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Case Report

Infective endocarditis caused by *Cardiobacterium hominis* endocarditis: A case report and review of the literature☆

Nobuhiro Asai [a, b], Daisuke Sakanashi [b], Hiroyuki Suematsu [b], Naoya Nishiyama [a, b], Hiroki Watanabe [a, b], Hideo Kato [b], Arufumi Shiota [b], Mao Hagihara [a], Yusuke Koizumi [a, b], Yuka Yamagishi [a, b], Hiroshige Mikamo [a, b, *]

[a] Department of Clinical Infectious Diseases, Aichi Medical University Hospital, Aichi, Japan
[b] Department of Infection Control and Prevention, Aichi Medical University Hospital, Japan

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ABSTRACT

Background: While it has been increasing cases of *C. hominis* endocarditis in the past decades due to advances of diagnostic methods, the epidemiology and clinical manifestations of IE caused by *C. hominis* is still unknown.

Case presentation: A 62-year old man was admitted to our institute with fever, anorexia and general fatigue for the preceding one month. He had a past medical history of both aortic and mitral valves replacement due to cardiac diseases. He was diagnosed as IE caused by *C. hominis* according to the modified duke criteria. The patient received 2 weeks of combination therapy of intravenous ceftriaxone (CTRX) 2g and gentamycin 180mg daily followed by 4 weeks CTRX 2g daily alone. Oral moxifloxacin 400mg once daily was given for an additional 4 weeks. After the antibiotic therapy was discontinued, disease recurrence was not observed. We reviewed previously reported *C. hominis* IE cases in 60 publications including ours. Of 73 patients enrolled, 53 were male, the mean age was 52 years. The most common risk factor of IE was past history of cardiac diseases in 44/73 (60%). As for antibiotics initially prescribed, third-generation cephalosporins was most frequently used in 28/69 (41%). While the cure rate was 67/73 (93%), 31/73 patients (43%) received a surgical intervention. Embolic lesions to the central nervous system and vertebrae were seen in 16/72 (22%) and 5/72 (7%).

Conclusion: IE caused by *C. hominis* has a favorable prognosis, showing the cure rate of 93%. Physicians should recognize the possible occurrence of emboli among IE patients.

1. Introduction

Cardiobacterium hominis, a fastidious, Gram-negative bacillus belonging to the HACEK group (*Haemophilus parainfluenzae*, *Haemophilus aphrophilus, Haemophilus paraphrophilus*, *Actinobacillus actinomycetemcomitans*, *C. hominis*, *Eikenella corrodens* and *Kingella* species), is a usual cause of infective endocarditis and is frequently associated with negative blood cultures [1–3]. These organisms account for appropriately 3–6% of cases of bacterial endocarditis [4,5]. It is general that the identification of *C. hominis* is difficult because this organism grows slowly. With the advancement of the diagnostic tools such as new blood culture system, broad-range PCR or positron emission tomography and matrix-assisted laser desorption ionization time of light (MALDI-TOF-MS), it has been increasing cases of *C. hominis* endocarditis in the past decades [6–8].

HACEK group are the potential causative pathogens of community-onset infective endocarditis. However, the clinical manifestations and prognosis are still unclear. We present a case of *C. hominis* endocarditis and review all reports previously published in English since 1962. This is the first review of *C. homonis* endocarditis since 2010 in English-language.

☆ All authors meet the ICMJE authorship criteria.

* Corresponding author. Department of Clinical Infectious Diseases, Aichi Medical University School of Medicine, 1-1 Yazakokarimata, 480-1195, Nagakute, Aichi, Japan.
E-mail address: mikamo@aichi-med-u.ac.jp (H. Mikamo).

