Aerococcus viridans native valve endocarditis

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Aerococcus viridans is an infrequent human pathogen and few cases of infective endocarditis have been reported. A case involving a 69-year-old man with colon cancer and hemicolectomy 14 years previously, without recurrence, is reported. A diagnosis of native mitral valve endocarditis was established on the basis of clinical presentation, characteristic echocardiographic findings and pathological specimen examination after urgent valve replacement. *A viridans* endocarditis appears to be particularly virulent, requiring a surgical approach in four of 10 cases reported and death in one of nine. Given the aggressive nature of *A viridans* endocarditis and the variable time to diagnosis (a few days to seven months), prompt recognition of symptoms and echocardiography, in addition to blood cultures, should be performed when symptoms persist.

Key Words: A viridans; *Endocarditis; Mitral valve*

Une endocardite à *Aerococcus viridans* de la valvule naturelle

L'*Aerococcus viridans* est un pathogène humain peu fréquent qui s'associe à peu de cas déclarés d'endocardite infectieuse. Les auteurs présentent le cas d'un homme de 69 ans atteint d'un cancer du côlon et ayant subi une hémicolectomie 14 ans auparavant, sans récurrence depuis. Les médecins ont posé un diagnostic d'endocardite de la valvule mitrale naturelle d'après la présentation clinique, les observations échocardiographiques caractéristiques et l'examen des échantillons pathologiques après un remplacement valvulaire d'urgence. L'endocardite à *A viridans* semble particulièrement virulente. Elle a exigé une approche chirurgicale dans quatre des dix cas déclarés, et a suscité un décès dans un cas sur neuf. Étant donné le caractère agressif de l'endocardite à *A viridans* et le délai variable avant le diagnostic (de quelques jours à quelques mois), il faut en reconnaître rapidement les symptômes et ajouter une échocardiographie aux hémocultures en cas de persistance des symptômes.

Aerococcus viridans is a microaerophilic, Gram-positive, catalase-negative coccus with a strong tendency toward tetrad formation. It has growth characteristics similar to that of streptococci and enterococci. Aerococci are environmental isolates ubiquitously found in the air of housing premises (hospitals, schoolrooms, factories, offices), dust, raw vegetables, animals and animal products, as well as human skin (1). Three *Aerococcus* species have been implicated as rare pathogens in humans. *Aerococcus urinae* causes endocarditis (2-11), septicemia, urinary tract infections/urosepsis, pyelonephritis, spondylodiscitis, spontaneous bacterial peritonitis, peritonitis, lymphadenitis and soft tissue infections (12-25). *Aerococcus sanguinicola* causes bacteremia (26), endocarditis (26), urosepsis (26) and cholecystitis (26). *A viridans* causes urinary tract infections (27,28), bacteremia, endocarditis (Table 1), para-aortic abscess, meningitis, spondylodiscitis and septic arthritis (29-44). Risk factors for *A viridans* systemic infections (bacteremia/endocarditis) have not yet been fully elucidated; however, granulocytopenia, oral mucositis, prolonged hospitalization, previous antibiotic therapy, invasive procedures and implantation of foreign bodies have been associated with severe infections with *A viridans* (36). Previous valvular abnormalities, such as rheumatic valve disease, have been described as predisposing conditions for infective endocarditis (38). Reports in which no obvious immunosuppressive factor could be found are rare. This was the case in our patient.

Studies from clinical cases and specimens demonstrated that strains are generally susceptible to β-lactam antimicrobials (eg, penicillin, ampicillin, amoxicillin-clavulanic acid) and vancomycin (40-44). On the other hand, resistance was found to quinolones, tetracycline, clindamycin and streptomycin (40-44); penicillin resistance was reported in two instances to levels >250 µg/mL (44). Resistance to gentamicin has also been reported occasionally for human clinical strains (39,41).

The present article describes a case of *A viridans* endocarditis in a patient with no obvious risk factor for immunosuppression or previous valvular abnormality.

