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**Case Series**

# Endocarditis: a case series with review on atypical presentations of infective endocarditis

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## ABSTRACT

Infective endocarditis is a well-known clinical entity. However, despite improved diagnostic techniques and advances in treatment options, clinical heterogeneity of infective endocarditis sometimes prevents rapid recognition, correct diagnosis and timely treatment which are very essential to reduce morbidity and mortality associated with this disease. We herein present a case series of seven patients who presented to Government Medical College, Kozhikode during the period 2018-2022 with atypical presentations of infective endocarditis.

**Keywords:** Infective endocarditis, Anterior mitral leaflet, Non-bacterial thrombotic endocarditis, Right sided infective endocarditis, Trans-oesophageal echo, Left sided infective endocarditis

## INTRODUCTION

Endocarditis first described by William Osler in 1885 is an infection of valves or lining of the heart.[1] As the microorganism move quickly past the endocardial lining, those strains which can strongly adhere to the surface are the bacteria which causes infective endocarditis (IE). Clinical features can be non-specific, and it is a syndromic diagnosis, which mandates high degree of clinical suspicion, on the basis of compatible clinical signs associated with predisposing conditions (example; intravenous drug use, prosthetic valve, and valvulopathy), rather than on a single definitive test result. Diagnosis can be tough during early stages of the disease and is often delayed until a serious infection has already happened. This article will discuss various clinical presentations of IE.

## CASE REPORT

### *Case 1*

A 50-year-old male patient with history of uncontrolled diabetes mellitus, hypertension, alcohol use disorder and smoking presented with fever 3 days prior to admission, associated with dyspnoea and dry cough. On admission to hospital patient also had severe myalgia and fatigue and later became restless and developed disorientation to time, place and person. There was no history of haemoptysis, altered bowel habits, headache, dysuria, joint pain.

On examination, patient was conscious, appeared ill, moderately built and nourished. Pallor and icterus present. Pulse -110/min regular, blood pressure 150/100 mmHg, temperature 101 F, respiratory rate 44/minute. Accessory muscles of respiration were active, Breath sounds diminished in right infra-axillary and infra-scapular areas. Stony-dullness elicited over these areas. Crepitations heard bilaterally over mammary, infra-axillary and infra-scapular areas. Tip of spleen palpable. Cardio-vascular system revealed, pansystolic murmur in the tricuspid area. After analysing the history and clinical examination possibilities considered were multi-lobar consolidation with right sided syn-pneumonic effusion, leptospirosis with ARDS, IE, and enteric fever.

Investigations showed neutrophilic leucocytosis with TC 25200 (P82L5M13), Hb -8.5, platelet -2.37 lakh, ESR -130

first hour, RBS -463, total/direct bilirubin -3.5/1.6, albumin -2.5, SGOT/SGPT-45/94, and urine routine – normal. Initial chest X-ray PA view revealed multifocal patchy alveolar opacities involving the right middle and bilateral lower zones (Figure 1). Pleural fluid study was consistent with an exudative pleural effusion with TC -600 (polymorphs predominant), protein 5.1 gm, sugar -67, albumin 2.4 gm, pleural fluid LDH-2407, ADA -84. Sputum AFB, culture and sensitivity showed no organisms. Pleural-fluid gene expert, culture and sensitivity and Mantoux test were negative.