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2. Case presentation

A 62-year old man was admitted to our institute with fever, anorexia and general fatigue for the preceding one month. He did not have a recent dental procedure nor any medical history of diabetes mellitus or medication with immunosuppressants. He had had both aortic and mitral valves replacement using mechanical valves due to disturbance of aortic regurgitation (AR) and mitral regurgitation (MR). Laboratory studies on admission showed an elevation of white blood cell counts of 12,000/mm3 with 87% neutrophils and 5% lymphocytes. The erythrocyte sedimentation rate was 63 mm/h. Serum PR-ANCA was also elevated, even though symptoms of collagen vascular diseases were not seen. Computed tomography (CT) scan showed splenomegaly, even though his previous spleen was normal in the previous CT findings. He did not demonstrate retinal hemorrhages, Roth' spots or Janeway nodule. Two sets of blood cultures were obtained. By 48 hours, all blood cultures yielded a Gram negative bacillus identified as *Cardiobacterium hominis* by MALDI-TOF-MS. A repeated blood culture admitted on day 3 showed that *C. hominis* was positive. Both transthoracic echocardiogram (TTE) and transesophageal echocardiogram (TEE) demonstrated no vegetation. MRI of brain revealed multiple brain infarctions without any symptoms. He was diagnosed as having IE caused by *C. hominis* according to the modified duke criteria. The patient received 2 weeks of combination therapy of intravenous ceftriaxone (CTRX) 2g and gentamycin 180mg daily followed by 4 weeks CTRX 2g daily alone. Oral moxifloxacin 400mg once daily was given for an additional 4 weeks according to the result of susceptibility testing. Antimicrobial susceptibility testing was performed for the strain using the broth microdilution method (Dry Plate®Eiken Chemical co., Ltd, Tokyo, Japan) according to the Clinical and Laboratory Standards Institute guidelines [9]. The isolate was susceptible to ampicillin, CTRX, carbapenems, and fluoroquinolones (Table 1). A total of 10 weeks antibiotic therapy was performed, rather than a standard 4 weeks course, because of his septic cerebral and vertebral embolus. After he completed the therapy, infections did not recur during the observation period. A total of 10 weeks antibiotic therapy was performed, rather than a standard 4 weeks course, because of his septic cerebral and vertebral embolus. After he completed the therapy, infections did not recur during the observation period.

2.1. Literature review

We reviewed 60 manuscripts and a total of 73 cases were enrolled in this study, including our case as shown in Table 2. Non-English-language cases were not included [7,9–66]. Some cases lacked sufficient clinical courses and data for the analysis. The mean age was 51 ± 14 years. They were 53 males (73%) and 20 females (27%). The most common risk factor among previous history was cardiac diseases in 44/73 (60%), followed by the presence of prosthetic valves in 23/72 (32%). In terms of the infection site of IE, aortic valve was the most commonly seen in 33/72 (46%), followed by mitral valve in 20/72 (28%), and 11/72 (15%) were unknown. As for the diagnosis, echocardiogram was performed in 49 patients (67%), which showed vegetations in 29/49 (59%). TTE and TEE were performed in 40 and 18, respectively. Nine patients had received both TTE and TEE. While 70 of the 73 patients had a positive blood culture of *C. hominis*, three patients showed negative blood cultures. In the 3, a diagnosis as IE was based on cultures of the valve at surgery [50] or by PCR genome amplification on either the resected valve [40] or arterial embolus [7]. As for symptoms, fever was the most frequent in 54/70 (77%), followed by fatigue in 41/70 (59%). Embolic lesions to the central nervous system and the vertebrae were found in 16/72 (22%) and 5/72 (7%), respectively.

The most frequent treatment regimen was third-generation cephalosporin. A combination therapy of β-lactams and aminoglycoside was performed in 8/68 (12%). The mean length of antibiotic therapy in 59 patients for whom the data were described was 6.8 ± 3.4 weeks. Prior dental work was seen in 13/71 (18%). Embolic

Table 1
Antimicrobial susceptibility of *Cardiobacterium hominis* isolated from blood culture.

Antimicrobial agents	MIC (μg/mL)	Interpretation
Ampicillin	≦0.01	S
Amoxicillin/Clavulanic acid	≦0.5	S
Ceftriaxone	≦1	S
Imipenem	≦0.5	S
Meropenem	≦0.5	S
Ciprofloxacin	≦0.12	S
Levofloxacin	≦0.25	S

MIC, minimum inhibitory concentration; S, susceptible.

Table 2
Patients' characteristics (n = 73).

Characteristics and outcomes	number (percentage)
Patient' characteristics	
Median age (range, years)	52 (17–82)
Sex	
male	53 (73)
female	20 (27)
Risk factors for infective endocarditis	
Past history of cardiac diseases	44/73 (60)
Prior dental work	13/71 (18)
Prosthetic valves	23/72 (31)
Prior endocarditis	5/71 (7)
Recent endoscopy	3/70 (4)
Site of infection of *C. hominis* endocarditis	
Aortic	31/73 (42)
Mitral	20/73 (27)
Aortic and mitral	9/73 (12)
Pulmonic	1/73 (1)
Tricuspid	1/73 (1)
Unknown	11/73 (15)
Symptoms and physical examinations	
Fever	54/70 (77)
Fatigue	41/70 (59)
Anorexia	27/70 (39)
Night sweat	21/70 (30)
Splenomegaly	27/65 (42)
Heart failure	25/69 (36)
Arrhythmia	15/73 (20)
Glomerulonephritis	4/63 (6)
Embolic lesions	
To central nervous system	5/72 (7)
To vertebrals	16/72 (22)
Procedure of echocardiogram	49/73 (67)
Transthoracic echocardiogram	40
Transesophageal echocardiogram	18
Presence of vegetations	29/49 (59)
Antibiotics by initial treatment (n = 70)	
Penicillins alone	10/70 (14)
Cephalosporins alone	6/70 (9)
Fluoroquinolones alone	3/70 (4)
Penicillins+cephalosporins+others	11/70 (16)
Combination with aminoglycoside	28/70 (40)
Others	12/70 (17)
Mean length of treatment (weeks±SD)[a]	6.8 (±3.4)
Outcome	
Cure	67/72 (93)
Death	5/72 (7)
Surgical procedure	
Yes	31/72 (43)
No	41/72 (57)

