CASE REPORT OPEN ACCESS

Mitral valve endocarditis with high level aminoglycoside resistant Enterococcus faecalis in breast cancer patient

Ashish Bhargava, Vasavi Paidpally, Pragati Bhargava

ABSTRACT

Introduction: Enterococci represent the third most common cause of infective endocarditis, after streptococcus **and** Staphylococcus aureus**, and are responsible for 5–20% of all cases of endocarditis. We present a rare case of native valve** Enterococcus faecalis **(**E. faecalis**) endocarditis of mitral valve in a breast cancer patient. Case Report: A 56-year-old breast cancer patient presented with complains of fever and found to have** E. faecalis **bacteremia. Echocardiogram showed mitral valve vegetations. This** E. faecalis **strain was also found to have high level aminoglycoside resistance (HLAR). She responded well to six weeks ampicillin and ceftriaxone combination therapy despite loss of aminoglycoside synergy. Conclusion: Most commonly observed risk factors for enterococcal endocarditis were rheumatic fever, valvular heart abnormalities, gastrointestinal neoplasia, surgery (dental surgery, cardiovascular surgery, and abdominal surgery), gastrointestinal procedures and diabetes. Left-sided enterococcal endocarditis in our patient responded well to combination regimen with ampicillin and ceftriaxone despite loss of aminoglycoside synergism.**

Keywords: Enterococcus faecalis**, Endocarditis, Mitral valve, Breast cancer**

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INTRODUCTION

Enterococci are feared nosocomial pathogen since the emergence of resistant strains, which are challenging to treat. Despite the common occurrence of E. faecium bacteremia, endocarditis caused by this organism is relatively rare, with frequency occurrence less than 10% among patients with enterococcal bacteremia [1, 2]. Infective endocarditis is also unusual in cancer patient in absence of intravenous drug abuse. According to our medline literature search, there is no case reported about enterococcal endocarditis associated with breast carcinoma till now. We present a rare case of native valve E. faecalis endocarditis of mitral valve in a breast cancer patient. This challenging case was also complicated with loss of treatment synergism due to high level aminoglycoside resistance (HLAR).

CASE REPORT

A 56-year-old African-American female patient came to the infusion centre for her chemotherapy and found

to have high fever. She had stage IV estrogen/progesterone and her 2/neu receptor negative invasive ductal carcinoma of right breast status post palliative mastectomy which was diagnosed in 2010. For this locally advanced tumor she was started on chemotherapy with carboplatin and gemcitabine. Three months prior to her current admission, she received her last dose. During that visit, she was noted to have positive blood cultures with E. faecalis. This bacteremia last for four days and was noted secondary to an infected PICC line. She was given intravenous ampicillin and bacteremia resolved. Due to prolonged bacteremia, a transesophageal echocardiogram was done which revealed no valvular vegetations. She was then treated with line removal and total two weeks of ampicillin treatment from PICC line removal and negative culture.

At this admission, patient was noted to have temperature of 38.4°C. She denied any other complaints such as chest pain, shortness of breath, palpitations, nausea, vomiting, diarrhea, dysuria, rash, chills or mediport site pain. Her blood pressures were stable with normal range pulse rate. On examination, mediport was noted on right side of the chest. There was no erythema, swelling or tenderness over the site. She was noted to have chronic lymphedema of her right arm since her mastectomy. Laboratory findings were normal except for anemia (see Table 1). Chest X-ray showed a left internal jugular port catheter tip over upper cavoatrial junction without any other significant findings. She was started on empiric therapy with vancomycin.

Blood cultures drawn upon admission showed E. faecalis which was ampicillin sensitive but resistant to aminoglycosides. So, she was switched to intravenous ampicillin 2 g every 4 h. She was noted to have persistent bacteremia for four days. Transthoracic echocardiogram showed 2 nodular, immobile echogenic densities measuring 0.8x0.6 cm attached to tip of the anterior mitral valve leaflet along atrial and ventricular aspects. Transesophageal echocardiogram revealed a large mobile bilobar echodensity measuring 1.7x0.8 cm attached to the atrial aspect of anterior mitral leaflet tip, consistent with vegetation. She was then started on ceftriaxone 2 g daily for synergy as E. faecalis had high level aminoglycoside resistance. Her blood cultures became negative after 48 h of combination therapy. She was discharged on intravenous ampicillin and ceftriaxone for six weeks. Repeat cultures done after discharge remained negative. During her three months follow up after completion of her intravenous therapy, patient has been doing well.

