

Unconventional Infective Endocarditis: Case Series Of Unusual Vegetation Locations And Complications With Systemic Embolization

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Abstract

Infective endocarditis (IE) is a potentially fatal infection that is becoming more common among high-risk populations such as intravenous drug users, patients on hemodialysis for end-stage renal disease (ESRD), and people with chronic bacteremia. This case series focuses on three unique manifestations of IE. (1) a 28-year-old intravenous drug user with mitral valve endocarditis complicated by multi-organ septic emboli, (2) a postpartum woman with methicillin-resistant *Staphylococcus aureus* (MRSA) IE and multiple embolic infarctions, including a breast abscess, and (3) a 60-year-old ESRD with Permcath patient on hemodialysis with *Staphylococcus aureus*-related mitral valve IE. Each case highlights the diagnostic problems, consequences, and the need of early detection and vigorous treatment. This case series also looks at the function of echocardiography, antibiotic therapy, and the consequences of delayed interventions in these high-risk patients.

Keywords: Unconventional Infective Endocarditis; Vegetation Locations; Systemic Embolization.

Introduction

Infective endocarditis (IE) is an infection of the heart's endocardial surface (4). According to recent epidemiologic statistics, the incidence ranges between 3 and 10 cases per 100,000 person-years throughout both low and high-income regions, with over 25,000 hospital admissions for definite or suspected IE in the United States alone each year (5,6). The in-hospital mortality rate remains as high as 15-20%, emphasizing the importance of rapid identification and treatment (7).

Staphylococci species have surpassed viridians group streptococci as the most common pathogenic organism in developed countries (8).

This case series features three patients with mitral valve IE, each with unique risk factors and significant systemic consequences. It focuses on clinical signs, consequences, and treatment techniques, emphasizing the importance of early diagnosis and a multidisciplinary approach.

Case 1: A 28-year-old man with a history of injectable and oral drug usage arrived with four days of fever, chills, broad body weakness, diarrhea, and vomiting. He has also suffered from a loss of appetite for the past week. He had a stiff neck, yet his Kernig's sign was negative, and there were numerous injection needle marks spread throughout, as well as a visible tattoo.

When he arrived, he had a fever of 38°C, was aware but lethargic, answered simple orders, was tachycardic at 107 beats/min, tachypneic at 36 breaths/min, and had a blood pressure of 117/77 mmHg while maintaining oxygen saturation on room air. He exhibited both subconjunctival hemorrhages and Janeway lesions on his palms.

The chest examination revealed clear bilateral breath sounds. A cardiac examination indicated a pan systolic murmur at the apex that spread to the axilla. There were no other signs of endocarditis, such as splinter hemorrhages or splenomegaly. The neurological exam indicated no meningeal or cerebellar abnormalities, and a computed tomography (CT) scan showed no evidence of acute intracranial abnormalities (Figure 1). His chest examination revealed that both lungs were clear, which was corroborated by the chest X-ray.

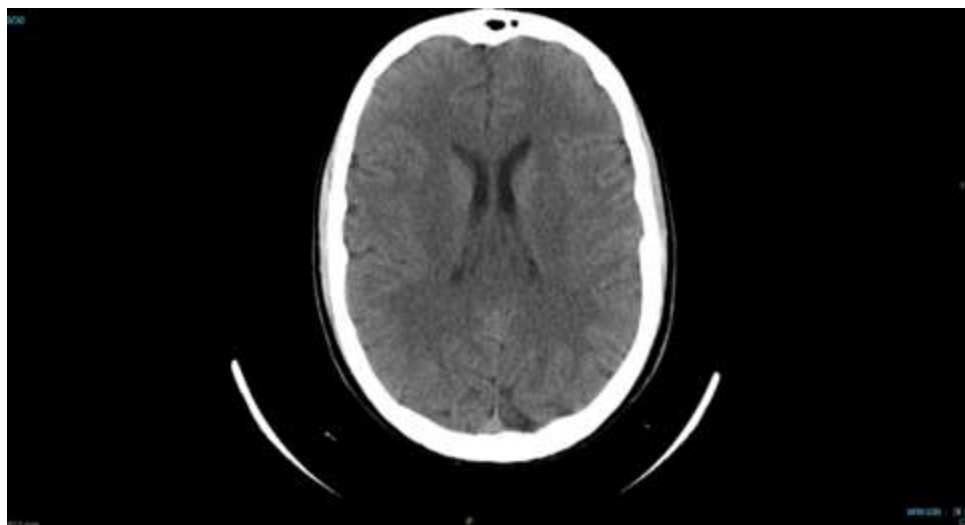


Figure 1: First CT brain on admission -Normal.

The admission lab results revealed leukocytosis of 23,000/mm³, hemoglobin 10 g/dL, high inflammatory markers (C-reactive protein 216 mg/L, erythrocyte sedimentation rate 120 mm/hr, procalcitonin 11.7 µg/L, and D dimer 2.2 µg/ml), creatinine 1 mg/dL, and normal liver function tests. Serology and blood toxicology tests were negative, however serial Troponin I levels remained continuously elevated. However, concomitant urine testing indicated positive results for benzodiazepines and amphetamines.