[a] Mean length of treatment was in 59 patients. In 13 patients, lengths of treatment were not described.

lesions to the central nervous system and the vertebrae were seen in 16/72 (22%) and 5/72 (7%), respectively.

As for the outcome, 67 of the 72 (93%) patients survived and in-hospital mortality rate was 7%. Finally, 31 of the 72 (43%) patients underwent surgical operations.

3. Discussion

Although *C. hominis* is of relatively low virulence, endovascular infection complicates 95% of all cases of bacteremia, with the aortic valve being most commonly affected [3,4]. In our study, peripheral and central nervous system emboli occur frequently in *C. homonis* IE in 51% and 21%, respectively [3,5,6]. These results might be because *C. hominis* tends to form large friable vegetations that are associated with a significant risk for congestive heart failure, emboli to peripheral and CNS system Formation of emboli to the peripheral and CNS system may be attributable to the fact that *C. hominis* tends to form large friable vegetations that are associated with a significant risk for congestive heart failure [9]. Thirty-one out of 72 (43%) patients presented with IE caused by *C. hominis* had received surgical valve replacement, which may be related to frequent heart failure. Heart failure could be a poor prognostic factor of IE caused by non-HACEK organisms. Although IE patients caused by *C. hominis* were complicated by heart failure, the mortality rate was lower than non-HACEK IE patients [67]. This discrepancy may be due to the low-virulence and subacute progression of *C. hominis* IE.

As for an invasion door of *C. hominis*, although the patient had neither a recent dental procedure nor a dental disease, it is considered to be from the mouth. While a systematic review and some guidelines for IE do not always recommend an antibiotic prophylaxis for IE after dental procedures [68], the antibiotic prophylaxis for prevention should be considered in case of patients with a high risk of IE.

While HACEK organisms are responsible for approximately 3% of infectious endocarditis, these organisms are difficult to be detected due to their low growth, nutritional needs and as oropharyngeal flora [69]. MALDI-TOF-MS is more rapid, and accurate than conventional cultures. It could lead to shorten the time to diagnosis and an initial appropriate antibiotic treatment for infections [70]. The efficacy and accuracy of MALDI-TOF-MS has been reported in the detection of HACEK group organisms [71–73]. The number of IE caused by HACEK organisms is estimated to increase by using MALDI-TOF-MS, and it could contribute to early diagnosis as IE caused by HACEK organisms.

It has been estimated that intracranial mycotic aneurysms developed in 1%–3% of all IE patients [10]. The result of our study found that 6 patients were complicated by mycotic aneurysms, and 3 of which were intracranial mycotic aneurysms. Of the 3, prognosis may vary as follows: cured following aneurysm removal with medical management, cured following a surgical interventional procedure and medical management of aneurysm only or death following aneurysm rupture. The early diagnosis of a mycotic aneurysm is very challenging. However, appropriate management of mycotic aneurysm could be associated with a good prognosis for *C. hominis* IE patients.

In terms of antibiotic susceptibility, *C. homonis* produce β-lactamase resulting in resistance to penicillins. This contributed to the fact that American Heart Association guideline recommended third-generation cephalosporins for the treatment for HACEK IE. In addition, since central nervous system emboli and intracranial mycotic aneurysm could occur, third-generation cephalosporin's such as CTRX, which has a good transitivity to cerebrospinal fluid, should be recommended.

In conclusion, IE patients caused by *C. hominis* frequently present emboli to the CNS and vertebrae. Cerebral emboli and intracranial mycotic aneurysm should be pursued. Otherwise, they might be overlooked resulting in a poor outcome. Physicians must be aware of these characteristics of IE caused by *C. hominis*.

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