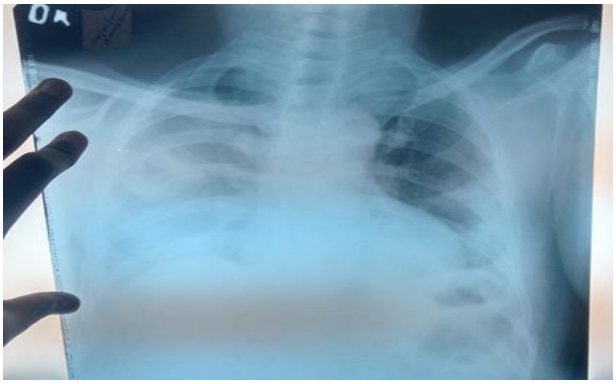

**Figure 1: Chest X-ray – right synpneumonic effusion with multi-lobar consolidation.**

Blood culture yielded methicillin sensitive staphylococcus aureus. Urine-culture and bone marrow cultures were sterile. C-reactive protein was 90.3 mg/l, serum ferritin -2048. Peripheral smear –dimorphic RBC. DCT and ICT-negative. Stool occult blood - negative. Subsequent chest radiographs showed cavitation in right middle zone. Contrast enhanced CT- thorax showed right sided pleural effusion, subsegmental collapse of right lower lobe and multi-lobar consolidation. ECG sinus-tachycardia. Widal-test, leptospirosis-IgM, Weil-Felix, IgM mono-spot, HIV, HBsAg, Anti HCV ELISA were negative. Troponin I quantitative, ANA-IF – negative.

In the background of a prolonged fever, multi-lobar consolidation, pansystolic murmur in the tricuspid area , splenomegaly and staphylococcal septicaemia a very high clinical suspicion of a right sided infective endocarditis with septic embolization was considered and transthoracic ECHO done initially was normal. Due to a high index of suspicion of a right sided endocarditis a repeat transthoracic ECHO was done after 10 days of initial ECHO showed freely mobile mass attached to tricuspid valve suggestive of a tricuspid valve endocarditis (Figure 2).

Patient was treated with intravenous antibiotics (cefazolin and amikacin), glycaemic control attained with basal bolus regime of insulin and antihypertensives were continued. Patients became afebrile, breathlessness and cough subsided, chest signs resolved, total count normalized, inflammatory markers (ESR, CRP) became reduced. Patient was treated for a period of six weeks.

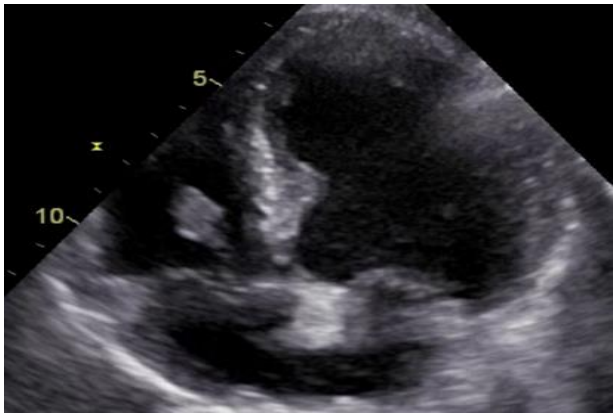


**Figure 2: Tricuspid valve vegetation.**

***Case 2***

23-year-old primigravida with history of congenital heart disease –VSD closure with aortic valve replacement performed 8 years back was admitted at 39 weeks of gestation with chief complaints of fever & dysuria of 1 day duration. Her vitals: pulse -96/min regular, blood pressure-110/70 mmHg, respiratory rate-16/min. Her general and systemic examination were unremarkable. Initial lab reports showed total count-11700 (P84L10), Hb-11.7, platelet-2.49 lakhs. Urine routine – numerous pus cells and 3-5 RBCs. Clinically diagnosed as UTI, initiated intravenous ampicillin and gentamycin. On post-admission day2 patient developed labour pain and foetal distress. Emergency LSCS done and delivered the baby.

