



Case report

Apyretic pulmonary oedema revealing *Cardiobacterium hominis* endocarditis: Case report and review of literature

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ARTICLE INFO

Keywords:

Endocarditis
Cardiobacterium hominis
 Apyrexia
 MALDI TOF MS
 16S RNA PCR
 HACEK

ABSTRACT

Cardiobacterium hominis is a member of the HACEK group of bacteria, responsible for infective endocarditis, mainly in patients with damaged or prosthetic valves. The low virulence of this organism can explain the insidious presentation and subacute or chronic progression of *C. hominis* infective endocarditis. Here, a 41-year-old man with a past history of surgery for a Waldhausen type aortic coarctation was hospitalised with dyspnea and chest pains revealing an acute pulmonary oedema, without fever. Transesophageal echocardiography indicated a 20 mm vegetation on bicuspid aortic valve. Six sets of blood culture were positive with *Cardiobacterium hominis*. In case of lack of fever, the diagnosis of infectious endocarditis is difficult because other symptoms are non-specific and biological markers of inflammatory syndrome are quiet or non-existent. This is the first case of *C. hominis* infectious endocarditis with a clinical presentation of acute pulmonary oedema in the literature. We report here an apyretic pulmonary oedema revealing *C. hominis* endocarditis and a review of the literature on apyretic infective endocarditis due to *C. hominis*.

The HACEK group of bacteria, *Haemophilus-Aggregatibacter-Cardiobacterium-Eikenella-Kingella*, are small Gram-negative rods involved in 1.3–1.4% of endocarditis [1,2]. These microorganisms colonize the oropharynx, are slow growing, and their growth is enhanced by the presence of CO₂. First identified as a *Pasteurella-like organism*, Slotnick and Dougherty described *Cardiobacterium hominis* in 1964 and gave it its present name [3]. Subsequently, *C. hominis* was reclassified with *Suttonella indologenes* in the family *Cardiobacteriaceae* on the basis of 16 S rRNA analysis [4]. The low virulence of this organism may explain the insidious presentation and subacute or chronic progression of *C. hominis* infective endocarditis, with a tendency to infect damaged or prosthetic valves [5]. Occasionally, complications may arise such as haemodynamic disturbances. We report here an apyretic pulmonary oedema revealing *C. hominis* endocarditis and a review of the literature on apyretic *C. hominis* infective endocarditis.

Case report

A 41-year-old man, with a Waldhausen type aortic coarctation

operated in childhood was admitted to our hospital in a context of dyspnea and chest pains revealing an acute pulmonary oedema typical of cardiac decompensation, confirmed by X chest ray. The initial examination showed tachycardia (113/min) with blood pressure asymmetry: 130/60 mmHg in left arm and 180/80 in right arm suggesting an aortic dissection. His body temperature was 37.1 °C, respiratory rate 44 breaths/min and oxygen saturation 96%. He had a stage III dyspnea (NYHA). There were no palpable spleen and no peripheral cutaneous endocarditis symptoms. The angio CT scan performed did not reveal aortic dissection. Considering of his cardiac past, the patient was transferred in the cardiac surgery ward. Transesophageal echocardiography demonstrated a 20 mm vegetation on bicuspid aortic valve, with severe aortic insufficiency. Blood test reveal C-reactive protein level at 35 mg/L (normal range < 5 mg/L). The white blood cell count was 9.1 × 10⁹/L with 81% of polynuclear neutrophil, the hemoglobin concentration was 11.1 g/dL, and the platelet count was 284 × 10⁹/L. Six peripheral blood culture sets were performed and incubated in BacT/Alert Virtuo (bioMérieux, Marcy l'Etoile, France). All blood cultures became positive after 34 h of incubation and confirmed the infective

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Table 1
Review of the literature about *Cardiobacterium hominis* apyretic infectious endocarditis.

