Fatal Bioprosthetic Aortic Valve Endocarditis Due to *Cardiobacterium valvarum*

Walter Geißdoerfer,1* René Tandler,2 Christian Schlundt,3 Michael Weyand,2 Werner G. Daniel,3 and Christoph Schoerner1

Institute of Clinical Microbiology, Immunology and Hygiene,1 Center of Cardiac Surgery,2 and Department of Internal Medicine 2 (Cardiology),3 University of Erlangen-Nuremberg, Erlangen, Germany

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*Corresponding author. Address: Institut für Klinische Mikrobiologie, Immunologie und Hygiene, Universität Erlangen-Nürnberg, Wasserturmstrasse 3, D-91054 Erlangen, Germany. Phone: 49-9131-852-2647. Fax: 49-9131-852-1001. E-mail: walter.geissdoerfer@ mikrobio.med.uni-erlangen.de.

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*Cardiobacterium valvarum* was isolated from the blood of a 71-year-old man with fatal aortic valve endocarditis. The API NH system was used for phenotypic characterization of the *C. valvarum* strain. This is the first case of infective endocarditis caused by *C. valvarum* in Germany and the first case worldwide affecting a prosthetic valve and lacking an obvious dental focus.

CASE REPORT

A 71-year-old patient was admitted to our cardiac department due to complicated severe endocarditis. His medical history revealed surgery 2 years previously with insertion of bypasses and replacement of a stenotic aortic valve with a bioprosthesis. No infective endocarditis was diagnosed at that time. Two months prior to admission, he had suffered backache resulting from a disc prolapse, which was conservatively treated with repeated local injections of nonsteroidal anti-inflammatory drugs. In the last weeks before admission, he developed a general weakness accompanied by fever, chills, edema and petechiae in the legs, and psychomotoric slowing. Upon admission to a nearby hospital (day 1), arterial hypotension was treated with noradrenalin. Transesophageal echocardiography revealed endocarditis with vegetations on the bioprosthetic aortic valve. Blood cultures were taken immediately and showed growth of fastidious gram-negative rods after 4 days of incubation. In response to this finding, empirical antibiotic therapy was adjusted to ceftriaxone, rifampin, and amikacin. When an atrioventricular block, grade III, appeared on day 6, the patient was transferred in stable cardiorespiratory condition to our department of cardiology. The API 20NE (bioMérieux) system was used for phenotypic characterization of the *C. valvarum* strain. This is the first case of infective endocarditis caused by *C. valvarum* in Germany and the first case worldwide affecting a prosthetic valve and lacking an obvious dental focus.

In a nearby laboratory, the blood culture isolate (VA1941/06) was tentatively identified as a probable HACEK organism on the basis of gram staining (gram-negative rods) and testing for oxidase (positive), catalase (negative), and indole (positive). Because conventional identification of these organisms can be challenging, and because of the patient’s severe clinical condition, the strain was sent to our department of clinical microbiology for fast characterization. 16S rRNA gene sequence analysis revealed 99.8% identity to the sequence of *Cardiobacterium valvarum* (GenBank accession number AF506987). Routine PCR testing of the explanted aortic valve prosthesis by broad-range (”eubacterial”) PCR (8) revealed the identical 16S rRNA gene sequence, confirming *C. valvarum* as the etiological agent of endocarditis.

Cultures from the explanted valve specimen were incubated for 13 days but remained negative, indicating the effectiveness of the antibiotic treatment. Strain VA1941/06 grew slightly better on chocolate agar at 37°C with 5% CO₂ than on sheep blood agar and formed round, opaque, weakly alpha-hemolytic, glistening colonies of 0.5 mm after 3 days (Fig. 1). Bacterial cells appeared as straight gram-negative rods, located singly or in pairs and of variable length depending on the medium (Fig. 1). The API 20NE (bioMérieux) system was
positive for tryptophanase only, and the resulting identification code 2000004 was unsuitable for identification, as previously described by Han et al. (3, 4). With the API NH system, reactions for glucose, fructose, maltose, sucrose, indole, lipase (weak), and alkaline phosphatase were positive, whereas penicillinase, ornithine decarboxylase, urease, beta-galactosidase, proline arylamidase, and gamma-glutamyl transferase were negative. The respective API NH algorithm resulted in identification code 7134, corresponding to *Haemophilus parainfluenzae*.