On post-admission day 3, patient developed altered sensorium and high-grade fever. Her vitals: pulse-130/minutes regular, blood pressure - 90/60mmHg, Temperature-102.8C. Her TC -18600(P88L7), Hb-9.5, platelet -74000, ESR -86 mm 1st hour, PT -16, INR-2.24, Na -137, K-3.6, urea-54, serum creatinine-1.6, liver function test –TB/DB-2.1/0.6, TP/Alb-6/3.4, AST/ALT-98/79, ALP- 56, ECG –sinus tachycardia. Possibilities kept was urosepsis with disseminated intravascular coagulation and in view of aortic valve replacement a possibility of acute endocarditis also considered. Antibiotics hiked to intravenous piperacillin-tazobactam and vancomycin. Screening ECHO revealed no vegetations. Meanwhile, triple blood-cultures were sent in infective endocarditis protocol. All three samples grew MRSA sensitive to vancomycin, linezolid. However, patient expired on day 4.

***Case 3***

29-year-old male with no known co-morbidities presented with chief complaint of on and off vomiting, of 3-month duration. Patient had multiple admissions for the evaluation of vomiting. He had no documented fever, dysuria, constitutional symptoms, high risk behaviour or iv drug abuse. Gastro-intestinal imaging including ultrasound, esophago-gastro-duodenoscopy was within normal limit. Endocrine evaluation including fasting

cortisol, thyroid function test, prolactin was within normal limit.

On examination, vitals: pulse rate -80/min, BP-120/80 mmHg, respiratory rate -16/min, temperature-98.6 F. No pallor, icterus, clubbing, lymphadenopathy, oedema, hepatosplenomegaly. Neurological examination was unremarkable with no papilledema. Cardiovascular auscultation revealed pansystolic murmur at the apex with radiation to axilla.

Laboratory results showed total count -11800 (P87L8), ESR-80 mm 1st hour, Hb-11.8, platelet-3.7 lakhs, C reactive protein -126. Other biochemical tests were within normal limit. Chest X-ray –normal. In view of the murmur and high inflammatory markers ECHO done which revealed vegetation attached to tip of AML (Figure 3). Six cultures send and all the samples showed growth of streptococcus species sensitive to Ampicillin, ceftriaxone and vancomycin. Patient was treated with intravenous ceftriaxone for 6 weeks. Patient improved clinically and inflammatory markers normalized.

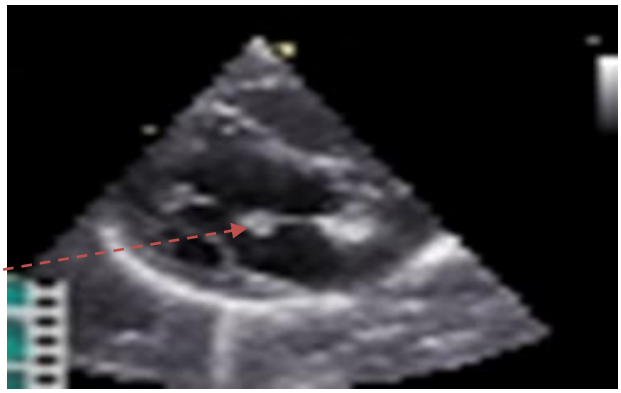

**Figure 3: Vegetations attached to tip of AML.**

***Case 4***

19-year-old male with history of recent hospitalisation for fever with thrombocytopenia recovered and discharged, got re-admitted with symptoms of fever-4 days, headache -3 days and altered sensorium of 2-day duration. On examination, vitals: pulse-120/minute, blood pressure-100/60 mmHg, respiratory rate-20/min, temperature-102.6 C. peripheral stigmata of IE was present including splinter haemorrhages, Osler's node, Janeway lesions, clubbing and fundus showed Roth spots and retinal haemorrhages (Figure 4a-d). Neurological examination revealed positive release reflexes and signs of meningeal irritation and patient was drowsy. Cardiovascular system- pansystolic murmur over mitral area.

Investigations: Hb-11.3, total count -21700 (P88L5), platelet-53000, ESR-95, other routines within normal limits. URE normal. ECG – sinus tachycardia, chest X-ray –normal. CT brain normal. ECHO-perforation of base of AML with vegetation. Culture grew methicillin resistant *Staphylococcus aureus*. Patient was initiated on intravenous ceftriaxone and vancomycin.

