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Case Report

Infected Thoracic Aortic Aneurysm Caused by *Helicobacter cinaedi*

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The causative organism is not identified in some cases of infected aneurysms, a life-threatening condition. A 68-year-old man presented with chest/back pain and a 1-year history of intermittent fever and fatigue. Computed tomography revealed a thoracic aortic aneurysm. After several negative blood cultures, he was eventually diagnosed with an infected aneurysm caused by *Helicobacter cinaedi* via gene analysis of an aortic tissue specimen. As *H. cinaedi* is a low-virulence bacterium, infection with this pathogen should be suspected in cases of aortic aneurysms with unidentified causative organism and a long history of subjective symptoms. Detailed examinations, including polymerase chain reaction, should be conducted in such cases.

Keywords: infected aneurysm, *Helicobacter cinaedi*, thoracic aortic aneurysm

Introduction

An infected aneurysm is a serious clinical condition associated with a rapid clinical course and a high rate of rupture and, consequently, with significant morbidity and mortality.[1)] Many pathogens have been implicated in infected aneurysms, with *Staphylococcus* and *Salmonella* spp. being the most common; however, the causative organism is not identified in 25% of patients.[2)] The identification of the pathogen is essential for diagnosing and treating the infection.

In this report, we present a case of an infected thoracic aortic aneurysm caused by *Helicobacter cinaedi* that was diagnosed using gene analysis of an aortic tissue specimen. In cases of infected aneurysms in which the causative organism is difficult to identify, tissue polymerase chain reaction (PCR) and a clinical history of persistent subjective symptoms may prove useful in diagnosing aneurysms infected by *H. cinaedi*.

A small number of cases of infected aneurysm caused by *H. cinaedi*, mainly involving the abdominal aorta, have been reported, but this disease is rarely detected in the thoracic region.[7–9)] This report includes histopathological observations and sequential changes in computed tomography (CT) findings as well as a literature review.

Case Report

A 68-year-old Japanese man with a history of hypertension and hyperuricemia was referred to our hospital with complaints of new-onset chest and back pain and a 1-year history of intermittent fatigue and fever. Eight months previously, he had visited another department of our hospital with a chief complaint of fatigue and slight fever, and his laboratory tests had revealed low levels of the inflammatory marker C-reactive protein (CRP, 3.0 mg/dL). CT had not revealed any abnormalities (**Fig. 1A**). He had been diagnosed with viral infection and was not prescribed an antimicrobial agent. However, his symptoms repeatedly waxed and waned after that visit. Four days prior to his eventual admission, he had consulted a doctor at a nearby medical clinic and was prescribed a 4-day course of cefcapene pivoxil hydrochloride (300 mg/day) on an outpatient basis.

During admission, his physical examination revealed the following findings: temperature, 38.0°C; blood pressure, 115/79 mmHg; and pulse, 75 beats/min (normal pulse). He exhibited relative bradycardia. Laboratory tests revealed no specific signs of a bacteria-induced inflammatory response [white blood cell count, 7230/μL (segmented neutrophils, 61.7%; lymphocytes, 20.5%); procalcitonin, 0.12 ng/mL]; however, CRP level was elevated (13.81 mg/dL). CT revealed a saccular aneurysm

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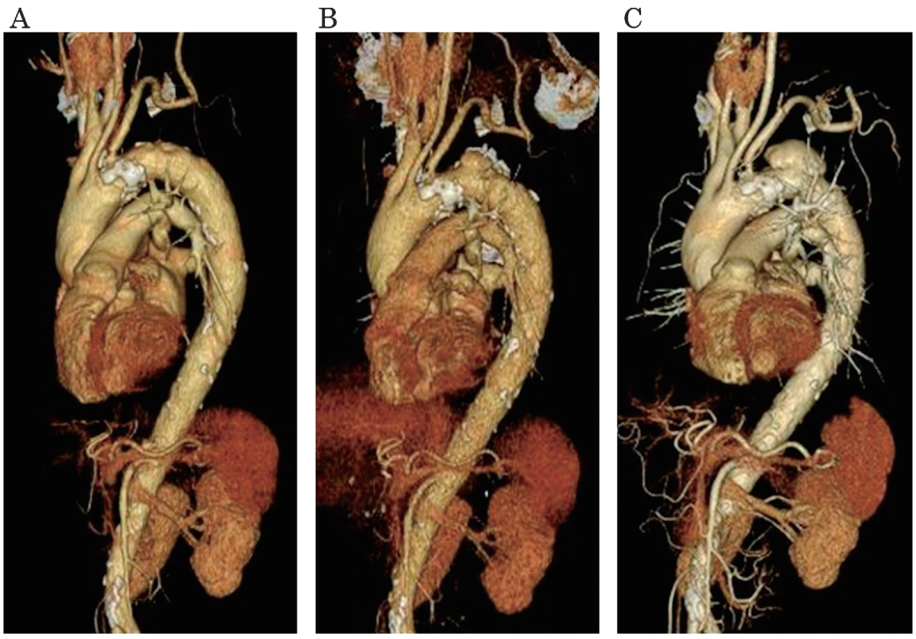

