

Case Reports

Enterococcus faecalis endocarditis

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ABSTRACT

The increasing usage of cephalosporins, to which the enterococci are resistant, has resulted in the rising number of enterococcal infections worldwide. Enterococci are a normal part of the flora of the human gastrointestinal tract, buccal cavity, perineal skin, vagina, urethra and gallbladder, but may occur as pathogens in a number of sites causing urinary tract infections, intra-abdominal infections, fatal bacteremia, meningitis and endocarditis. A Saudi male who developed enterococcal endocarditis with vegetations on both aortic and mitral valves required mitral and aortic valve replacement. The attention of physicians is drawn to the increasing frequency of enterococcus as a cause of nosocomial infections, the risk factors, and antibiotic resistance pattern including resistance to vancomycin as well as its potential for virulence.

Keywords: Endocarditis, enterococcal.

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In the last decade, there have been numerous reports of the increasing incidence of enterococcal infections.¹⁻³ The increasing number of enterococcal infections has been associated with increasing cephalosporin usage, to which enterococci are usually resistant.⁴ Enterococci are normally part of the flora of the human gastrointestinal tract, buccal cavity, perineal skin, vagina, urethra and gallbladder, but may occur as pathogens in a number of sites causing urinary tract infections, intra-abdominal infections, fatal bacteremia and endocarditis.^{2,5-11} Debilitated or immunocompromised patients are highly susceptible to enterococcal infections, which frequently arise from the urinary or gastrointestinal tracts.⁹ Enterococcal infections may also occur as a result of abdominal wounds and surgery, where their role may be underestimated.¹⁰ Furthermore, enterococci may invade the blood stream to cause endocarditis, meningitis and septicemia with associated high mortality rates.^{11,12} Antibiotic therapy with 3rd generation cephalosporins, imipenem, ciprofloxacin, aztreonam and ticarcillin/clavulanate has been reported as a high risk factor for the

development of enterococcal bacteremia.⁸ There have been very few reports of systemic human enterococcal infections in the Kingdom of Saudi Arabia (KSA).^{5,7,13-15} In this report, we present the case of a Saudi male who developed enterococcal endocarditis requiring mitral and aortic valve replacement. As far as we are aware, this is the first case of enterococcal endocarditis reported in KSA.

Case Report. This 33-year-old man was seen at our Nephrology Clinic where he was being followed up for minimal change glomerulonephritis causing nephrotic syndrome and hypertension. He was on treatment with prednisolone, atorvastatin and captopril. At a routine follow-up appointment, he was noted to be pyrexial with temperature of 38°C, without any localizing symptoms. On examination, he had a pansystolic murmur at the cardiac apex and an early diastolic murmur at the aortic area. There were no other clinical indicators of infective endocarditis. His blood count showed a significant neutrophil leucocytosis. His erythrocyte sedimentation rate was 50 mm in one hour. Blood

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cultures were sent and *Enterococcus faecalis* (*E.faecalis*) was isolated from both aerobic and anaerobic blood culture bottles. For logistic reasons, he was admitted to another hospital and commenced on treatment with intravenous (IV) ampicillin 175 mg/kg/day in divided doses and gentamycin 1 mg/kg every 8 hours.¹⁶ His transthoracic and transesophageal echocardiograms confirmed infective endocarditis initially only at the aortic valve, but later also at the mitral valve. He was strongly advised to undergo surgery, but he declined. He was continued on IV antibiotics as an inpatient for 5 weeks, after which he was discharged and continued on IV antibiotics at home with the assistance of personnel from a nearby Polyclinic. Unfortunately, a week later, he sustained a cerebrovascular accident (CVA) with a dense left hemiplegia, facial weakness, and dysphagia and recurrent choking. His family brought him to our emergency room and on examination, he was very ill looking. His jugular venous pressure was elevated and he had peripheral manifestations of severe aortic regurgitation (AR). He was afebrile. He had mild clubbing of his fingers and toes, as well as splinter hemorrhages. He was in pulmonary edema and had features of aspiration pneumonia. On cardiac auscultation, he had features of severe AR, mild mitral regurgitation (MR) and mild tricuspid regurgitation. Examination of the abdomen showed no tenderness or hepatosplenomegaly. He was confused with a dense left hemiparesis, dysarthria and left VII nerve palsy. Investigations showed a neutrophil leucocytosis, mild anemia and elevated urea, with normal creatinine. His albumin ranged between 24 and 28 g/l and proteinuria was in the range of 200 mg/24 hours. His liver enzymes showed an elevated aspartate transaminase of 345 IU/L and alanine transaminase at 1,021 IU/L, which improved over the ensuing days. His electrocardiogram showed left ventricular hypertrophy and strain

pattern. His chest x-ray showed cardiomegaly with fluffy infiltrates in both lung fields, and a small right pleural effusion. An urgent transthoracic Echo-Doppler showed a normal looking aortic root with large vegetations on all 3 aortic valve leaflets (**Figure 1**). He also had severe AR with a dilated left ventricle (LV) but initially very well contracting with a normal LV ejection fraction. His LV contractility deteriorated rapidly over the ensuing days. His mitral valve leaflets were also thickened with a small echodense mass attached to anterior mitral leaflet and moderate MR (**Figure 1**). Computerized tomography of the brain showed a large infarct in his right parieto-occipital region (**Figure 2**).