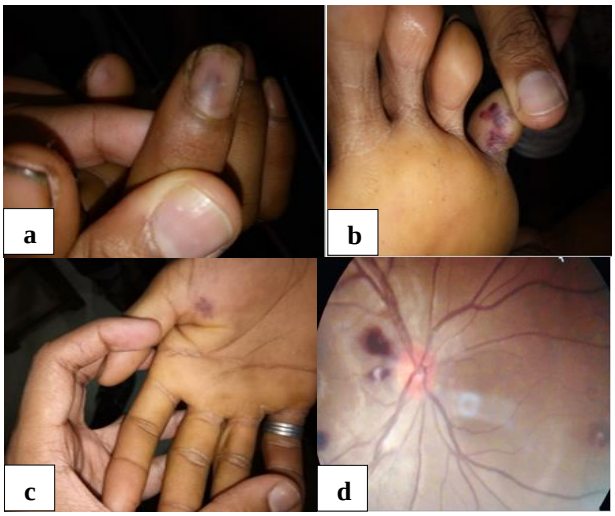


**Figure 4: (a) Splinter haemorrhage, (b) Osler's node, (c) Janeway lesions, and (d) roth spot and retinal haemorrhage.**

On post admission day 5 patient became stuporous. Clinical examination revealed paucity of movements right upper and lower limbs. MRI brain showed multiple septic emboli (Figure 5a). Eventually, there was progressive worsening of sensorium. Further imaging revealed haemorrhagic transformation of septic emboli and significant midline shift (Figure 5b). Emergency craniotomy and evacuation of intraparenchymal bleed done. Patient was on mechanical ventilation post operatively, was gradually weaned off. He was continued on intravenous antibiotics for 6 weeks. He had remarkable clinical improvement on discharge.

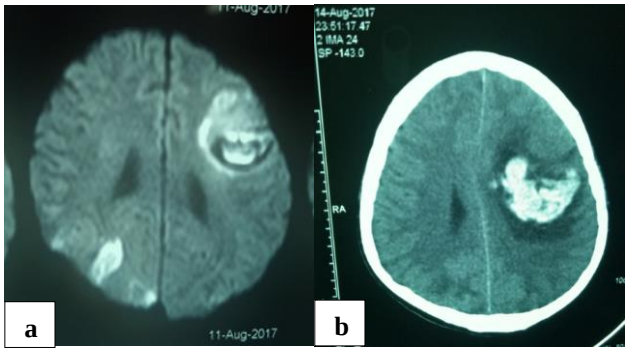


**Figure 5: (a) MRI -multiple septic emboli, and (b) CT showing haemorrhagic transformation).**

***Case 5***

16-year-old boy presented with complaints of 1 month history of fever and pain in the right lower back pain. He was evaluated for backpain and diagnosed with right sacroiliitis (clinically and MRI evidence). He was treated with NSAIDs from local hospital for 1 week following

which he had some relief of symptoms. But 1 week later he developed polyarthritis and was referred to Medical College Kozhikode.

On examination, clubbing present. Vitals: pulse - 80/min and blood pressure-110/70 mm Hg. The left hip joint, left elbow, left metacarpophalangeal joints were swollen, tender and warm. Cardiovascular system examination - apex in 5$^{th}$ left intercostal space in the mid clavicular line, and a short systolic murmur in the mitral area. Spleen tip was palpable. Other systems were within normal limits.

On investigation he had an elevated total count with a rise in inflammatory markers-ESR (70 mm/hour) and CRP (22). ECG showed normal sinus rhythm, chest X-ray revealed mild cardiomegaly with straightening of left heart border.

In view of the prolonged fever with the cardiovascular and musculoskeletal involvement, possibility of infective endocarditis was considered. Triple blood culture samples were sent, and he was started on empirical antibiotic therapy with vancomycin plus gentamicin.

