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CASE REPORT

Are Unusual Bacteria Becoming Common Causative Agents of Infective Endocarditis?

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Abstract

Infective endocarditis (IE) has been a burden to humanity for the last 300 years. It is a disease which is continuously evolving in its predisposing factors and microbiology. Earlier, the predominant risk factor for IE was rheumatic heat disease but recent studies have shown injection drug abuse as the major risk factor. Similarly, there is an increasing incidence of cases of IE caused by unusual microorganisms. Identification of the microbe responsible for IE is critical in deciding the best treatment. Here we report three cases of IE caused by unusual organisms.

Key Words

Rheumatic Heart Disease, Infective Endocarditis, Unusual Organisms

Introduction

Microbial infection of the endocardium or the valves of the heart is called Infective endocarditis (IE).[1] Diagnosis of IE is made based on Modified Duke/ 2015 clinical criteria of European Society of Cardiology (ESC).[2,3]

The causative agents of around 80-90% of the cases of IE are *Streptococci*, *Staphylococci and Enterococci*.[4] Other bacteria include HACEK group of organisms, *Coxiella burnetti*, *Brucella* species, *Chlamydia psittaci* and *Mycobacterium* species.[5] Recently many cases of IE has been reported to be caused by unusual microorganisms. Unusual microorganisms are defined as those "other than *Streptococci*, *Staphylococci* and *Enterococci*," and include (a) pathogens which have lower tendency to affect heart valves and are commonly seen in other sites (Example- *Pseudomonas aeruginosa*, *Enterobacteriaceae*), (b) bacteria which has established affinity towards cardiac valves but responsible for only a small percentage of the cases.[4] Diagnosing the cases of IE caused by unusual organisms is often difficult. Delay in diagnosis and ineffective empiric antibiotic therapy can result in higher risk of fatal outcomes in such cases of IE.[5]

In this article, we aim to study three cases of IE caused by unusual microorganisms. (Table 1)

Case Reports

Case 1

A 55-year-old male presented with fever, chest pain and weakness for two days. He gave a history of coronary artery bypass grafting for severe aortic stenosis four months back. His routine blood investigations were normal. Suspecting IE, three sets of blood were sent for culture in BAC-T alert bottles after which he was started on piperacillin-tazobactam. The patient had persistant fever spikes inspite of antibiotics. All three sets of blood culture bottles flagged positive after 3 days and grew *Achromobacter xylosoxidans*. Echocardiograph (Echo) showed vegetations in the aortic root. He was advised to undergo valvectomy. But due to financial constraints, the patient asked for discharge against medical advice (DAMA) and had to be discharged with intravenous

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antibiotics for four weeks.

Case 2

17-year-old male presented to our hospital with complaints of fever with chills, giddiness and dyspnoea for one day. He was diagnosed with chronic kidney disease six months ago for which he was on frequent hemodialysis. He had hemodialysis (HD) catheter in situ on right internal jugular vein. Suspecting catheter related blood stream infection, he was started on empiricantibiotics meropenem and teicoplanin after taking blood and urine samples for culture. His hemoglobin & platelet counts were low and procalcitonin was very high. Fever persisted and his blood pressure reduced from 110/80 to 90/60 mm mercury. Considering the possibility of shock he was shifted to critical care unit and his HD catheter was removed. One bag of single donor platelets was transfused and a cycle of hemodialysis was done due to the deranged RFT. Blood culture sent from HD catheter flagged positive after 2 days. Biofire detected *Methicillin Resistant Staphylococcus aureus* (MRSA) and *Stenotrophomonas maltophilia*. On the next day other blood cutures also flagged positive which grew MRSA & *Stenotrophomonas maltophilia* from HD catheter and *Stenotrophomonas maltophilia* fromleft cubital vein. Antibiotics were changed to cotrimoxazole, ceftaroline and vancomycin. Echo showed vegetation in the tricuspid valve. Tricuspid valve replacement surgery was adviced once he became hemodynamically stable. Due to financial issues, they wanted to shift the patient to a government hospital hence he was given DAMA after 45 days of hospitalisation.