CASE PRESENTATION

The patient was a 69-year-old man with colon cancer and hemicolectomy 14 years previously, without recurrence. He was admitted to hospital after five weeks of general deterioration, fatigue, weight loss, chills and sweats. He reported undergoing a dental cleaning one month before admission. Physical examination revealed a man with a heart rate of 82 beats/min, blood pressure of 122/86 mmHg, a respiratory rate of 22 breaths/min and a temperature of 37.2°C. His lungs were clear and cardiac sounds revealed a grade III/VI pansystolic blowing murmur at the apex radiating to the axilla with a laterally displaced apex. There were no heaves or thrills. The jugular venous pulse was noted at 2 cm above the sternal angle, at 30°. Abdominal examination revealed no hepatomegaly or splenomegaly. No peripheral stigmata of embolic phenomena were identified in the extremities, skin or retina. The neurological examination was unremarkable.

Blood work revealed a hemoglobin level of 126 g/L, a white blood cell count of 13.45×10^9/L , an absolute neutrophil count of 10.96×10^9/L and a platelet count of 243×10^9/L. Serum electrolytes and creatinine levels were normal, as were liver enzyme levels and coagulation profile. An electrocardiogram showed normal sinus rhythm with a normal QRS interval. Chest radiography showed no cardiomegaly or pulmonary edema. Transesophageal echocardiography demonstrated two large mitral valve vegetations; the first identified was a multilobulated vegetation on the anterior leaflet 2.4 cm ×1.4 cm with perforation of the leaflet, and another vegetation measuring 1.7 cm ×1.0 cm was identified on the posterior leaflet. Doppler interrogation confirmed moderate to severe mitral regurgitation. No abscesses were identified. The other valves were

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TABLE 1
Review of published reports on *Aerococcus viridans* endocarditis

Case	Age, years/ sex	Clinical presentation	Diagnosis	Treatment	Complications	Resistant	Ref
1	49/M	Subacute (7 months): Fever; polymyalgia; mild AR murmur	14×15 mm AV veg on TEE	Ampicillin/ amikacin	AV thickening/mild AR. Medical Rx. No relapse at 18 months	Quinolones/ aminoglycosides	40
2	62/M	Subacute (1 month): Fever; weight loss; dyspnea/MR murmur; Janeway lesion; splenomegaly	13×12 mm veg on anterior mitral leaflet	Ceftriaxone/ amikacin	Splenectomy for splenic abscesses. MVR. No relapse at 12 months	Quinolones	40
3	40/M	Subacute (3 weeks): Fever/ fatigue; arthralgias; Osler nodes	14×11 mm veg at aortic cusp on TEE	Penicillin G/ gentamicin	Medical Rx. No relapse at 38 months		40
4	45/F	Acute (3 days): Fever; dyspnea; ataxia; Janeway lesion; MR murmur; CHF	7×6 mm veg on anterior leaflet and posterior leaflet 5×3 mm	Penicillin G/ gentamicin	MVR		40
5	10/M	Subacute (1 month): Fever; dyspnea; arthralgia; hematuria; clubbing; MR murmur; CHF	Veg on mitral leaflet	Norfloxacin/ amikacin	Compensated MR. Medical Rx	Penicillin/ampicillin/ cefotaxime/gentamicin	41
6	28/M	Subacute (6 months): Fever; rheumatic complaints; hematuria; AR murmur	Flail aortic leaflet with veg	Penicillin G/ gentamicin	AoVR. No relapse at 6 months		44
7	44/M	Acute (few days): Fever; hematuria; splenomegaly; AR murmur	Not reported	Penicillin/ streptomycin	CHF 6 weeks post discharge. Sudden death		42
8	54/M	Subacute (4 months): Fever; back pain; systolic murmur	Billowing leaflet	Penicillin	Medical Rx. No relapse at 10 weeks	Sulfonamide	43
9	58/M	Acute (4 days): Fever; pyuria/ hematuria; altered LOC; diastolic murmur	10 mm veg on noncoronary cusp of AV on TEE	Cefotaxime/ vancomycin	Medical Rx. Well at 3 months outpatient follow-up	Chloramphenicol/ clindamycin/ erythromycin/ gentamicin/TMP-SMX	39
10	44/F	Subacute (2 weeks): Fever; AF; systolic murmur at AV area	Rheumatic AV and MV; moderate MS; oscillating mass 11×10 mm, MG 35 mmHg across AV on TEE	Ampicillin/ sulbactam/ gentamicin	Enlarging veg (21×10 mm) causing AV obstruction s/p 3 weeks of oral antibiotics requiring AoVR/MVR		38

