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Case Report

Helicobacter cinaedi-associated Carotid Arteritis

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A 65-year-old Japanese man with bilateral carotid atherosclerosis presented with right neck pain and fever. Contrast-enhanced computed tomography suggested carotid arteritis, and carotid ultrasonography showed an unstable plaque. The patient developed a cerebral embolism, causing a transient ischemic attack. *Helicobacter cinaedi* was detected in blood culture, and *H. cinaedi*-associated carotid arteritis was diagnosed. Empirical antibiotic therapy was administered for 6 weeks. After readmission for recurrent fever, he was treated another 8 weeks. Although the relationship between *H. cinaedi* infection and atherosclerosis development remains unclear, the atherosclerotic changes in our patient's carotid artery might have been attributable to *H. cinaedi* infection.

Key words: atherosclerosis, bacteremia, bacterial translocation, *Helicobacter cinaedi*, vascular infection

Helicobacter cinaedi is a Gram-negative spiral bacillus that generally colonizes the intestines of animals such as hamsters and rhesus monkeys [1]. In humans, *H. cinaedi* infection was first reported in 1984 in homosexual men with proctocolitis [2]. Since then, *H. cinaedi* infections have been increasingly reported, but the organism is still rare as a human pathogen, and its clinical characteristics and relevance remain elusive. *H. cinaedi* has been isolated from immunocompromised patients such as those with human immunodeficiency virus (HIV) infection, deficiency in humoral immunity [3], and solid organ transplantation [4, 5]. However, recent reviews have documented that immunocompetent individuals may also be infected with *H. cinaedi*, even in a community setting [6].

Clinical manifestations of *H. cinaedi* infection vary greatly. Bacteremia accompanying cellulitis is a typical form [7]; over 80% of community-acquired *H. cinaedi* bacteremia cases showed dermatologic symptoms [6]. However, the organism can potentially cause systemic infections, resulting in arthritis [8], infective endocarditis [9], spondylitis [10], and meningitis [11]. Notably, *H. cinaedi* has a higher vascular affinity [7], and it may induce fatal vascular infections. To date, *H. cinaedi* infections involving the abdominal aorta [12, 13] and common iliac artery [14] have been documented. To the best of our knowledge, however, cases involving the carotid artery have not yet been reported. In the present report, we describe a rare case of *H. cinaedi*-associated carotid arteritis that was successfully treated with prolonged antimicrobial therapy.

Case Presentation

A 65-year-old Japanese man presented with a 1-week history of fever accompanied by chills, malaise, and right neck pain. His medical history included bilateral

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carotid atherosclerosis (approx. 60% stenosis in the right carotid artery, 40% stenosis in the left) and an unruptured cerebral aneurysm, for which clopidogrel and pitavastatin were prescribed. He visited a dentist because the neck pain worsened during meals. The dentist found no abnormalities, and referred the patient to our hospital for a systemic evaluation.

Upon examination, the patient's vital signs were as follows: body temperature, 37.0°C; blood pressure, 100/57 mmHg; heart rate, 65 beats per minute; oxygen saturation, 98% in ambient air; and respiratory rate, 16 breaths per minute. He did not complain of any symptoms except right mandibular cervical pain. Carotid bruits were detected bilaterally upon auscultation. Skin rash was unapparent. Laboratory blood tests revealed a white cell count of 7,740 /μL (neutrophils 64%), C-reactive protein (CRP) level of 5.9 mg/dL, and erythrocyte sedimentation rate of 64 mm/h. The results of a test for HIV were negative, and immunoglobulin and complement levels were within normal range.

A contrast-enhanced computed tomography (CT) scan showed an area of increased density surrounding the patient's right common carotid artery, suggesting carotid arteritis. There were no significant findings in his chest or abdominal cavities. Carotid ultrasonography revealed a 3.1 mm × 1.3 mm bouncing plaque (Fig. 1A, B). The patient was started on 200 mg per day of cilostazol, and hospitalized for further investigation.

Two days after admission, he developed transient dysarthria. Diffusion-weighted MRI revealed a high-intensity area in the right corona radiate, suggesting a new-onset cerebral infarction. Repeated carotid ultrasonography on admission day 3 revealed that the unstable plaque had disappeared (Fig. 1C, D), whereas the right internal carotid artery was found to be surrounded by thickened arterial wall and low-echoic soft tissues (Fig. 1D). On day 5, a Gram-negative spiral bacillus was isolated from the aerobic blood culture bottles (BacT/ALERT system; bioMérieux, Marcy l'Etoile, France) that were inoculated at the time of the patient's admission (Fig. 2). We identified the organism as *H. cinaedi* via a polymerase chain reaction (PCR) assay targeted to gyrase subunit B (*gyrB*) by applying the following primers: Forward, 5'-AGG GAT TCC ACA AAG TGA GC-3'; Reverse, 5'-TCT TGT CCT GTG CGT TCA TC-3' [15].