Trans thoracic echo showed rheumatic mitral valve with AML doming, with thickness of 3 mm, restricted mobility of posterior mitral leaflet, Vegetation on Anterior Mitral Leaflet of 6mm size and moderate mitral regurgitation. The findings were confirmed by TEE.

On third day of hospitalization on daily routine examination his radial artery pulse was found to be absent. Suspecting an arterial embolism, an arterial Doppler was done which revealed an echogenic thrombus in proximal part of radial artery with ischemic flow. He was continued on antibiotics. However, his blood culture revealed no organisms after three days of incubation.

Our patient had one major-criteria and 3 minor criteria as per modified Dukes criteria. Hence a diagnosis of sub-acute infective endocarditis on rheumatic mitral valve with emboli to right radial artery was made. Patient was continued on vancomycin plus gentamicin. He improved clinically, there were no further embolic events. He was discharged after the course of antibiotics and is currently under follow up.

***Case 6***

53year old lady with comorbidities of diabetes and hypothyroidism, with a recent hospital admission 1 month prior with complains of vertigo and ataxia and diagnosed as left cerebellar stroke, currently on antiplatelets and statins, now presented with chief complaints of pain over palm of right hand, sole of right foot and fatiguability of 2 weeks duration. Her past history was significant for polyarthritis involving bilateral shoulder joint, wrist joint and ankle joints.

On examination, patient was conscious yet confused, oriented to time, place, person. Pallor and clubbing present. Tender, tense, fluctuant swelling was present over sole of right foot and palm of right hand. Patient was febrile with temperature 101 F, pulse -112/minute regular, blood pressure – 110/80 mmHg, cardiovascular system – mid systolic murmur heard over mitral area. Nervous system examination- nominal aphasia with impaired working memory, bilateral ankle jerk absent. Other system examination was within normal limit.

Investigations revealed neutrophilic leucocytosis (13,500), anaemia (Hb-8.5), platelet 2.03 lakhs. Inflammatory markers were raised. ESR-95, CRP-49. Urine examination, renal and liver function test were within normal limits. HIV, HBsAg, HCV ELISA negative. Chest Xray – minimal right pleural effusion. Iron studies suggestive of anaemia of chronic disease. Repeat MRI brain showed acute infarct left temporo-parietal cortex. At this point analysing the clinical picture of fever, regurgitant murmur, multiple peripheral abscess, recurrent stroke and uncontrolled hyper-glycemia, raised the possibilities of left sided infective endocarditis with septic embolization and also melioidosis. Blood cultures and abscess drainage and culture was sent. Transthoracic ECHO done, which showed NBTE (Libman Sacks endocarditis), both AML and PML thickened, multiple small frons like vegetations seen on both AML and PML, mild mitral regurgitation. Blood cultures (all 3 sets) and abscess culture grew enterococcus. ANA -IF 2+ positive, ANA profile – anti dsDNA positive, anti-histone Ab and nucleosome Ab borderline positive. APLA panel negative.

Hence diagnosis of SLE with Libman sacks endocarditis with enterococcus superinfection was made. Patient was initiated on ceftriaxone 2 gm twice daily IV and vancomycin 15 mg/kg twice daily along with anticoagulation. Fever spikes subsided; patient developed acute kidney injury (AKI) with serum creatinine – 2.5 mg/dl. Vancomycin withheld in view of AKI. Renal function was monitored serially daily. In view of persistent AKI, patient was started on ampicillin 2 gm IV 4$^{th}$ hourly along with ceftriaxone. Renal parameters gradually improved. Patient was discharged with advice to follow up on outpatient basis and to continue antibiotic treatment for 6 weeks.

## DISCUSSION

Infective endocarditis due to its diverse presentation and lethal complication is often a diagnostic and management challenge. Neither the incidence nor mortality due to infective endocarditis have changed over the years. The clinical diagnosis of infective endocarditis requires a high index of suspicion because it may present as an acute, rapidly progressive infection, but also as a subacute or chronic disease. The symptoms are often only constitutional and many of the Oslerian manifestations are absent, except for subacute or chronic forms of the disease.