DISCUSSION

Enterococci are gram-positive, catalase-negative, facultative anaerobic bacteria, which usually inhabit the alimentary tract of humans in addition to being isolated from environmental and animal sources. Although initially enterococci were generally considered harmless commensals, studies have documented the pathogenic potential of these organisms and, in fact, shown to be the third most common cause of nosocomial bacteremia [3]. The other factor which draws attention is serious enterococcal infections are often refractory to treatment and with a higher mortality [4]. Enterococci represent the third most common cause of infective endocarditis, after Streptococcus and Staphylococcus aureus, and are responsible for 5% to 20% of all cases of endocarditis [5].

E. faecalis is responsible for the vast majority of cases of enterococcal endocarditis [6]. Only a minority of cases are caused by other species, such as E. durans, E. hirae, and E. avium. The presentation of enterococcal endocarditis is typically subacute and infrequently associated with peripheral stigmata of endocarditis. Most cases of enterococcal endocarditis are left-sided [7]. The most commonly observed risk factors were rheumatic fever, valvular heart abnormalities, gastrointestinal neoplasia, surgery (dental surgery, cardiovascular surgery, abdominal surgery), gastro-intestinal procedures and diabetes [4, 8] (see Table 2). From International collaboration of endocarditis database, enterococcal endocarditis was most frequently seen in elderly men, frequently involved the aortic valve and tended to produce heart failure rather than embolic events [7].

The other significant factor about enterococci is its notorious nature of increasing antibiotic resistance which makes it feared pathogen that is challenging to treat. After the first report, in the late 1970s, of clinical isolation of E. faecalis with high level of aminoglycoside resistance, the number of infections caused by HLAR strains are increasing. Enterococcus species do not possess cytochrome enzymes and thus cannot produce

Table 1: Biochemical profile of patient on admission.

Chemistry – Value (Range)	Complete Blood Cells	Microbiology (Blood Culture)
Sodium– 135 mmol/L (135–145) Potassium– 4.6 mmol/L (3.5–5.3) BUN– 24 mg/dL (7–20) Creatinine– 1.4 mg/dL (0.4–1.1) Anion gap– 8 mmol/L (3–20)	WBC– 8.3 K/CUMM (3.5–10.6) Hemoglobin– 8.7 g/dL (11–15) Hematocrit– 26.5% (34.4–44) Platelets– 282 K/CUMM (150–450)	Blood cultures (2 sets) – *E. faecalis*

Table 2: Risk factors for enterococcal endocarditis and HLAR enterococcal infection.

Risk factors for enterococcal endocarditis	Risk factors for HLAR enterococcal infection
1.Gastrointestinal malignancy 2.Surgery 3.Rheumatic fever 4.Diabetes 5.Valvular heart abnormalities 6.Gastro intestinal procedures	Prior antibiotic therapy Patient received more than four antibiotics Patient treated with cephalosporin Urinary catheter

the energy required to take up antibiotics into the cell. This means they show resistance to aminoglycosides at low levels [9]. But high-level aminoglycoside resistance in enterococci is mediated by aminoglycoside-modifying enzymes (AMEs) [10]. There is a study which demonstrated that patients are most likely to be infected with HLAR enterococci if they had prior antibiotic therapy, if they had received more than four antibiotics, if therapy had included a cephalosporin or if they had a urinary catheter [8]. This fact causes problems for the treatment of patients with endocarditis caused by these strains since it precludes bactericidal synergism between penicillin and aminoglycosides.

Gavalda et al. described an *in vitro* as well an observational study suggesting ampicillin and ceftriaxone combination as an alternative therapy for HLAR enterococci. The *in vitro* study showed, a strong anti-bacterial co-operation with more than 2-log10 decrease in CFU per million between the combination and its most active agent alone [11]. In the observational study, the cure rate was 100% in patients who completed the protocol [12]. Since then cases have been described which have been successfully treated with this combination therapy. Ceftriaxone provides bactericidal synergistic effect by totally saturating penicillin binding proteins.

