

Multidrug Resistant Pseudomonas Endocarditis

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Citation

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Abstract

Pseudomonas aeruginosa endocarditis is an uncommon disease except in parenteral drug abusers. While high dose combination antibiotics have improved the outcome of right-sided *pseudomonas* infection, the mortality and morbidity for left-sided valvular infection remains high. Factors contributing to this high mortality are frequent complications including systemic emboli, CHF, valve ring abscesses, high conduction abnormalities and higher relapse rates due to development of antibiotic resistance. However, medical therapy in combination with early surgical intervention appears to have improved the out come of left-sided *pseudomonas* endocarditis

CASE REPORT

A 44 yr old white female was admitted to one of the university hospitals to undergo bariatric surgery for morbid obesity. Her post op course was complicated by prolonged intubation leading to tracheostomy. She was transferred to a rehab facility for weaning. During her stay she developed a temperature spike of 102.F and blood cultures obtained at that time revealed *pseudomonas aeruginosa*. The source was thought to be an IV line as no other possible exposure site was identified and the patient had no prior history of IV drug abuse. A susceptibility report showed the organism to be resistant to Gentamycin, Ciprofloxacin and Ticarcillin clavulanate, but sensitive to Piperacillin and Ceftazidime. She was started on IV Piperacillin and Aztreonam. She remained afebrile and the antibiotics were stopped after 14 days of therapy. Two days after discontinuation of antibiotics she again spiked a temperature of 103F and was readmitted to this Hospital. Blood cultures were obtained and again showed *pseudomonas aeruginosa* but this time it was only sensitive to Ceftazidime. A systolic murmur was also noted on this admission. Patient was started on Immipenem 500 mg Iv q6hr and Ceftazidime 3 GM Iv q8hr. A Transthoracic Echocardiogram was obtained that showed normal LV ejection fraction, mod-severe aortic insufficiency and an ill-defined density in the Aortic outflow tract. A Transesophageal Echo was performed for better visualization and revealed a large Aortic valve vegetation with severe Aortic insufficiency but no evidence of an abscess. Her hospital course was complicated by CHF though no embolic events were noted. She subsequently had

a cardiac cath that showed four plus aortic insufficiency. Due to significant CHF she underwent surgery for Aortic valve replacement. At the time of surgery she was found to have a Sinus of Valsalva annular abscess with six cc of frank pus, perforation of the RT coronary cusp and complete destruction of the LT coronary cusp. She remained on IV antibiotics for six more weeks after valve replacement and did quite well with resolution of her CHF.

EPIDEMIOLOGY AND PATHOGENESIS

Pseudomonas aeruginosa has emerged as an important pathogen in major metropolitan cities especially in IV drug abusers. In Detroit, Michigan for example 10% of all cases of infective endocarditis were found to be caused by *pseudomonas aeruginosa*(¹). The high mortality associated with this disease necessitates early diagnosis and intervention(²). In a comprehensive review of 348 cases of infective endocarditis caused by gram negative bacteria from 1945-1977, Cohen et al (³) found *p-aeruginosa* to be the primary pathogen in 29% of all cases. Majority of these patients were intravenous drug abusers. Bennet al (⁴) in a review of infective endocarditis from 1984 through 1993 found that the incidence increased during the last decade with 17.4 episodes/million/yr in the first part of the decade and 36.5 episodes/million/yr in the second part($p<0.001$). The prognosis of Left-sided valvular involvement is far more disappointing than the Rt-sided, though the site of valvular involvement i.e. aortic vs. mitral has not been found to influence the outcome(²). Where as right-sided *pseudomonas* endocarditis presents as a subacute clinical picture associated with right heart failure, involvement of the

left side is a much more virulent disease complicated frequently by systemic emboli, neurologic sequelae, splenic abscesses, CHF and high conduction abnormalities. Mortality ranges from 50-89% in the literature (2). No clear evidence exists for this discrepancy in the clinical outcome. An enhanced exopolysaccharide production by a non mucoid strain of *P aeruginosa* at O2 tension reflective of the Left side of the heart and suboptimal aminoglycoside induced inhibition and killing has been put forward as one possible explanation (3). The development of resistance to antibiotics especially Penicillin due to production of beta-lactamase compounds the problem by leading to relapse of infection and failure of therapy (6). Experimental studies looking at the pathogenesis of infective endocarditis have also shown that a superficial layer of fibrin can form within 24 hrs of the introduction of bacteremia. This fibrin layer is devoid of leukocytes, which may offer additional protection to the bacterial colonies (7). Mortality also seems to be higher in the first week of hospitalization, hence the importance of early detection and treatment (4). Most of the insight into *pseudomonas aeruginosa* endocarditis is from studies involving IV drug abusers and experimental infection introduced in lab animals. To our knowledge there are very few reported cases of nosocomial *pseudomonas aeruginosa* endocarditis in a non parenteral drug abuse population. Benn et al (4) in a retrospective review of 62 cases of infective endocarditis found no case of documented *pseudomonas aeruginosa*. Our case points to the probability that long term intravenous catheters especially in ICU settings and long term care facilities remain a risk factor for *pseudomonas endocarditis*.

DIAGNOSIS

The diagnosis of IE has traditionally been made by the Von-Rye criteria until the Dukes criteria were introduced. The sensitivity of Dukes criteria is significantly higher than the Von-Rye criteria, though the specificities remained almost equal (8). Echocardiography remains the most important tool in diagnosing IE by detecting vegetations and hemodynamic consequences of valvular damage. TEE has emerged as a far more reliable method for detection than conventional trans thoracic echo due to better sensitivity. Shively et al (9) reported the sensitivity of TTE to be 44% compared to 94% for TEE with similar specificities at 98% and 100% respectively. TEE has also proved to be valuable for diagnosing perivalvular abscess with a sensitivity of 93% and specificity of 94%. The presence of an echo free space in more than one imaging access has been proposed to be

highly suggestive of Aortic valve ring abscess (10). Studies have also looked into the probability of clinical embolic events based on the size of the vegetation. Though some studies report a higher incidence of clinical embolic events with a vegetation larger than 1 cm (11), this observation has been challenged in other studies (12).

TREATMENT

Antibiotics remain the mainstay for treatment of endocarditis with cure rates for right-sided *pseudomonas endocarditis* close to 84% but only 33% in left-sided infection (2). Initial bacteremic cure is followed by a high relapse rate. The first line therapy remains a beta-lactam antibiotic in combination with an Aminoglycoside. Single agent therapy with either a beta-lactam or an aminoglycoside is more likely to be associated with failure to clear bacteremia, Where as combination of the two can achieve up to 25% eradication rate which can improve further by using higher than normal doses(2). Several studies have also proven the superiority of combination therapy in this setting (13).

Surgical intervention in endocarditis is usually undertaken when medical therapy fails or complications like CHF, embolic events occur. However in left-sided *pseudomonas endocarditis* early valve replacement is usually required for a complete cure. Numerous studies have shown significantly better outcome with combined medical/surgical treatment (14,15). Recommendations for surgical intervention in right-sided *pseudomonas endocarditis* are persistent bacteremia after two weeks of beta-lactam plus high dose Aminoglycoside. Tricuspid valvectomy has been shown to improve outcome and is considered by some to be the standard therapy for right-sided infective endocarditis(2). For left-sided *pseudomonas endocarditis* immediate valve replacement is recommended after confirmation of diagnosis. In both interventions surgery should be followed by six weeks of high dose combination antibiotics.

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