Fig. 1 **A**, **B**, and **C** show three-dimensional computed tomography (CT) reconstruction images obtained 8 months before admission, at admission, and before surgery, respectively. A saccular aneurysm of the distal aortic arch with a maximum diameter of 38 mm was forming on the cranial side at admission (**B**). Repeated CT after 2 weeks demonstrated an enlargement of the aneurysm to 44 mm in diameter (**C**).

of the distal aortic arch developing on the cranial side (**Fig. 1B**). Positron emission tomography–CT (PET–CT) revealed a local accumulation of the tracer fluorodeoxyglucose at the aneurysm. We suspected the aneurysm to be infected based on its characteristics, such as its saccular shape and low-density area around the aorta, on the CT image and PET–CT image findings, such as a local accumulation around the distal aortic arch. After admission, we ceased the antibiotic therapy and collected blood for culture (BacT/ALERT; bioMérieux, Tokyo, Japan) thrice on separate days (a total of six samples were submitted for culture: three each from arterial and venous punctures). However, no causative organism was detected after 6 days of incubation. Rapid plasma reagin and *Treponema pallidum* hemagglutination tests were negative.

We excluded other causes of chest/back pain, such as ischemic cardiac disease and aortic dissection, and initiated administering levofloxacin (250 mg/day) on the third day of hospitalization. A low dose of levofloxacin was administered because the patient's condition was gradually worsening, with evidence of reduced renal function (Cr, 1.58 mg/dL; CCr, 42 mL/min). Further, we suspected salmonella infection because of the relative bradycardia and position of the aneurysm. Fever subsided the day after commencing antibiotic therapy, and CRP levels were slowly declining. Although repeated blood cultures revealed no causative organism, an infected aneurysm continued to be suspected based on his clinical course and examinations.

On day 15 of hospitalization, CT revealed a sudden enlargement of the aneurysm (**Fig. 1C**). Therefore, we decided to perform surgery to replace the entire aortic arch and to perform omental wrapping. Surgical findings indicated that the surface of the aorta was contaminated, confirming our suspicions of infection. Dense adhesion was noted around the aneurysm, and a fragile septic thrombus was noted within the aneurysm.

As our attempts to identify the causative pathogen through postoperative tissue culture and Gram staining were unsuccessful, we attempted to detect bacterial gene products in the resected specimen. Firstly, 16S rRNA gene analysis was performed. The bacterial gene products obtained were subjected to DNA analysis, which revealed *H. cinaedi*.[3] *H. cinaedi*-specific PCR, which was designed to amplify the gyrB gene region specific to *H. cinaedi*, was also performed, which confirmed the presence of *H. cinaedi*.[4] The patient was diagnosed with an infected aortic aneurysm caused by this bacterium. Antimicrobial susceptibility testing using DNA analysis was not performed. As most reported cases of *H. cinaedi* infection have occurred in immunocompromised hosts,[5] we conducted HIV antibody testing and confirmed the patient's negative status. No other risk factors for infection were found in this patient.

We continued to administer the same antibiotic agent (levofloxacin) after surgery; however, the CRP level re-

mained elevated (approximately 7.0 mg/dL). Therefore, postoperative day 19, we changed the antibiotic agent to minocycline (200 mg/day), which has been reported to have a relatively low minimum inhibitory concentration against *H. cinaedi*; there have also been several reports on the resistance of *H. cinaedi* to fluoroquinolones.[6] A reduction in the CRP level was observed soon after changing the antibiotic, and the patient was subsequently discharged from the hospital. He was confirmed to be CRP-negative after discharge. We intend to continue his treatment with oral antibiotic for as long as possible.

Discussion

This case provided two important clinical insights. Detailed follow-up testing, including PCR, to identify *H. cinaedi* is required in cases of infected aneurysms in which the causative agent is difficult to identify. A relatively long clinical course of subjective symptoms may reflect the characteristics of *H. cinaedi* infection.

Firstly, when it is difficult to identify the causative bacterium of an infected aneurysm, detailed testing, including PCR, is necessary to detect potential pathogens, such as *H. cinaedi*. Cases of infected aortic aneurysm caused by *H. cinaedi*, primarily affecting the abdominal aorta, have previously been reported.[7–9] In one study, tissue gene tests performed on samples of eight patients with infected abdominal aortic aneurysm revealed *H. cinaedi* in three cases, thereby indicating that *H. cinaedi* may be involved in many cases of infected abdominal aortic aneurysm.[8] *H. cinaedi* is generally difficult to culture,[5] and the antibiotics prescribed to our patient by the previous physician may have made this more difficult. *H. cinaedi* is resistant to fluoroquinolones, and our patient's clinical course improved rapidly after the antibiotic was switched to minocycline, to which *H. cinaedi* is more susceptible.[6] Appropriate antibiotic selection results in easier infection control and improvements in therapeutic response and prognosis. Although most previous reports were on abdominal infection, the present case of an infected thoracic aortic aneurysm caused by *H. cinaedi* indicates the necessity to assess the possible involvement of *H. cinaedi* whenever identifying the causative bacterium is difficult, regardless of the affected site.