The results of a repeated blood culture examination were positive for *H. cinaedi*, indicating persistent bacteremia. We performed transthoracic and transesophageal echocardiography, which revealed no intracardiac vegetation. The gastroscopy and colonoscopy performed during the patient's hospitalization showed no remarkable findings.

On the basis of the above findings, we diagnosed the case as carotid arteritis caused by *H. cinaedi* and a subsequent cerebral embolism, and we initially administered intravenous meropenem 2 g every 8 h. Although surgical resection of the infected carotid artery was considered, we did not perform it since the tenderness and swelling ameliorated after antibiotic treatment and carotid echography revealed an improvement of the inflammatory finding. The persistent bacteremia was also confirmed to disappear, and antimicrobial therapy was switched to intravenous ceftriaxone at a dose of 2 g every 12 h.

After 2 weeks of intravenous treatment, laboratory findings were recovered to normal ranges: peripheral white cell count, 5,380 /μL (neutrophil 53%); CRP level, 0.16 mg/dL; and erythrocyte sedimentation rate, 34 mm/h. The patient's treatment was switched to 100 mg oral minocycline 2×/day for 2 weeks, and he was then discharged.

Three days after discharge, however, he revisited us complaining of fever and chills. Neck pain was absent and carotid ultrasonography did not indicate worsening of the carotid arteritis. The results of a blood culture examination were negative. However, we diagnosed the case as a recurrence of *H. cinaedi* infection and administered intravenous ceftriaxone 2 g every 12 h. The patient's clinical condition improved after 2 weeks of intravenous treatment. He was then discharged with a prescription for 500 mg oral ampicillin 3×/day plus 200 mg oral doxycycline 2×/day, which was continued for 6 weeks. Two months after the completion of this treatment, a follow-up carotid ultrasonography demonstrated an improvement of the thickened arterial wall (Fig. 1E). No recurrence of symptoms has been reported since then for >6 months.

Discussion

We have described a rare case of *H. cinaedi*-associated carotid arteritis. Persistent bacteremia suggested an intravascular infection, and the clinical symptoms as well as imaging findings were consistent with the diagnosis. This case highlights the relevance of *H. cinaedi* infection to atherosclerosis, as has been recently pro-