Our patient did had a prior line related episode of enterococcal bacteremia which was adequately treated. Esophageal echocardiogram then showed no evidence of valvular vegetations. She then had a mediport placement outpatient one month prior in anticipation of her chemotherapy initiation. She had no recent history of urinary tract infection. Her previous surgery and antibiotics exposure might have played a role in acquisition of HLAR *E. faecalis*. She was started on synergistic combination therapy of intravenous ampicillin 2 g every 4 h and ceftriaxone 2 g every 12 h. Her bacteremia cleared with in 48 h and clinical symptoms resolved in few days. Repeated culture done after completion of therapy also remained negative. So, prompt effective therapy for these resistant strains can give you favorable results, as with our case. Delayed or ineffective initial treatment may require valve replacement for cure [13] or can be devastating with loss of patient life even with valve replacement [14].

CONCLUSION

In conclusion our patient with left-sided enterococcal endocarditis responded well to combination regimen despite loss of aminoglycoside synergism.

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Author Contributions

Ashish Bhargava – Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Critical revision of the article, Final approval of the version to be published
Vasavi Paidpally – Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Critical revision of the article, Final approval of the version to be published
Pragati Bhargava – Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Critical revision of the article, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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REFERENCES

1. Fernandez-Guerrero ML, Verdejo C, Azofra J, de Gorgolas M. Hospital-acquired infective endocarditis not associated with cardiac surgery: an emerging problem. Clin Infect Dis 1995;20:16–23.
2. Patterson JE, Sweeney AH, Simms M, et al. An analysis of 110 serious enterococcal infections: epidemiology, antibiotic susceptibility, and outcome. Medicine (Baltimore) 1995;74:191–200.
3. M Edmond, S Wallace, D McClish Nosocomial Bloodstream Infections in United States Hospitals: A Three-Year Analysis Clin Infect Dis 1999;29(2):239–44.
4. Murray BE. The life and times of the Enterococcus. Clin Microbiol Rev 1990;3:46–5.

5. McDonald JR, Olaison L, Anderson DJ, Hoen B, Miro JM, Eykyn S. Enterococcal endocarditis: 107 cases from the international collaboration on endocarditis merged database. Am J Med 2005 Jul;118(7):759–66.
6. Mylonakis E, Calderwood SB. Infective endocarditis in adults. N Engl J Med 2001;345:1318–30.
7. M Giusti de Marle, A Sgreccia, E Carmenini, S Morelli. Infective endocarditis from Enterococcus faecalis complicating colonoscopy in Heyde's syndrome Postgrad Med J 2004;80:619–20.
8. M Viagappan, R Holliman. Risk factors for acquisition of gentamicin resistant enterococcal infection: a case-controlled study Postgrad Med J. June 1999;75(884):342–5.
9. Klare, I, Konstabel, C, Badstubner, D, Werner, G. & Witte, W. Occurrence and spread of antibiotic resistances in Enterococcus faecium. Int J Food Microbiol 2003;88;269–90.
10. Wade JJ, Uttley AHC. Resistant enterococci mechanisms, laboratory detection and control in hospitals. J Clin Pathol 1996; 49:700–703.
11. Gavalda Joan, Oscar Len, Benito Alamirante, and Albert Pahissa. Ampicillin plus Ceftriaxone for High-Level Aminoglycoside Resistant Enterococcus faecalis Endocarditis. Annals of Internal Medicine February 5, 2008;148(3):243.
12. Gavalda Joan, Oscar Len, Jose Miro M, Munoz Patricia, Miguel Montejo, Aristides Alarcon, et al. Brief Communication: Treatment of Enterococcus faecalis Endocarditis with Ampicillin plus Ceftriaxone. Annals of Internal Medicine April 17, 2007; 146: 574–9.
13. Fernandez-Guerrero ML, Barros C, Rodriguez Tudela JL, Fernandez Roblas R, Soriano F. Aortic endocarditis caused by gentamicin-resistant Enterococcus faecalis. Eur J Clin Microbiol Infect Dis. Aug 1988;7(4):525–7.
14. Lee PY, Das SS. Endocarditis due to high-level gentamicin-resistant Enterococcus faecalis. Postgrad Med J. 1995; 71(832): 117–9.