Secondly, a relatively long clinical course of subjective symptoms may be specific to low-virulence *H. cinaedi*

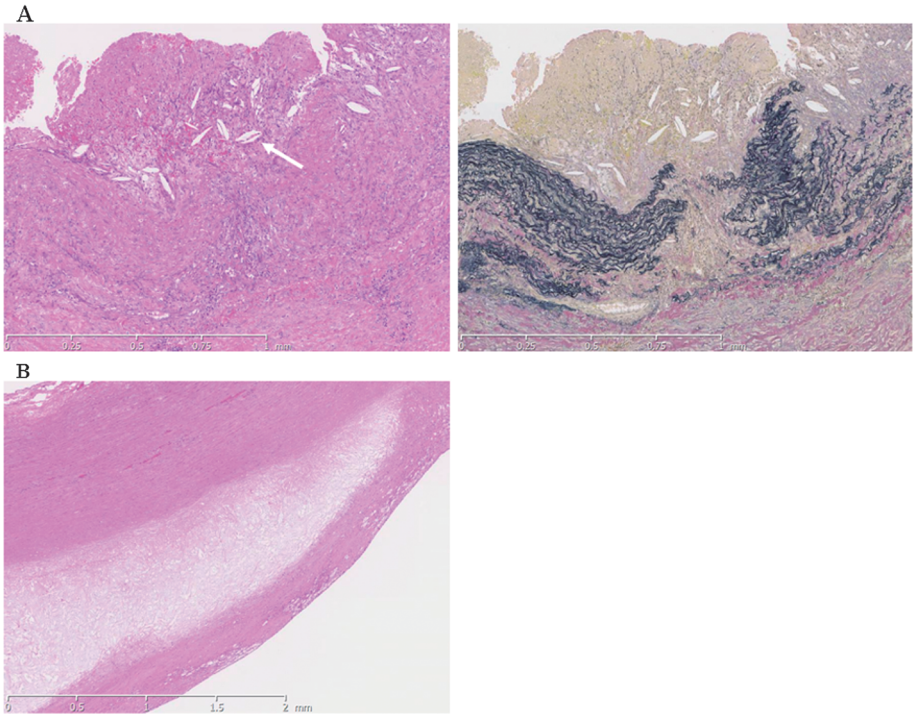

Fig. 2 Histopathologic examination. (**A**) Left: hematoxylin and eosin (H&E) staining, right: elastica van Gieson staining: A resected specimen in which most vascular structures were destroyed. The intima was detached, and the media was slightly retained. Several cholesterol clefts are noted adjacent to the intravascular area (arrow). Reactive fibrosis was observed in the adventitia. (**B**) H&E staining: A resected specimen in which the vascular structure was relatively maintained. Most lesions spanned the intima area and were mainly comprised foam cells.

infection. An infected aneurysm is generally characterized by rapid progression, but our patient intermittently experienced general fatigue and fever for 1 year, suggesting that an aneurysm infected by *H. cinaedi*, a low-virulence bacterium, can have a longer clinical course. Consistent with the findings in a previous report on a murine model demonstrating that *H. cinaedi* infection is closely associated with arteriosclerosis induction,[10] advanced arteriosclerotic lesions were observed in aneurysm tissue in the present case (**Fig. 2**). Despite marked neutrophilic infiltration, it is highly likely that other findings, such as abscess, indicative of infection disappeared because of preoperative antibiotic therapy. The patient's tissue samples also displayed signs of tissue repair, such as the formation of granulation tissue. Given the fact that CT performed 8 months prior to admission did not indicate aneurysm formation, it is possible that the relatively long clinical course observed in the present case is unique to *H. cinaedi* infection. The long course may reflect relatively slow tissue destruction at the infected arteriosclerotic site that began prior to aneurysm formation, rather than the rapidly developing inflammation normally observed at the infection site.

Conclusion

We reported a case of an infected aortic aneurysm in which the causative agent was difficult to identify but was eventually identified to be *H. cinaedi* using tissue PCR. When an infected aortic aneurysm is strongly suspected but blood and tissue cultures fail to identify the causative bacterium, it is necessary to aggressively perform gene analysis to identify the causative agent. If the patient's subjective symptoms persist over a relatively long term, *H. cinaedi* should be suspected and detailed follow-up tests should be performed. The findings from the present study emphasize that the identification of causative bacteria and the selection of appropriate antibiotics are extremely important in controlling infection in aortic aneurysms.

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Disclosure Statement

The authors have no conflict of interest to disclose.

Author Contributions

Critical review and revision: all authors
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Accountability for all aspects of the work: all authors

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