TABLE 1 : Case Details

CASE	CASE 1	CASE 2	CASE 3
AGE (in years)	55	17	42
Presenting complaints	Fever, chest pain, weakness	Fever, giddiness, dyspnoea	Fever, DOE
Past history	RHD- Severe AS	CKD- MHD	RHD- MS
Blood culture	Blood (Rt, Lt,) sent in 3 different timings- *Achromobacter xylosoxidans*	Blood (Lt cubital (Sample 2), HD cath (Sample 1) and (Sample 2), left femoral (Sample 3)- *Stenotrophomonas maltophilia* HD Cath (Sample 1), (Sample 2)- MRSA Blood (Sample 4)-No growth after 5 days	Blood (Lt & Rt Brachial, 3rd site)- *Abiotrophia defectiva*
Multiplex PCR	None detected	MRSA and *Stenotrophomonas maltophilia*	Not performed
Antibiotic susceptibility testing	Ceftazidime, cefepime- R Piperacillin-tazobactam, Meropenem, Minocycline- S Levofloxacin- S	Levofloxacin, Minocycline, Cotrimoxazole- S	Penicillin, ciprofloxacin-S Cotrimoxazole, Chloramphenicol-R
Imaging	Echo-Vegetation (aortic root) 23 X10mm PET-CT- Superiormesentric artery thrombosis	Echo- Vegetation on Tricuspid root (23X 13mm)	Echo-RHD, severe MS,No vegetation
Other cultures	Urine culture, sputum culture- No growth	Urine culture-No growth, ETT culture- Acineto and Ecoli	
Outcome	Advised- Valvectomy- Not done DAMA	PCV Transfusion Advised-Tricuspid valve Surgery- not done DAMA	Discharge on improvement

Abbreviations used-RHD: Rheumatic heart Disease, AS: Aortic stenosis, MS: Mitral Stenosis, DOE: Dyspnoea on exertion, CKD: Chronic Kidney Disease, MHD- Maintenance hemodialysis, Rt:Right, Lt:Left, HD Cath: Hemodialysis catheter, MRSA:Methicillin Resistant Staphylococcus aureus, PCR:Polymerase chain reaction, EET: Endotracheal tube, Echo: Echocardiography, PCV:Packed cell volume.

Case 3

A 42-year-old male came with complaints of dyspnoea on exertion and recurrent episodes of fever for one month duration. He had a history of rheumatic heart disease (mitral stenosis) for which baloon mitral valvuloplasty was

done four years ago. Suspecting IE, he was admitted, and three sets of blood culture were sent at an interval of half an hour. His routine blood investigation showed raised total leukocyte count with predominant neutrophilia, raised erythrocye sedimentation rate (ESR) and C-reactive protein (CRP) suggestive of impending bacterial infection. He was started on intravenous ceftriaxone. Rhematoid arthritis factor was positive.All three sets of blood culture flagged positive after two days which grew *Abiotrophia defectiva*. The identity of the organism was confirmed by MALDI-TOF-MS (score 1.99). Echo did not show any vegetation. As the patient improved symptomatically and his vitals were stable, he was discharged after ten days of admission.

Discussion

Inspite of the advances in surgical, diagnostic and treatment protocols, the morbidity and mortality due to IE is still on the higher side.[1] It still poses clinical, diagnostic and treatment challenges. In IE caused by unusual organisms, false negative culture can be obtained as a result of (a) their decreased tendency to colonize the heart valves, resulting in infrequent bacteremia (continuos bacteremia is seen in IE caused by common organisms) (b)their inability to grow on routine culture media and (c) Being slow growing and requiring more than six weeks for its growth.[2,5] On the contrary to this, in our study blood culture from all three patients grew the unusual organisms in routine culture media. Often IE caused by unusual organisms can also pose a treatment challenge due to their tendency to show resistance to commonly used empiric antibiotics.

*Achromobacter xylosoxidans*is an opportunistic pathogen which can cause serious infections like meningitis,osteomyelitis, peritonitis, pneumonia and bacteremia.[6] Only 22 cases of endocarditis due to Achromobacter has been reported in literature with a mortality rate of 43%.[7] Combination therapy with trimethoprim-sulphamethoxazole and piperacillin-tazobactam is recommended along with valve replacement surgery.[6,7]

Stenotrophomonas maltophilia is a nosocomial pathogen capable of causing pulmonary infection, urinary tract infections, wound infections and septicemia.[8] IE due to *Stenotrophomonas maltophilia* is very rare with only 41 cases reported worldwide and 35% mortality rate.[9] In a hospital setting, when the skin barrier is broken, Stenotrophomonasis notorious to cause IE from contaminated intravascular lines like cerebro atrial shunt, central lineor a subcutaneous reservoir.[8] Treatment includes a combination of antibiotics like trimethoprim-sulphamethoxazole, aminoglycoside or fluroquinolones with removal of the indwelling device. Valve replacement is required in patients who do not respond to medical therapy.[9]

Abiotrophia defectiva is also known as nutritionally variant Streptococci which is a part of normal human microbiome of the gut, oral cavity and genitourinary system. Endocarditis is one of the most encountered infections due to Abiotrophia. Around 125 cases of IE due to A. defectiva have been reported till the year 2023.[10]

Conclusion

Though IE caused by unusual organisms is rare, they are still relevant. As most of these bacteria are intrinsically resistant to many empiric antibiotics, treating such cases may be challenging. Hence, to reduce the morbidity and mortality due to IE caused by such unusual organisms, microbiologists and clinicians should have continuous communication from the early stage of these infections for administering effective and prompt therapy.

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