In summary, he had partially treated infective endocarditis with multiple complications including severe AR, MR, embolic CVA with suspected aspiration pneumonia, sepsis, prerenal azotemia and hepatitis probably secondary to an acute ischemic insult. Unfortunately, a few hours after admission, he continued to deteriorate and became acutely distressed with marked tachypnea and desaturation despite supplemental oxygen. He was therefore electively intubated and transferred to our intensive care unit, where he had a Swan-Ganz catheter inserted. This showed a reduced cardiac index (2.24 litres/min/m²) despite inotropic support; and a slightly elevated systemic vascular resistance index (1,680 dynes-sec-cm⁻⁵/m²). His pulmonary capillary wedge pressure was also elevated. He was commenced on imipenem 500 mg twice daily and metronidazole 500 mg IV twice daily for presumed aspiration pneumonia and uncontrolled sepsis, as well as the ampicillin and gentamycin after the appropriate cultures were taken. He was transferred to the regional cardiothoracic surgical center where he underwent emergency aortic and mitral valve replacement. A piece of the vegetation was sent to the Microbiology Laboratory for culture. In spite of being a high risk surgical patient, he made an

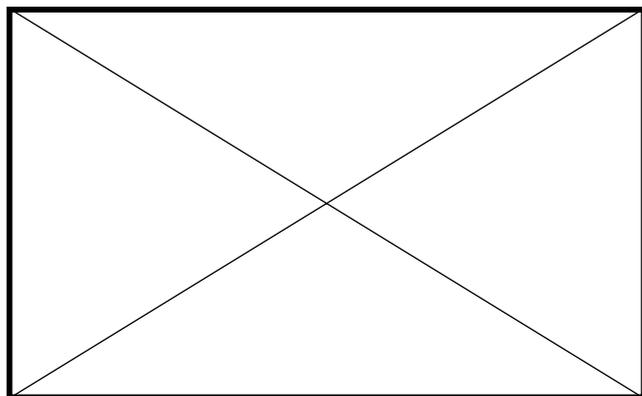


Figure 1 - Echocardiogram showing multiple vegetations on aortic valve. RV - right ventricle, RA - right atrium, LA - left atrium, PA - pulmonary artery, AOV - Aortic valve.

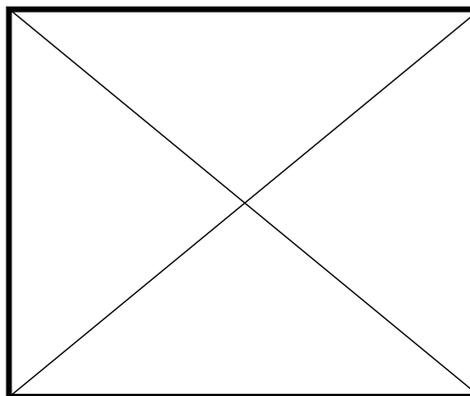


Figure 2 - Computerized tomography of the brain showing large right parieto-occipital infarction.

excellent post operative recovery and was transferred back to our hospital 48 hours after his double valve replacement on no inotropic support and minimal anti-failure measures. He remained afebrile and continued to show remarkable improvement. Since the vegetations removed at surgery were still positive for *E. faecalis*, he was continued on ampicillin and gentamycin for 4 weeks. He made an excellent recovery from his CVA and was able to perform all the activities of daily living unaided prior to his discharge. His LV dimensions and function normalized over 3 months, at which time he returned to work.

Microbiological investigations. All 4 blood cultures taken at the initial admission were positive for growth. On gram stain, the organisms were gram-positive spherical cocci in pairs and short chains. The culture was identified as *E. faecalis* based on negative catalase and oxidase tests, presence of group D antigen, absence of hemolysis on blood agar, growth in broth containing 6.5% sodium chloride, growth on and blackening of bile-esculin agar and positive identification by the API 20 Strep (BioMerieux sa, Lyon, France). The susceptibility test of the isolate by Kirby-Bauer disk diffusion method according to National Committee for Clinical Laboratory Standards guidelines showed it to be sensitive to penicillin (10 units), ampicillin (10 ug), gentamycin (120 ug) and vancomycin (30 ug). The vegetation tissue was ground and cultured on blood agar aerobically and anaerobically. *Enterococcus faecalis* was isolated and identified as above. The minimum inhibitory concentration as determined by Vitek System (Vitek Systems, Inc, Hazelwood, MO, USA) was penicillin 2.0 mg/L, ampicillin 1.0 mg/L, vancomycin 0.5 mg/L, gentamycin <500 mg/L.