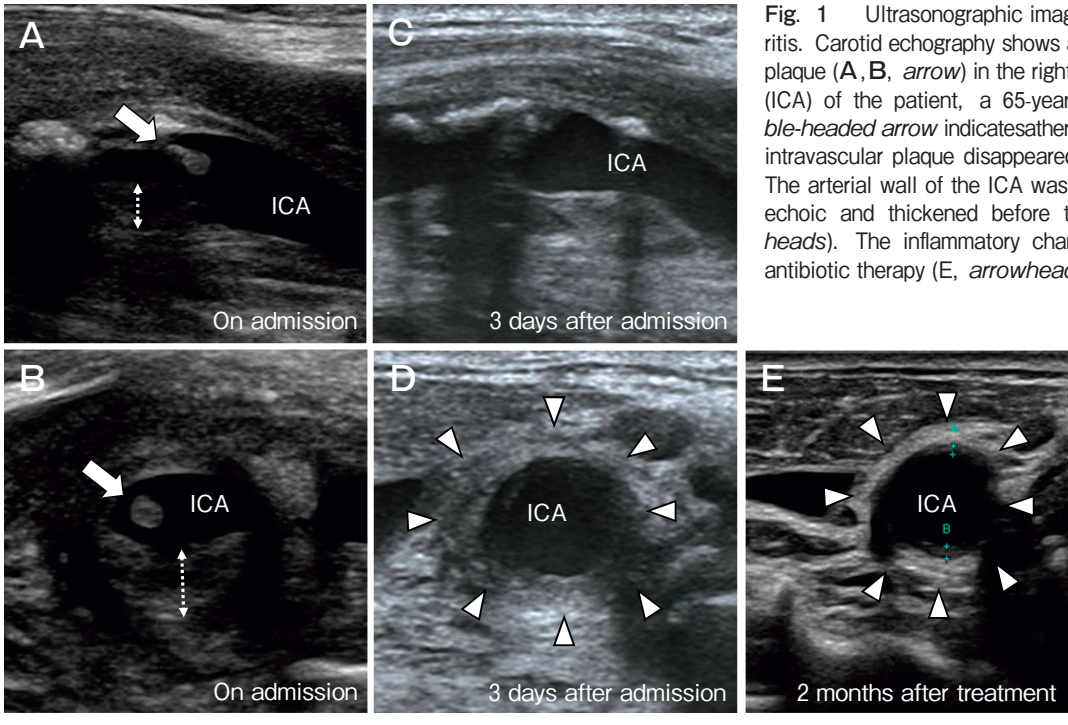

Fig. 1 Ultrasonographic images of the carotid arteritis. Carotid echography shows an unstable, bouncing plaque (**A**, **B**, *arrow*) in the right internal carotid artery (ICA) of the patient, a 65-year-old male. The *double-headed arrow* indicatesatherosclerotic plaque. The intravascular plaque disappeared 3 days later (**C**, **D**). The arterial wall of the ICA was circumferentially low-echoic and thickened before treatment (D, *arrowheads*). The inflammatory change ameliorated after antibiotic therapy (E, *arrowheads*).

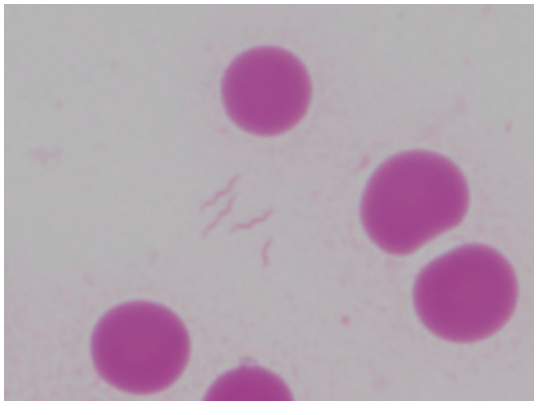

Fig. 2 Gram-negative spiral rods detected in blood culture.

posed in the literature.

The clinical features of *H. cinaedi* infections have long been undetermined because of the low incidence and the difficulty in the microbiological identification of *H. cinaedi*. According to a Japanese multicenter study, *H. cinaedi* accounts for <1% of positive blood cultures [16]. Additionally, because of the slow growth and microaerophilic features of *H. cinaedi*, some cases may remain undiagnosed [17]. A review reported that nearly half the cases of *H. cinaedi* infection required >5 days for positive blood culture results [18], which is consistent with our patient's case.

The atherosclerotic lesion in our patient's carotid artery could be related to the onset of this rare infection. A report suggested the clinical relevance of *H. cinaedi* infection to the progression of atherosclerosis [19], which has been demonstrated in experimental atherosclerosis models as well [7, 20]. It is unclear whether a converse relationship exists; *i.e.*, whether the presence of atherosclerosis affects the onset of vascular *H. cinaedi* infections. However, previous cases of *H. cinaedi* involvement in atherosclerotic plaques support this possibility [13, 14]. We believe that the atherosclerotic lesion in the carotid artery could be attributable to the occurrence of the rare infection in the present case.

H. cinaedi is considered highly invasive to the peripheral vascular system of gastrointestines, triggering bacterial translocation to the systemic circulation [7]. In a study, *H. cinaedi* was detected in stool samples from more than half of 63 patients with bacteremia, indicating that the blood stream infections had gastrointestinal origins [18]. Gastrointestinal complications associated with *H. cinaedi* bacteremia were also documented in another case series [5]. In contrast, our patient did not have any previous history of abdominal symptoms before the onset, and radiographic and endoscopic investigations did not reveal any clinically significant findings. Thus, the origin of the pathogen

was not identified.

No guidelines are currently available concerning *H. cinaedi* susceptibility testing, or regarding the choice of antibiotic therapy for *H. cinaedi* infection. The minimum inhibitory concentrations of carbapenems, tetracycline, and aminoglycosides for *H. cinaedi* are low, but this organism is comparatively resistant to penicillins, cephalosporins, fluoroquinolones, and macrolides [7]. Some reports recommend the clinical use of tetracycline and aminoglycosides rather than cephalosporins, macrolides, or fluoroquinolones [17]. In the present case, we administered meropenem as an empirical treatment, and then switched to ceftriaxone. Both of these agents were administered at high doses, considering the possibility of central nervous system infection.

Although the optimal treatment duration for *H. cinaedi* infections is unclear, long-term therapy (2 to 6 weeks) is preferred [8, 21]. *H. cinaedi* potentially causes obstinate infections with a high recurrence rate [7], which was also indicated in our patient's case. Physicians need to be aware of the persistence of this pathogen.

In summary, we describe a rare case of *H. cinaedi*-associated carotid arteritis. The patient developed a cerebral embolism that caused a transient ischemic attack, but was successfully treated with antimicrobial therapy. The atherosclerotic changes in his carotid artery might be attributable to the *H. cinaedi* vascular infection.

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