References	Age (y) / Sex	Medical history	Symptoms at admission	Cardiac symptoms at admission	Initial laboratory investigations	Outcome
[7]	58/M	Attacks of chest pain	Malaise and shortness of breath following an influenza-like illness	Signs of aortic incompetence Congestive heart failure	L: $6,5 \times 10^9/L$ ESR: 25 mm/h	Aortic valve replacement Good outcome
[8]	28/M	Murmurs of aortic stenosis and aortic regurgitation	Fatigue Leg pain of 2 month's duration	Systolic and diastolic murmur TTE: Aortic vegetations	L: $10,3 \times 10^9/L$	Aortic valve replacement Good outcome
[9]	28/M	None	2 years history of transient vertiginous attacks Intermittent vertical diplopia Tendency to weave towards the left side while walking Slurring of his speech	Systolic murmur Carotid arteriography: an embolus of cerebral artery	Blood count normal	Good outcome
[5]	63/F	Rheumatic fever and a heart murmur Dyspnea following exertion and atrial fibrillation Aortic and mitral stenosis, mitral regurgitation Right hemiparesis: a cerebral hemorrhagic infarction	Progressive symptoms of congestive heart failure	Systolic murmur Echocardiogram: mitral stenosis, right ventricular dilation, abnormal septal motion, a dilated left atrium, and abnormal aortic valve closure. No vegetations At surgery, aortic vegetations	L: $9,1 \times 10^9/L$ ESR: 96 mm/h	Aortic and mitral valve replacement and tricuspid valve annuloplasty Good outcome
[10]	55/M	Congestive heart failure secondary to bicuspid aortic valve Carpentier-Edwards prosthesis aortic valve replacement	Weakness Emesis and melena After Upper Gastrointestinal Endoscopy	Systolic murmur Echocardiogram: Dilated, hypokinetic left ventricle with hypertrophy At surgery, prosthetic aortic valve had vegetations	L: $29,9 \times 10^9/L$	Aortic valve replacement Good outcome
[11]	40/M	Emboloc occlusion of the right popliteal artery	Sudden pain left calf (= embolic occlusion of the left fibular artery)	Diastolic murmur TOE: Bicuspid aortic vegetations	ESR: 6 mm/h CRP: 37 mg/L	Aortic valve replacement Good outcome
[12]	17/M	Congenital aortic stenosis Homograft aortic valve replacement Dental treatment	Lethargy Night sweats for 3 weeks	Diastolic and systolic murmur Echocardiogram: left ventricular hypertrophy TTE: Non-coronary cusp of the aortic homograft vegetation	Blood count normal ESR: 4 mm/h CRP undetectable	Aortic valve replacement Good outcome
[13]	66/F	Diabetes mellitus Dental caries	Chest discomfort Fatigability	Systolic and diastolic murmur TOE: Aortic vegetations	L: $8,5 \times 10^9/L$	Aortic valve replacement Good outcome
[14]	63/M	Porcine aortic valve for severe stenosis across his native bicuspid aortic valve Dental caries and tooth erosions	Nightly sweats Weight loss Immune thrombocytopenic purpura refractory to steroids Splenomegaly	Holosystolic murmur TTE: A degenerated aortic valve prosthesis with moderate aortic stenosis and aortic insufficiency No vegetation	L: $9,3 \times 10^9/L$	Good outcome
[15]	61/M	Carpentier-Edwards prosthesis aortic valve replacement 3 episodes of <i>Streptococcus sanguinis</i> endocarditis	Lethargy Weight loss Chills Night sweats for 2 months	TTE: Minimal calcifications and an aortic insufficiency TOE: No signs of endocarditis	L: $8,2 \times 10^9/L$ CRP: 17 mg/L	Good outcome
[16]	60/M	Dermatological lesion treated with corticoids	Atypical chest Constrictive pain	Diastolic murmur TOE: Large valvular vegetation right coronary aortic cusp	L: $9,1 \times 10^9/L$ CRP: 24 mg/L	Valve replacement
[17]	12/M	Tetralogy of Fallot Replacements of right ventricle to pulmonary artery complicated by <i>Staphylococcus aureus</i> mediastinitis Poor dentition	Fatigue Decreased endurance of 2-3 weeks duration	Systolic and diastolic murmur Echocardiogram: Valve with a suggestion of mass attached to the leaflet TTE: Mass on a pulmonary valve leaflet concerning for a possible vegetation	L: $5,9 \times 10^9/L$ ESR: 25 mm/h CRP: 11.5 mg/L	Not stated
[18]	47/M	Dyspnea, orthopnea, exertional chest heaviness and hemoptysis 4 months previously Dental procedure	Worsening malaise Fatigue Drenching night sweats Anorexia Weight loss	Aortic and diastolic murmur TOE: Bicuspid aortic vegetations Magnetic resonance angiography: Septic cerebral embolus	L: $14,1 \times 10^9/L$ CRP: 64 mg/L ESR: 28 mm/h	Aortic valve replacement Residual left-sided numbness at three-month follow-up
[19]	56/M	Weaned smoking Overweight	Pelvic girdle and scapular pain Anemia	TTE: Tricuspid valve endocarditis TOE: Tricuspid valve vegetation Chest scan: Septic pulmonary embolism	CRP: 69 mg/L	Tricuspid valve replacement Good outcome
[20]	60/M	Valve-sparing aortic root replacement for aortic regurgitation Dental procedure	Fatigue with anemia over a 3-month period	Holosystolic murmur TTE and TOE: Aortic valve vegetation	L: $8,3 \times 10^9/L$ CRP: 5.2 mg/L	Aortic valve replacement Good outcome

