A Case of Vascular Graft Infection Caused by Haemophilus parainfluenzae

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Haemophilus parainfluenzae is a gram-negative coccobacillus that is part of the normal flora in the human upper airway and sometimes causes infective endocarditis. We present a case of a 68-year-old Japanese man who had vascular graft infection caused by H. parainfluenzae 4 years after surgery for chronic aortic dissection.

Keywords. vascular graft infection; oral suppressive therapy; pseudoaneurysm.

Members of the genus Haemophilus are small gram-negative coccobacilli with fastidious growth requirements. Haemophilus parainfluenzae accounts for ~75% of the Haemophilus flora of the human upper airway. It is now increasingly recognized as a cause of infective endocarditis, causing up to 5% of cases of endocarditis, along with other slow-growing organisms, the so-called HACEK organisms (Haemophilus spp., Aggregatibacter spp., Cardiobacterium spp., Eikenella spp., and Kingella spp.) [1]. However, reports of other infections caused by H. parainfluenzae, such as surgical site infections or infections of prosthetic materials, are rare [2–4]. Here, we present a case of vascular graft infection (VGI) caused by H. parainfluenzae.

CASE PRESENTATION

A 68-year-old Japanese man with hypertension was discovered to have a pseudoaneurysm at the anastomosis section of the ascending aorta on a computed tomography (CT) scan (Figure 1) during a routine follow-up visit to the outpatient clinic in 2021. He had undergone total arch replacement with an elephant trunk procedure and right coronary artery–saphenous vein graft bypass for chronic DeBakey I/Stanford A thoracic aortic dissection in 2017. The aorta was repaired with a 3-layer knitted Dacron graft (22 mm). As a complication, he had renal failure, for which he was on hemodialysis temporarily. He successfully weaned from dialysis on postoperative day (POD) 21. He had no other postoperative complications other than this event.

After that, he was followed up at the outpatient clinic by a cardiovascular surgeon. In addition to routine blood tests every 3 months, the surgeon was taking CT scan images to monitor any postoperative complications every 6 months. In the CT scan taken in 2021, despite the absence of symptoms, including fever and chest pain, the cardiovascular surgeon suspected VGI based on a newly formed pseudoaneurysm in the anastomosis section, which was not present in previous CT images. A decision was made to perform re-replacement of the ascending aorta. The patient had smoked 3 packs of cigarettes per day until quitting 8 prior. He denied any illegal drug use, recent dental procedures, and recent antibiotic treatment within the 3 months prior. His preoperative laboratory data taken 1 day before the surgery showed a mild increase in inflammatory markers, with a white blood cell count of 9270 cells/μL (neutrophil 85.0%) and C-reactive protein of 4.47 mg/dL. Other than that, his blood test results were unremarkable.

At the time of surgery, blood cultures from the peripheral blood were not collected before initiation of prophylactic antimicrobials (cefazolin 1 g). During the surgery, there was some pus around the graft, but no aorto-enteric fistulas. The infected graft was partially replaced with a woven gelatin-coated graft, Gelweave (24 mm). No flap coverage procedures were done. A total of 13 samples were collected from the anastomosis site, the felt, pseudoaneurysm, pericardial sac, and the removed graft, and all were submitted for culture. After the surgery, the patient was administered intravenous (IV) meropenem (1 g every 8 hours) and vancomycin with a target trough level of 15–20 μg/mL for suspected VGI.

All 13 samples were found to be positive for H. parainfluenzae ~24 hours after inoculation on chocolate agar, which was identified by matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) [5]. Antimicrobial susceptibility testing was performed using the microbroth dilution method (MICroFAST 6); Beckman Coulter, Inc.) according to the Clinical and Laboratory Standards Institute recommendations [6] (Table 1). Based on the culture results,
the patient was diagnosed with intrathoracic VGI caused by *H. parainfluenzae*.

On POD 4, an infectious diseases (ID) consultation team was consulted on the selection of antibiotics and the further management of the *H. parainfluenzae* VGI. The patient’s postoperative clinical course was uneventful. At the time of ID consultation, his vital signs were stable, with a body temperature of 36.0°C, oxygen saturation of 98% on oxygen 4 L/min via nasal cannula, blood pressure of 126/80 mmHg, and heart rate of 73 bpm. On physical examination, several cavities in his teeth were noted, which were also confirmed by dentists. None of them were infected or complicated with gingivitis. Although they were no culture tests performed preoperatively in this case, we performed culture tests with a nasal swab and sputum on POD 5 to evaluate the entry point of *H. parainfluenzae*; the tests were negative for *H. parainfluenzae*. In addition, the transthoracic echocardiography done on POD 7 did not show any signs of endocarditis.

