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A successful outcome of a Rare Case of Infective Endocarditis due to MDR Enterococcus faecium

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Abstract

With the emergence of resistance to the most common anti - entero coccal anti biotics, treatment of these infections is an important clinical challenge, particularly in infective endo carditis (IE)

The management of infective endocarditis (IE) due to Entero coccus faecium with high level aminoglycoside resistance (HLAR) is a challenge.

Reporting a case of IE of the mitral valve due to Entero coccus faecium MDR with HLAR that was success fully managed with intravenous vanco mycin and tigecycline for 6 weeks along with valve replacement surgery.

In addition to limited drug availability had difficulties like drug resistance and adverse drug effects during prolonged treatment, Tigecycline remained the last salvage treatment. Being Redo high risk surgery, decision of operating at right time with optimization of patient was very important. Successful outcome achieved in spite of post operative complications like stress cardio myopathy and pancreatitis.

While tigecycline achieves poor serum levels, penetra tion into vegetations is significant. The use of tigecyc line in combination with cell wall active agents merits further investigation as a potential therapeutic option for IE due to Enter ococcus faecium with HLAR.

Keywords: Enter ococcus faecium, HLAR, tigecyc line, resistance, vancomycin, MDR, Endocarditis, vegetation

Introduction

In a prospective cohort study by international collabo ration on endo carditis,90% of entero coccal endocarditis are due to Enter ococcus faecalis. Endo carditis due to Enter ococcus faecium is rare.[1] Enter ococcus faecium strains are associated with hospital -associated (HA) infections.[2]

The successful treatment of endovascular infections due to Enter ococcus spp. requires a synergistic bactericidal combination of a cell wall active agent (penicillin G, ampicillin or vanco mycin) along with a second anti biotic. The traditional choice for this second agent has been an amino glycoside (streptomycin or gentamicin). In IE due to Enter ococcus faecalis with high level resistance to amino glycosides (HLAR), the addition of a third - generation cephalosporin (ceftriaxone or cefota xime) has been shown to have a similar efficacy but with a lower incidence of nephrotoxicity. However, the management of IE due to Enter ococcus faecium with HLAR remains a challenge.

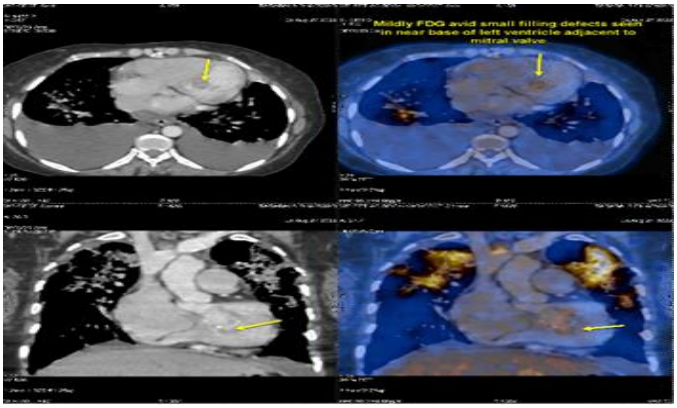
MDR resistant enterococcal faecium pose significant problems in medical management of infective endo carditis. Clinicians are forced to make decisions based on limited clinical data.[3] We present a case of native valve IE due to ampicillin resistant, vancomycin sensitive Enter ococcus faecium with HLAR that was managed with a combination of Vanco mycin, Tigecyc line and valve replacement surgery.

Case Report

A 58-yearfemale, known case of type II diabetes mellitus, hyper tension and rheumatic valvular heart disease with mitral stenosis and atrial fibrillation under treatment for fever since 40 days. She had previously undergone an open mitral valvulotomy in 1990 and a balloon mitral valvuloplasty in 2004. She had covid in 2020. Most recent pre-morbid trans thoracic echo cardio gram (TTE) documented a mitral valve area of 1 sq.cm with no mitral regurgitation and no pulmonary hyper tension with atrial fibrillation. She also had a history of recurrent urinary tract infections during the preceding one year.