(continued on next page)

Table 1 (continued)

References	Age (y) / Sex	Medical history	Symptoms at admission	Cardiac symptoms at admission	Initial laboratory investigations	Outcome
		Esophagogastroduodenoscopy and colonoscopy 4 weeks before		Brain magnetic resonance imaging (MRI): multiple acute lacunar infarctions (= cerebral embolism)		

L: leukocytes, ESR: erythrocyte sedimentation rate, TTE: transthoracic echocardiography, TOE: transesophageal echocardiography, CRP: C-reactive protein

endocarditis diagnosis. Gram stain showed pleiomorphic Gram-negative rods with swollen ends arranged in rosette clusters suggesting *Cardiobacterium hominis*. The first antimicrobial therapy initiating with oxacillin and amoxicillin was modified by ceftriaxone (4 g/day). After 72 h of incubation at 37 °C in 5–10% CO₂ in a humid atmosphere, subcultures on chocolate agar plate yielded pale yellow to white colonies, measuring 1 mm (oxidase positive, catalase negative and indole positive). Identification was performed using MALDI-TOF-mass spectrometry (Bruker Daltonics, Wissembourg) giving a 1.96 score for *Cardiobacterium hominis*.

Antibiotic susceptibility testing was performed using disk diffusion method (BioMérieux, Marcy l'Etoile, France) on Mueller-Hinton agar supplemented with 5% horse blood and 20 mg/L β-NAD (MHF). The strain was susceptible to amoxicillin, amoxicillin-clavulanic acid, piperacillin, cefotaxime, carbapenems, aminoglycosides and fluoroquinolones. The nitrocefin-based test (Nitrocefin SR112, Oxoid microbiology Products, USA) for beta-lactamase production was negative. The treatment with ceftriaxone (4 g/day) was therefore switched to amoxicillin (8 g/day) for 4 weeks. The evolution of infectious process was favorable and the patient remained afebrile throughout his stay. The aortic insufficiency was treated using a mechanical prosthesis after 4 days of medical antibiotic treatment. The culture of the native valve remained sterile and molecular typing with 16 S rRNA gene sequencing confirming *Cardiobacterium hominis* identification (accession number LR134365.1) based on a 100% identity, using the NCBI database.