The ID consultation team recommended de-escalation of the antimicrobials, from meropenem and vancomycin to ceftriaxone 2 g per day every 24 hours. From POD 12, the patient experienced hospital-acquired pneumonia due to *Pseudomonas aeruginosa*, which was treated with piperacillin-tazobactam. His postoperative course was otherwise uneventful. A CT image taken on POD 27 did not show any worsening signs around the newly replaced graft. The inside of the graft and each branch of the arch were enhanced well by the contrast material, which showed that the graft was functioning properly. No ectopic gas was observed. Thus, we decided to discontinue his IV ceftriaxone and switch to oral long-acting cephalixin (1 g twice daily) on POD 29. The patient was discharged home on POD 32.

After 5 months of surgery, his renal function started to get worse, so we discontinued oral long-acting cephalixin and switched to clarithromycin 500 mg once daily, suspecting drug-induced kidney injury due to cephalixin. After changing the antibiotics, his renal function recovered. During this time, he received endoscopic mucosal resection (EMR) for colon cancer 5 months after the surgery and underwent another surgery for lung cancer 7 months after the surgery for VGI; these cancers were both incidentally found in the preoperative CT scan for VGI. Because of these surgeries, we decided to extend his antibiotic therapy until both EMR and the surgery are safely complete.

### Table 1. Results of Antimicrobial Susceptibility Tests of *Haemophilus parainfluenzae*

| Antimicrobial | MIC µg/mL | Interpretive Categories |
|---------------|-----------|------------------------|
| ABPC         | =2        | I                      |
| ABPC/CVA     | =2        | S                      |
| ABPC/SBT     | =2        | S                      |
| CCL          | =2        | S                      |
| CTM          | =2        | S                      |
| CTX          | =1        | S                      |
| CTRX         | =0.25     | S                      |
| CPM          | ≥4        | *                     |
| MEPM         | =0.5      | S                      |
| CAM          | =8        | S                      |
| MINO         | ≤0.5      | S                      |
| CP           | =1        | S                      |
| ST           | ≤0.25     | S                      |
| LVFX         | ≤0.03     | S                      |
| CPFX         | ≤0.03     | S                      |
| RFP          | ≤0.5      | S                      |

Abbreviations: ABPC, ampicillin; CAM, chloramphenicol; CCL, cefpodoxime; CPM, cefpodoxime; CP, cefoperazone; CPFX, ciprofloxacin; CTM, cefotiam; CTRX, ceftriaxone; CTX, cefotaxime; CVA, clavulanic acid; I, intermediate susceptibility; LVFX, levofloxacin; MEPM, meropenem; MIC, minimal inhibitory concentration; MINO, minocycline; RFP, rifampicin; S, susceptible; SBT, sulbactam; ST, trimethoprim-sulfamethoxazole.

*MIC breakpoints are not set.*

**Figure 1.** Computed tomography scan images of the aorta and the vascular graft. **A**, Computed tomography scan performed immediately after the surgery in 2017. **B**, Follow-up contrast-enhanced CT scan performed at an outpatient clinic follow-up visit in 2021 showing a new pseudoaneurysm in the ascending aorta (white arrow). Abbreviation: CT, computed tomography.
done. He is currently being followed up at our outpatient clinic and is still taking clarithromycin. His postoperative clinical symptoms, vital signs, laboratory data, and CT scans in the outpatient clinic have not shown any evidence of a recurrence of VGI during the past 8 months of follow-up. We are considering discontinuation of his antibiotics ≏ 9 months after the surgery.