She was being managed in another hospital where her nasopharyngeal swab was positive for influenza H1N1 by polymerase chain reaction. Her first blood culture immediate on admission showed no growth. During her stay, due to persistent fever, a repeat blood culture was sent which grew Enter ococcus faecium (table 1) for which she was given tablet linezolid 600 mg twice daily for 14 days. Her fever subsided initially but her platelet count dropped to 24000 / cu.mm. Linezolid was dis continued. She was readmitted with recurrence of fever and signs of cardiac failure. Repeat blood cultures were sent which again grew Enter ococcus faecium. TTE did not reveal any vegetation and trans-oesophageal echo cardio gram was not done due to pulmonary oedema. She underwent a full body 18-fluoro deoxy glucose (FDG) positron emission tomography CT scan (PET/CT) which revealed a mildly FDG avid filling defect near the base of the left ventricle adjacent to mitral valve, suggestive of a possible vegetation (figure 1). Suspecting IE, she was started on high dose injectable daptomycin 700 mg IV once daily as well Tab Linezolid 600 mg twice daily.

Figure 1: Full body 18 FDG PET/CT done on August 27, 2022, showing a mildly FDG avid filling defect near the base of the left ventricle adjacent to mitral valve, suggestive of a possible vegetation (yellow arrow).



She was subsequently admitted to our hospital. Surgical opinion was taken on admission and decided to operate once fever settles.

Blood cultures again grew Enter ococcus faecium which was ampicillin and daptomycin resistant, vancomycin sensitive and HLAR. So Dap to mycin was discontinued and injectable vancomycin was started. Linezolid was initially continued but sub sequently stopped due to persistent thrombocyte penia.

Haema to logist opinion was taken. Other causes of throm bocyte paenia were ruled out. Injectable Tigecycline was added as per the culture report at a dose of 50mg IV twice daily after a loading dose of 100mg.

Table 1:

BLOOD AEROBIC CULTURE & SENSITIVITY										
Selected Organism: Enterococcus faecium										
Antimicrobial	20-Jul-22	26 July 2022		15 August 2022		26 August 2022		06Sept 2022	08Sept 2022	14 Sept 2022
		MIC		MIC		MIC				
Benzylpeniciillin	No Growth	>=64	R	>64	R	>64	R	No Growth	No Growth	No Growth
Ciprofloxacin		>=8	R	>=8	R	>=8	R			
Daptomycin		<=2	S	-	-	>8	R			
Erythromycin		>=8	R	>=8	R	>=8	R			
Levofloxacin		>=8	R	>=8	R	>=8	R			
Linezolid		2	S	2	S	2	S			
Teicoplanin		<=8	S	>32	R	0.5	S			
Tetracycline		-	-	>16	R	>16	R			
Tigecycline		<=0.12	S	<=0.12	S	0.25	S			
Vancomycin		<=4	S	1	S	0.5	S			
Gentamicin synergy		HLAR		HLAR		HLAR				

Her fever stopped with vancomycin and tigecycline. Three sets of blood cultures sent over the next two weeks showed no growth. Platelet counts normalised and inflammatory markers (ESR and hsCRP) reduced by <50% from previous values on admission.

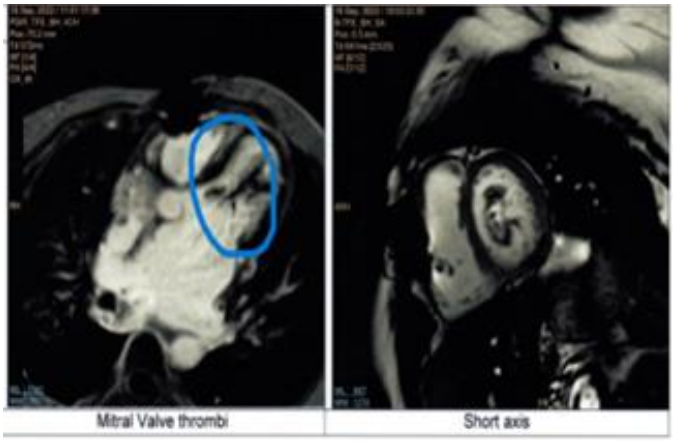
It was decided to plan a valve replacement surgery in order to increase the chances of treatment success considering the aetiology of her IE was a difficult to treat organism.