Discussion

Cardiobacterium hominis is a Gram-negative facultative anaerobic, non-motile rod. It can be arranged in pairs, short chains, teardrop forms, rosettes, or clusters. *C. hominis* tend to retain gentian violet at apical points after Gram staining. It is a commensal species of the human oral cavity and nasopharynx but has also been described in the genital tract of some people. The low virulence of *C. hominis* explains the opportunistic role of this bacterium recognized as a cause of subacute or chronic infective endocarditis [5]. In 2018, a study including 17 patients with HACEK infective endocarditis was reported. The most frequent clinical characteristic was fever at admission, in 16 patients (94%) [2]. In 2019, in a review of the literature, 73 cases of infective endocarditis caused by *C. hominis* were described and the mainly clinical feature of these patients was also fever in 54/70 (77%) [6]. In our case, the patient presented an acute pulmonary oedema without fever on admission. Fifteen other cases of *C. hominis* afebrile endocarditis have been reported in the literature over the last 50 years (Table 1).

The majority of patients was male 13/15 (87%) with a median age of 56 years. Native-valve endocarditis was more common than prosthetic-valve endocarditis. Aortic valve was the site of infection the most frequently found in 12/15 (80%), the remaining sites being 1 case of tricuspid valve infection, 1 case of pulmonary valve infection and 1 case unknown. As for clinical characteristics at admission, fatigue and malaise were the most frequent in 9/15 (60%), followed by night sweats in 4/15 (27%) and weight loss in 3/15 (20%). Other symptoms found were leg pain, splenomegaly, chest pain and shortness of breath. In terms of laboratory data, in the majority of cases white blood cell count was normal in 11/15 (73%). The C-reactive protein concentration and the erythrocyte sedimentation rate were increased in 6/15 and 4/15

respectively, however the level remains low. The clinical presentation of *C. hominis* endocarditis is known to be insidious, particularly in the absence of fever: indeed, other symptoms are non-specific and biological markers of inflammatory syndrome are discrete or non-existent.

We note here that no case associating acute pulmonary oedema and *C. hominis* have been reported in the literature. This presentation was probably due to the evolution of the cardiac process complicated by *C. hominis* endocarditis.

In our case, six blood cultures were positive for *C. hominis* with a relatively short delay of 34 h. As described previously, improvements to conventional blood culture techniques allow the detection of *C. hominis* with available automated blood culture systems within the standard incubation period of 5–6 days in 95% of the cases if the patient did not received antibiotics [21,22]. For all studies presented in Table 1, the microbiological diagnosis of *Cardiobacterium* endocarditis was made by detection of the pathogen in blood cultures, except for one case [11] diagnosed in the embolic material by broad range polymerase chain reaction amplification of 16 S ribosomal RNA.

The standard treatment of endocarditis caused by HACEK microorganisms is intravenous ceftriaxone (2 g/day) for 4 weeks in native valve and 6 weeks in prosthetic valve [23,24]. Due to the emergence of β-lactamase producing strains [25], the detection of production of β-lactamase is required. In absence of the enzyme, the strain is susceptible to ampicillin and the treatment may be de-escalated to a more restrictive-spectrum antibiotic. Endly, ciprofloxacin may be an option for penicillin and cephalosporin intolerance [23,24].

In the review of the 15 cases, the most common complications were embolic events in 6/15 (40%), including 3 patients with embolic lesions to the central nervous system (CNS) (50%) and 3 patients with peripheral emboli (2 patients with embolic occlusion of the fibular artery and 1 patient with pulmonary embolism). These results are in line with Wormser et al.: embolic events were seen in 44% of patients [5]. Nevertheless, CNS emboli were observed in 21–22% of cases of complications of *C. hominis* endocarditis [6,26]. In most cases, the prognosis of patients is favourable [6], however valve replacement is required in the majority of cases. In our review, 11/15 patients (73%) underwent surgery therapy in addition to medical treatment.

In conclusion, this case illustrates the importance of suspecting *C. hominis* infective endocarditis in patient with a clinical presentation of acute pulmonary oedema. Endocarditis should be suspected even in absence of fever.

Conflicts of interest

The authors declare that they have no conflict of interest.

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