AF Atrial fibrillation AoVR Aortic valve replacement; AR Aortic regurgitation; AV Aortic valve; CHF Congestive heart failure; F Female; LOC Level of consciousness; M Male; MG Mean gradient; MR Mitral regurgitation; MS Mitral stenosis; MV Mitral valve; MVR Mitral valve replacement; Ref Reference; Rx Treatment; s/p Status post; TEE Transesophageal echocardiogram; TMP-SMX Trimethoprim-sulfamethoxazole; Veg Vegetation

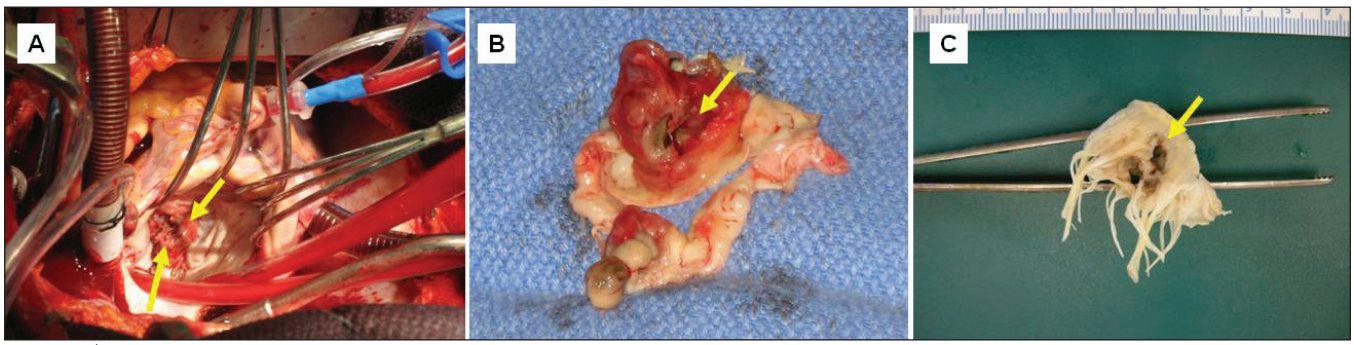

Figure 1) A *Intraoperative view of the mitral valve through a left atreiotomy. Vegetations (arrows are seen on the anterior and posterior valve leaflets).* **B** *Resected specimen. The anterior valve leaflet is perforated (arrow). Large vegetations are seen on the anterior valve leaflet and the Pi segment of the posterior leaflet. Note the intense inflammation and fibrotic reaction contributing to the distorsion of the valve apparatus.* **C** *Ventricular aspect of the resected mitral valve showing the perforation of the anterior leaflet (arrow)*

otherwise normal on echocardiography. Two different sets of blood cultures grew *A viridans*, with sensitivities to ceftriaxone (0.25 µg/mL) and penicillin (0.03 µg/mL).

Surgery was performed six days after admission because of general deterioration, evidence of moderate to severe mitral regurgitation and fenestration of the anterior mitral valve leaflet. Blood-based cardioplegia was administered for myocardial protection. Through a left atriotomy, direct visualization of the mitral valve revealed large vegetations on the anterior and posterior leaflets with marked anatomical destruction of the valve (Figure 1A). Closer examination showed marked distortion of the valve apparatus, with a fenestration of the anterior leaflet (Figure 1B and 1C). The annulus was preserved. Mitral valve replacement using a bioprosthetic valve was performed. Care was taken to preserve the papillary-annular continuity to maintain ventricular function by saving as much of the mitral subvalvular apparatus as possible. Both the surgery and the postoperative course were uneventful. On postoperative day 7, he was discharged home without complications. A six-week treatment of penicillin was provided via pump through an indwelling intravenous line. Repeat postoperative blood cultures were negative for any growth.

