fluid collection. The diagnosis of graft infection is usually based on clinical findings supported by the clinical course and radiological and microbiological investigations.

In the clinical course, noninfectious persistent fluid collection or soft-tissue attenuation was observed for up to 3 months postoperatively.\(^4\) In some cases, peri-graft fluid may be seen for up to 1 year without infection.\(^5\)

On CT, abscesses may present as low-attenuation masses, exhibiting rim enhancement following contrast agent injection.\(^6-10\) Other findings suggestive of infection include air bubbles within the abscess cavity and adjacent soft tissue.\(^6,7,9,11-13\)

Regarding CT values and SUV max, it has been reported that an abscess is > 25 HU and a seroma is < 25 HU\(^14\); and some authors have reported 6.3 SUV is a good cut-off value for the differential diagnosis of inflammation and infection\(^15\), even though there are no general criteria published for these two
processes. It has also been reported that SUV max cut off values could serve as an interesting monitoring tool for the response to antibiotic treatment\textsuperscript{16}. In this case, (18)F-FDG PET-CT was negative 2 years after the second surgery (Fig. 3. a,b). Blood culture can be false negative, or the same bacteria as graft infection may not be detected. CT-guided needle aspiration for culture has been proposed to obtain fluid collection around the graft\textsuperscript{17}. In addition, bacteria may not be detected even though a large number of specimens can be collected.

Possibilities include attenuated bacteria, such as Staphylococcus epidermidis, in which a large amount of WBC is observed but no microorganisms are detected\textsuperscript{18}, and the culture becomes negative when antibiotics are preceded. In that case, the sensitivity can be increased by extending the culture period\textsuperscript{19} or by transferring to enriched medium. Furthermore, PCR is more sensitive and contributes to the diagnosis of graft infection in patients with culture-negative infections\textsuperscript{20}.

We conducted CT-guided needle aspiration for peri-graft fluid collection around the prosthetic and stent grafts and collected approximately 70 cc of a highly viscous, yellowish-white WBC specimen. The culture showed negative findings even on liquid medium for enrichment culture, and the PCR findings were confirmed as negative. We also suspected that seromas, accompanied by a capsule, represent the most common noninfectious cases\textsuperscript{21–23}. However, no such capsule was observed during the re-do surgery. This time, the stent graft was exposed during surgery, and no native blood vessels were observed. It is thought that this might be related to fluid collection around the stent graft in this study. In fact, it has been reported that stent-graft placement causes a thinning of blood vessels. The aortic wall is nourished by the vasa vasorum and endoluminal diffusion;\textsuperscript{23–25} in TEVAR, an endovascular stent graft covers the vessel luminal wall, disrupting both trophic pathways. As a result, necrosis of the intima,\textsuperscript{26} media,\textsuperscript{27} and adventitia\textsuperscript{28} has been reported. In our patient, the cause of fluid collection around the vascular prosthesis was compression of the vaso-vasorum due to the use of an oversized stent and excessive stress being applied, resulting in aortic ischaemia and inflammatory changes, with inflammation potentially forming a non-infectious abscess. There are some limitations in this report. First, the infection may be controlled only by the omentum, although it is rare to have no recurrence of the infection without long-term antibiotic use and removal of prosthetic or stent grafts. Second, the patient was followed for only 2 years without antibiotics. Since peri-graft fluid collection occurred 2 years after the first surgery, there is a possibility that symptoms will appear in the future if it is the same microbe.

We cannot conclude that extending the culture period, submitting additional enriched culture and PCR can exclude the infection completely, but it can successfully avoid increased drug-resistant bacteria count, elevated medical costs, and drug side effects due to the improper use of antibiotics through proper diagnosis.

**Conclusion**
We report a case of rapid peri-graft fluid collection 2 years after 2d-TEVAR. When graft infection is suspected when normal culture tests for general bacteria and fungi are all negative, we emphasize the importance of medium selection, additional medium orders, extension of culture, genetic testing, and communication with microbiology laboratories. We successfully avoided increased drug-resistant bacterial counts, elevated medical costs, and drug side effects due to the improper use of antibiotics through proper diagnosis.

**Declarations**

**Ethics approval and consent to participate**

Not applicable

**Consent for publication**

The author obtained consent for publishing this case report from the patient.

**Availability of data and materials**

All data generated or analyzed during this study are included in this published article.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors’ contributions**

AM drafted the manuscript, provided the original images, and performed the aortic surgery. YM performed the aortic surgery and was in review. YA was in review and editing. TN managed perioperative care. All authors read and approved the final manuscript.

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Figures
Figure 1

The CT value of peri-graft fluid collection (Blue color) was 30-40 HU.

Figure 2

(18)F-fluorodeoxyglucose ((18)F-FDG) positron-emission tomography (PET) before surgery.
2a: The fluid in the mediastinum had expanded and extended to the right neck side (Green arrow).

2b: The PET confirmed 14.2 standardized uptake values max (SUV max) around prosthetic and stent graft.

Figure 3

(18)F-fluorodeoxyglucose ((18)F-FDG) positron-emission tomography (PET) 2 years after surgery.

3a,b: The PET confirmed decreased standardized uptake values max (SUV max) around prosthetic and stent graft.