Discussion. Enterococci have been reported to be the 3rd leading cause of bacterial endocarditis, following viridans streptococci and staphylococci and are responsible for approximately 20% of all cases of bacterial endocarditis, whether on previously normal heart valves or on abnormal or prosthetic valves.^{8,17-21} It has been reported that *E. faecalis* adheres to heart valve tissue more strongly than viridans streptococci or staphylococci.²¹ The aggregation substance surface protein has been implicated as a virulence factor for endocarditis. The patients at high risk of developing enterococcal endocarditis include, elderly men, subjected to multiple genitourinary procedures, young women with postpartum and genitourinary infections and intravenous drug abusers.⁸ Most infections are endogenously acquired from the patient's own gastro-intestinal or genitourinary flora.^{17,21} It is probable that the infection in this patient was acquired endogenously through the genitourinary tract of the patient. The predisposing factor in this

patient was the glomerulonephritis and the treatment with prednisolone, which might have precipitated the blood invasion by the enterococcus. Patients with enterococcal endocarditis commonly present with fever, night sweats, weight loss malaise, heart murmurs, and symptoms due to cardiac failure. Neurological abnormalities occur in up to 40% of the patients, as in our patient. Clinical diagnosis is usually confirmed by positive blood cultures and evidence of endocardial involvement at echocardiography, the development of a new cardiac murmur or both.¹⁸ The most important pathogenic feature of the enterococci, is their high level of resistance to many common antibiotics. Enterococci are intrinsically resistant to cephalosporins, clindamycin and aminoglycosides.^{1,3,16,22} Therefore, therapy of enterococcal infections is greatly complicated. One of the major reasons these organisms have thrived in a hospital environment is not only due to their inherent resistance to the commonly used antibiotics but also to their ability to acquire resistance plasmids and transposons, which confer on them resistance to other antibiotics, such as erythromycin, tetracycline and chloramphenicol.^{1,16,19,22} Penicillin, ampicillin and vancomycin are bacteriostatic against enterococci hence bactericidal synergy between one of these antibiotics and an aminoglycoside is usually required to treat the most serious enterococcal infections such as endocarditis and meningitis.^{1,2} Aminoglycosides alone are usually ineffective to treat enterococcal infections due to their inability to penetrate the bacterial cell wall, hence the action of a penicillin is required to disrupt the cell wall synthesis thus allowing the aminoglycoside to penetrate inside the cell and bind to the bacterial ribosomes. However, the synergistic effect is lost, if there is high-level resistance to either class of antibiotic. Resistance to high concentration of aminoglycosides, usually due to aminoglycoside-modifying enzymes is widespread among the enterococci.^{1,2,20,22} Our patient responded to the combination of ampicillin and gentamycin, in addition to vancomycin at one stage, when he was rapidly deteriorating.

Specific anti-enterococcal therapy is indicated when enterococcal endocarditis or septicemia is present, especially when the enterococci are persistent in samples, particularly in elderly or immunocompromised patients.¹² In high-risk patients, delaying specific anti-enterococcal therapy is associated with high mortality.⁹ For endocarditis, 4 to 6 weeks of antibiotic treatment is generally recommended.^{16,21} The overall cure rate for patients with enterococcal endocarditis in which the isolate is susceptible to penicillin, gentamycin and vancomycin is approximately 75%.^{16,21} Teicoplanin and ampicillin combined with sulbactam have also been reported to be very effective in enterococcal

endocarditis with a cure rate of 89%.¹⁹ Recently enterococci, particularly *Enterococcus faecium*, acquired a plasmid-mediated resistance to vancomycin, resulting in a modification of the target site to vancomycin. Since vancomycin-resistant enterococcus has been described in KSA,^{7,13,14} it is mandatory that Microbiology Laboratories should screen all isolates of enterococci for vancomycin resistance and also determine the level of aminoglycoside resistance, since this has implications for therapy.

In conclusion, the increasing frequency of enterococcus as a cause of nosocomial infections demands increased awareness of attending physicians of the risk factors, antibiotic resistance pattern and potential for virulence of the enterococci. It is also to be borne in mind that vancomycin-resistant enterococci have been reported in KSA, hence the need for screening all enterococcal isolates for vancomycin resistance.

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