A coronary angiography was done which revealed patent coronaries. Cardiac catheterization showed severe pulmonary hypertension with reversibility. Repeat ECHO showed decreased pulmonary hypertension (79 as compared to 100 on admission) but there were no convincing vegetations.

TEE could not be done as patient was breathless. A cardiac magnetic resonance imaging study showed normal left ventricular ejection fraction, severe mitral

stenosis with thickened mitral valve and small thrombi on anterior leaflet (figure 2).

Figure 2: Cardiac magnetic resonance imaging study done on Sept 16th 2022 showing severe mitral stenosis with small thrombi on the anterior leaflet (yellow arrow inside blue circle).



On day 21 of vancomycin / tigecycline, the patient underwent mitral valve replacement surgery with a 25 mm peri mount (Magna EASE) bioprosthetic valve. Vegetations were observed intra-operatively on the mitral valve, the culture of which yielded no growth.

Post-operative TTE showed stress cardiomyopathy with ejection fraction of 40%, a normally functioning bioprosthetic mitral valve and a reduction in pulmonary artery pressures from 79 to 46 mmHg. Patient was in atrial fibrillation with fast ventricular rate in congestive cardiac failure. The patient completed six weeks of intravenous vancomycin and tigecycline. She remained afebrile throughout and was dis charged.

On follow up after one month of discharge, the patient was doing well with no signs of heart failure and in normal sinus rhythm. TTE showed a left ventricular ejection fraction of 55%, normal mitral valve gradient and a normal pulmonary artery pressure.

She had post operative pancreatitis with pseudo cyst which required drainage with stent. Her repeat blood culture, urine culture and pancreatic fluid cultures showed no growth, as she had fever spikes for few days due to pancreatitis. Stent removal was done after 6 weeks.

She remains afebrile and well at five months of follow up.

Discussion

In cases of enterococcal endocarditis, both native and previously damaged valves can be involved. It presents in a subacute manner. Diagnosis is based on clinical criteria of IE with positive blood cultures.[4]

The clinical presentation of enterococcal IE is usually subacute, with fever. The main complication of Enterococcal IE is heart failure. It occurs in almost half of the patients with an important impact on outcome. Our patient also presented with fever and later cardiac failure.[5]

Entero coccal IE is increased by in infection by MDR E. faecium. This species shift has important clinical conse quences [6]

Blood culture of our patient showed E. faecium (ampicillin resistant, vancomycin sensitive, HLAR).

Forrest et al. compared the clinical characteristics and out comes of patients with E. faecium and E. Faecalis VRE IE. It showed a higher mortality (p=0.002) and a longer duration of bacteraemia (p=0.002) in patients with E. faecium IE. [7]

The combination of Tigecycline with vacomycin, gentamyc in, doxycycline and rifampin has been shown to be additive in vitro against Enter ococcus spp. [8]

Bakul K N in 2021 reported a rare case of infective endo carditis due to Enterococcus faecium. Combination of anti-biotics was given along with aortic valve replace Ment. [9]

For our patient due to daptomycin resistance during treatment, vanco mycin was started along with linidazole. Initially it worked but due to throm bo cytopaenia had to switch to tigecyc line from linidazole as second drug.

The indication for surgery in patients with native valve endo carditis are heart failure due to valvular dys function, un controlled endo car dial infection (para valvular extension or

Persistent bacteraemia) and prevention of systemic emboli. With standard treatment and appropriate use of valve replacement a cure rate of 85% is possible.

Our patient also doing well with valve replace Ment and total 6 weeks of combination of anti-biotic therapy.

Conclusion

The best treatment of IE MDR enter ococcal endo carditis is unknown.

This clinical case intends to share our experience with physicians that use of combination of Tigecycline in standard doses only with vanco mycin for 6 weeks and early surgical intervention produced good clinical outcome.

In spite of limited therapeutic options in hand, drug resistance and drug adverse effects during prolonged treatment, high risk of redo surgery and post operative complications still good outcome is possible.

The use of intravenous Tigecycline in combination with another antibiotic is a potential therapeutic option for IE due to E. faecium with HLAR.

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