DISCUSSION

Since the early 1950s, synthetic materials have been widely employed in reconstructive vascular surgery. As a result, VGI has been observed as an infrequent but serious complication and is associated with a high morbidity, and is sometimes fatal [7, 8]. The major complications of VGI include sepsis, disruption of the infected anastomotic suture line with rupture or pseudoaneurysm formation, and reinfection of reconstructed vascular grafts. The infection rate is 1%–5%, and coagulase-negative staphylococci are the most common pathogens (42%), followed by *Staphylococcus aureus* (29%) [9]. *Pseudomonas aeruginosa* is the most common cause of gram-negative infections and accounts for at least 10% of VGIs [10]. The clinical manifestations vary depending on whether the infection occurs within 2 months postoperatively or is delayed. As shown in this case, late-onset infection is less often characterized by signs of systemic sepsis. In these cases, the infection is often indolent, with a lack of graft incorporation by the surrounding tissue and pseudoaneurysm at the anastomotic site. The basic treatment strategy recommended by the American Heart Association guidelines is the administration of antibiotics and operative repair of the infected graft [7].

To the best of our knowledge, there has been only 1 case of VGI caused by *H. parainfluenzae* reported previously [3]. This case was about an early-onset, extracavitary VGI in the groin after common femoral artery endarterectomy and superficial femoral artery angioplasty. In this case report, the VGI was polymicrobial, with initial culture tests of the surgical wound showing *Staphylococcus epidermidis* and *Escherichia coli*, and only later growing *H. parainfluenzae*. In contrast to this case, our case was a late-onset, intracavitary VGI that occurred 4 years after the initial surgery. In addition, compared with the complicated clinical course of the patient and uncertainties in the previous case report, the current case highlights 2 main points: *H. parainfluenzae* was clearly identified as the causative pathogen of the VGI because (i) 13 samples collected during the surgery were all positive for *H. parainfluenzae* and no other pathogens were detected; and (ii) antibiotics for *H. parainfluenzae* were effective, and the patient’s postoperative clinical course was favorable.

Given the late-onset presentation of this case and the fact that *H. parainfluenzae* is a part of the normal flora in the oropharynx, we suspected that this infection was caused by some factors that were not directly related to the initial surgery 4 years prior, such as the patient’s poor condition. Moreover, in the past literature on *H. parainfluenzae* prosthetic joint infections [11, 12], patients had received recent dental procedures before the prosthetic materials becoming infected. However, we were not able to confirm a link between the cavities and the VGI in our case. Even so, we still referred the patient to a dentist for treatment of his cavities.

This case also suggests that first-generation cephalosporins may be effective for chronic suppressive therapy for *H. parainfluenzae* VGI. Traditionally, third-generation cephalosporins, fluoroquinolones, and sulfamethoxazole-trimethoprim have been used as antimicrobials with generally good activity against *H. parainfluenzae* [1]. Because this is a rare pathogen for VGI, there is no established management strategy regarding the choice of antibiotics or the duration of antimicrobial treatment. The strain of *H. parainfluenzae* isolated from our patient was sensitive to first-generation cephalosporin, cefaclor, and clarithromycin (Table 1). Therefore, we decided to use cefalexin,

![Figure 2](image_url)
a first-generation cephalosporin, and later clarithromycin as the choice of oral antibiotics.

The American Heart Association guidelines [7] recommend that antibiotic therapy be continued for 4–6 weeks for VGI. However, they also recommend considering continuing the administration of oral antibiotics for at least 3 to 6 months, and possibly lifelong, as suppressive therapy given the risk of recurrence of infection, the high morbidity and mortality, and the inability of many patients to tolerate undergoing another extensive surgical reconstruction. Moreover, in this case, the patient had to go through both EMR and surgery for cancers. Because of these surgeries, we decided to extend his antibiotics therapy until both procedures are safely done instead of discontinuing early. At the 8-month follow-up, we decided to discontinue the therapy ~9 months after the surgery as the patient is now fully recovered from both procedures with no postoperative complications.

CONCLUSIONS

We report a case of VGI caused by *H. parainfluenzae* that was diagnosed 4 years after surgery for chronic aortic dissection. This is the first report to clearly confirm that *H. parainfluenzae* can cause VGI. As seen in our case, even when the patient is asymptomatic, it is crucial to collect specimens intraoperatively for microbiological identification when VGI is suspected. This case indicates the importance of a combination of graft replacement surgery and antibiotic treatment, along with a close collaboration between ID specialists and cardiovascular surgeons in managing this rare case of VGI. As there is no established strategy of antibiotic therapy for VGI due to *H. parainfluenzae*, this patient is still on oral antibiotics even 8 months after surgery. We need further reports and investigations on the management of VGI caused by *H. parainfluenzae*.

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Consent for publication. The patient has provided consent for the publication of his case details.

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