Gross pathological examination (Figure 1) of the mitral valve revealed a firm thrombus, 2.0 cm in its greatest dimension, attached

to the ventricular aspect of a somewhat thickened valve. The thrombotic lesion appeared to have eroded into the valve, creating full-thickness valvular perforations measuring 1.0 cm and 0.7 cm in its greatest dimension (Figures 1B and 1C). Histological assessment of the valve revealed a prominent fibrinous exudate with neutrophils and tissue destruction, as well as areas of organization and fibrosis (Figures 2A to 2D). Furthermore, microscopy revealed a prominent population of Gram-positive cocci in clusters (Figure 2E), consistent with the *A viridans* found in the patient's blood. Nectrotic debris and fibrotic destruction of the valve are shown in Figure 2F.

DISCUSSION

We identified 10 previously reported cases of *A viridans* endocarditis (Table 1). In all reported cases, vegetations were identified on the mitral or aortic valves. One case resulted in congestive heart failure and death after discharge. In three cases, the isolated strain of *A viridans* was resistant to penicillin or quinolones. The laboratory findings were often nonspecific, with elevation in markers of inflammation (C-reactive protein, erythrocyte sedimentation rate and a mild leukocytosis). Blood cultures and echocardiography provided the diagnosis in all instances reported.

As in the present case, the symptoms of endocarditis are often nonspecific. From the onset of symptoms to first medical contact, a delay of at least five weeks was reported. This delay likely contributed to the destruction and perforation of the mitral valve leaflet.

CONCLUSION

A viridans endocarditis appears to be particularly virulent, despite its often long latency period (subacute 73% [eight of 11 cases] and acute 23% [three of 11 cases]) and comparably lower mortality rates (9% [one of 11 cases]) as opposed to left-sided, native valve *Staphylococcus aureus* infective endocarditis (30% to 40%). It nonetheless required a surgical approach in 45% (five of 11) of the cases reported. Given the aggressive nature of *A viridans* endocarditis and the variable time to diagnosis (a few days to seven months), prompt recognition of symptoms, blood cultures and echocardiography, including transesophageal echocardiography, should be performed when blood cultures are positive and suspicion index is high.

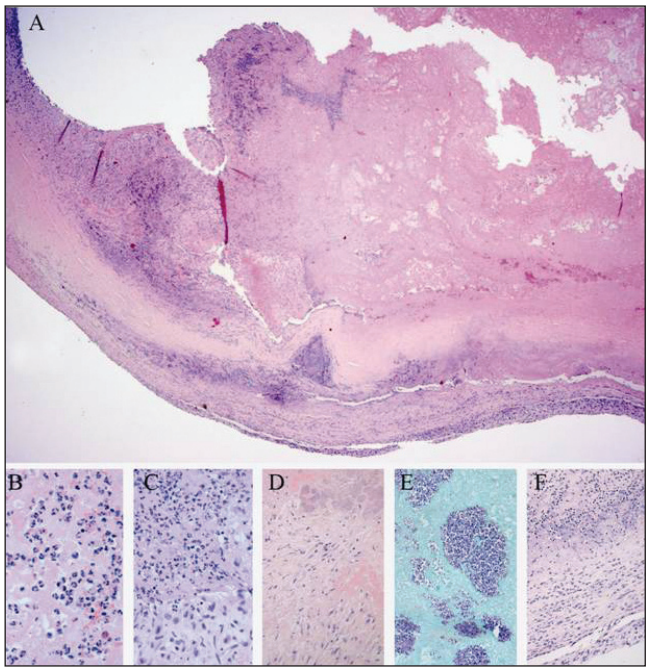

Figure 2) *Organizing mitral valve vegetation with bacterial growth and inflammatory infiltrate*. **A** *Hematoxylin and eosin stain of a representative section of the anterior mitral valve. Fibrotic remnant of the valve is seen at bottom of pictogram with fibrinous material on its ventricular surface. High magnification of* **A** *demonstrating focal infiltration by neutrophils* (**B**)*, with areas of early-stage organization* (**C**) *and later-stage organization* (**D**)*, as well as colonies of Gram-positive cocci in clusters* (**E**; *Gram-stain*)*. High magnification of the valve* (**F**) *reveals necrotic debris and fibrotic destruction of the valve*

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