In an agar diffusion test and determination of the MIC with Etest (Biodisk, Solna, Sweden) on nonstandardized chocolate tryptone agar, the *C. valvarum* strain showed high susceptibility to penicillin (MIC, 0.008 mg/liter), amoxicillin (MIC, 0.016 mg/liter), piperacillin, cefazolin, cefotiam, ceftriaxone (MIC, 0.016 mg/liter), ceftazidine, imipenem (MIC, 0.012 mg/liter), meropenem, gentamicin, tobramycin, amikacin, ciprofloxacin, moxifloxacin (MIC, 0.006 mg/liter), fosfomycin, erythromycin, tetracycline, chloramphenicol, vancomycin, and linezolid.

The genus *Cardiobacterium*, with its sole species, *C. hominis*, was established in 1964 for a group of fastidious gram-negative bacteria of the HACEK group (9). *C. hominis* is found in most (70%) individuals as part of the normal flora of the nose and throat. It appears to be the rarest agent of infective endocarditis within the HACEK group, with a total of 61 reported cases (1, 2, 6). The species *C. valvarum*, as a new member of the HACEK group, was first described in 2004 in Houston, TX, as the agent of endocarditis (4). Two additional cases have been reported, from Washington, DC (5), and Marseilles, France (1). A fourth case, from Chicago, IL, has been published without clinical data (7). Ours is therefore the fifth case of endocarditis caused by *C. valvarum* worldwide, the second in Europe, and the first in Germany. From our experience of 175 cases of infective endocarditis diagnosed from explanted heart valves, this case is the only one caused by a HACEK organism.

Strain VA1941/06 is available from the Culture Collection of the University of Göteborg, Göteborg, Sweden (CCUG 53031). Its phenotypic and biochemical features resemble those of the reported strains (1, 3–5), including their sensitivity to a broad range of antibiotics. In contrast, however, it grew better on chocolate agar than on sheep blood agar. Indole production, as a key reaction for identification of gram-negative bacteria, was reported to be positive for two (1, 4) and negative in five (3, 5) isolates of *C. valvarum*. Our strain tested indole positive. This confirms that indole production is variable within *C. valvarum* and is therefore not appropriate for differentiating *C. valvarum* from indole-positive *C. hominis*. Because API 20NE is not suitable for identification of *C. valvarum* due to its fastidious growth, we used the API NH identification system, which is commonly used for identification of *Haemophilus* spp. and *Neisseria* spp. of clinical importance. The outcome of the reactions was well defined but resulted in a misidentification as *Haemophilus parainfluenzae*, which does not grow on sheep blood agar. Therefore, API NH may be used for determination of key reactions in the case of fastidious gram-negative rods such as *C. valvarum*, but for final identification, molecular tools, e.g., 16S rRNA gene sequence analysis, are indispensable.

**FIG. 1.** (A) Colony morphology of *C. valvarum* on chocolate agar after 4 days of growth at 37°C with 5% CO₂. (B to D) Gram stains from blood culture (B), agar with sheep blood (C), and chocolate agar (D).
As with the other cases described in the literature, the onset of disease in our case was insidious, with moderate or no fever, and infection resulted in extensive tissue destruction, necessitating valvular replacement. Unlike all other published reports, in which the patients had a congenital bicuspid aortic valve, our patient had a prosthetic aortic valve as a risk factor, and he could not be restored to health as a consequence of the massive destruction of heart tissue. A fatal outcome is also unusual in cases of endocarditis caused by *C. hominis*, where the prognosis for both native and prosthetic valve endocarditis is usually favorable (6). The oral cavity is the probable reservoir of *C. valvarum*, because in all three of the published cases the patients experienced oral abscesses or dental treatment without antibiotic prophylaxis prior to endocarditis. In addition, other *C. valvarum* strains have all been isolated from subgingival pockets and tooth plaque (3). In contrast, our patient had no significant dental treatment prior to the onset of disease, and no further focus was known. However, the condition of his teeth and gums was poor, and they may have been a reservoir for *C. valvarum*.

In conclusion, this is the first case of endocarditis due to *C. valvarum* affecting a prosthetic valve, and it shows that physicians should be aware of *C. valvarum* as a rare cause of endocarditis. In addition, our case supports the value of applying molecular methods in the detection and identification of unusual agents of infective endocarditis.

**Nucleotide sequence accession number.** The 16S rRNA gene sequence of strain VA1941/06 has been deposited in the GenBank database under accession number DQ645464.

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**REFERENCES**