RSIE represents only 5-10% of IE cases. It frequently affects people with intravenous drug abuse. However, another susceptible population includes: haemodialysis patients, patients with congenital heart disease, intracardiac devices, uncontrolled diabetes, cancer chemotherapy, retroviral infection.[3] Right-sided endocarditis should be suspected in the presence of the so-called "tricuspid syndrome": recurrent respiratory events, anaemia, and microscopic haematuria as in case report 1. Patients with tricuspid valve IE often do not have a detectable heart murmur. Heart failure is unusual. Septic pulmonary emboli are common, occurring in up to three-fourths of patients with tricuspid involvement.[2] Peripheral manifestations, such as splinter or conjunctival haemorrhages, are observed less frequently. If peripheral manifestations are present an associated left sided endocarditis or a paradoxical embolism should be suspected. RSIE, has a lower mortality than LSIE. Majority of cases responds to IV antibiotics. In some cases, surgical treatment is indicated such as right heart failure due to severe TR, resistant bacteraemia or organism to culture directed antibiotics within 7 days and tricuspid valve vegetations >20 mm.[4] RSIE carries better prognosis than LSIE, while concomitant LSIE carries a worse prognosis due to high likelihood of systemic embolization and abscess formation.

In the case report 2, IE was suspected because predisposing condition (prosthetic valve) and persistent bacteraemia. The case highlights its dramatic presentation and failure to recognize it will lead to devastating outcomes. Staphylococcus aureus endocarditis has a mortality rate of 30-40%. Due to high risk of IE in patients with staphylococcal bacteraemia TEE should be done, even if transthoracic echo does not show evidence of IE and TEE has much higher sensitivity (90-100% versus 40-63%) respectively, than TTE in detecting vegetations.[5] The isolation of *Staphylococcus aureus* from urine may indicate a more severe condition (example; bacteraemia or endocarditis), where the microorganisms reach the kidney through hematogenous spread.[6]

The highlight of case report 3 is the clinical presentation of endocarditis as intermittent vomiting as part of systemic toxaemia. This patient didn't have any risk factors, fever, peripheral stigmata of endocarditis. Meticulous clinical examination of all systems should be done in all patients which would make breakthrough in the diagnosis. In developing countries, heart damage caused by rheumatic heart disease is the leading predisposing condition for the development of IE.[7] The case report 5 describes an atypical presentation of infective endocarditis as right sacroiliitis. An infective etiology should always be considered and excluded in patients presenting with mono-arthritis.

Libman sacks endocarditis also known as verrucous or marantic endocarditis is a form of non-bacterial thrombotic endocarditis, characterised by the presence of sterile vegetations and may be associated with malignancy, systemic lupus erythematosus or antiphospholipid antibody syndrome.[8] Most commonly affects mitral valve. Case report 6 describes a rare case of SLE- Libman sacks endocarditis superinfected with enterococcus. Patients are usually asymptomatic, but clinical manifestations are usually due to embolism. Our patient had peripheral embolism as well as cerebrovascular embolism. Enterococci is the third most common organism causing infective endocarditis in the world, contributing up to 5-15% cases after streptococcus and staphylococcus. It is usually a minor commensal-bacteria of intestinal microbiota.[9,11] Some data suggest, similar to streptococcus gallolyticus endocarditis, enterococci endocarditis may be associated with a colonic neoplasm, which highlights the importance of screening colonoscopy, although this was not performed in our patient.[10]

## CONCLUSION

Although technology have changed ever since Osler elucidated the fundamental mechanisms in the late 1800s, IE remains a disease of high morbidity and mortality, especially because of its clinical heterogeneity. The key is to make a prompt diagnosis, early antimicrobial therapy, and surgical treatment when necessary.

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