An ECG revealed sinus tachycardia with no symptoms of pulmonary embolism. Transthoracic echocardiography (TTE) revealed thickness, limited mobility, and vegetation on the posterior mitral valve leaflet. The anterior leaflet exhibited flail mobility, with a spherical, mobile vegetation on the tip and another extremely mobile vegetation linked to the chordae tendineae measuring 1.8 × 1.2 cm. There was a pedunculated intraventricular mass emerging from the mid-interventricular septum with restricted motility, most likely indicating vegetation, with no evidence of paravalvular expansion or abscess. The tricuspid valve was normal in structure and motion, with the exception of slight tricuspid regurgitation, and the left ventricle remained systolic. function

Figure 2 shows three blood cultures that tested positive for *Staphylococcus aureus*. As a result, surgical intervention for the mitral valve was explored, but due to the patient's condition and history, medicinal treatment was preferred.



Figure2: Long paracentral view showed mitral valve Vegetation

On day 3, the patient remained drowsy with neck stiffness. A CT head with contrast was ordered and showed a new Left occipital non-hemorrhagic infarction at the left posterior cerebral artery territory (**Figure 3**). A lumbar puncture was conducted, revealing a white blood cell count of 83 cells/microliter with 84% of these cells being neutrophils.

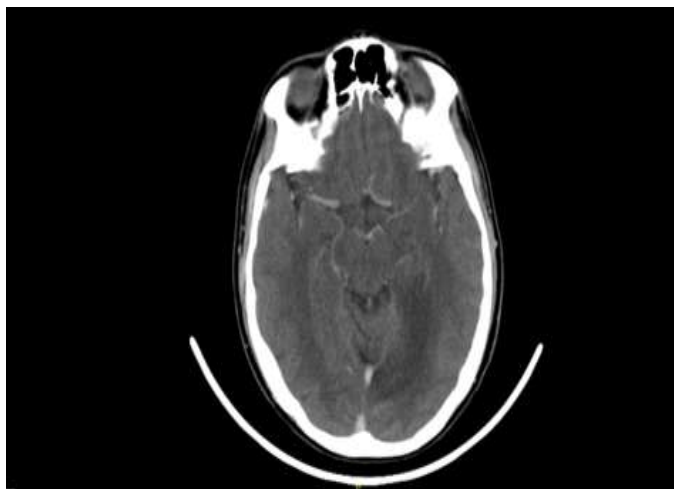


Figure 3: CT brain with contrast showed: development of hypodensity in medial temporal region on the left side acute infarction

On hospital day 5, the patient suffered bloody diarrhea, necessitating a blood transfusion, as well as abdominal pain. Stool tests revealed yeast, a few pus cells, and the rare RBC. A CT abdomen/pelvis with contrast revealed a fresh upper pole splenic infarction and a little right kidney infarction. It also revealed

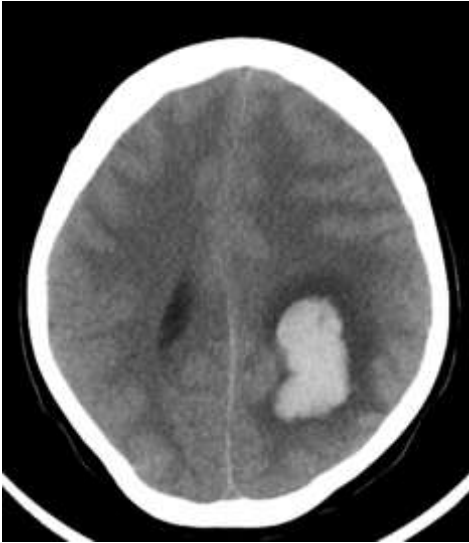


Figure 6: CT brain left parietal 2 hemorrhagic lesions with surrounding edema causing effacing the left lateral ventricle

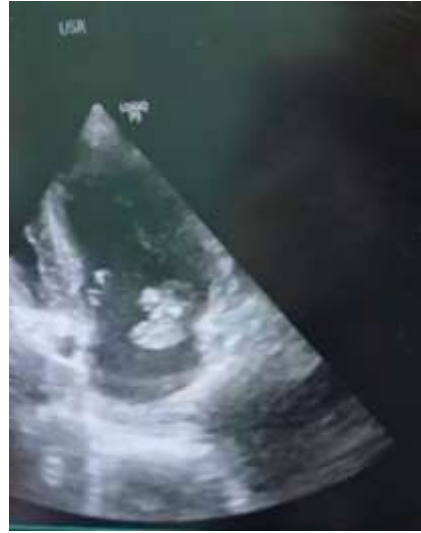


Figure 7. Modified 2 chamber view revealed mitral valve Vegetation

On Day 3, As the neurological condition worsened, MRI done revealed progressive multiple embolic infarcts with hemorrhagic transformation affecting the left parietal, right frontoparietal, occipital lobes, and cerebellum, with worsening edema causing a midline shift from 5 mm to 10 mm (**Figure 8&9**). This necessitated aggressive management with hypertonic saline and seizure prophylaxis (levetiracetam/Keppra). Despite these measures, the patient's condition deteriorated further. Blood cultures continued to show persistent MRSA bacteremia, and the patient developed septic shock and multi-organ failure.

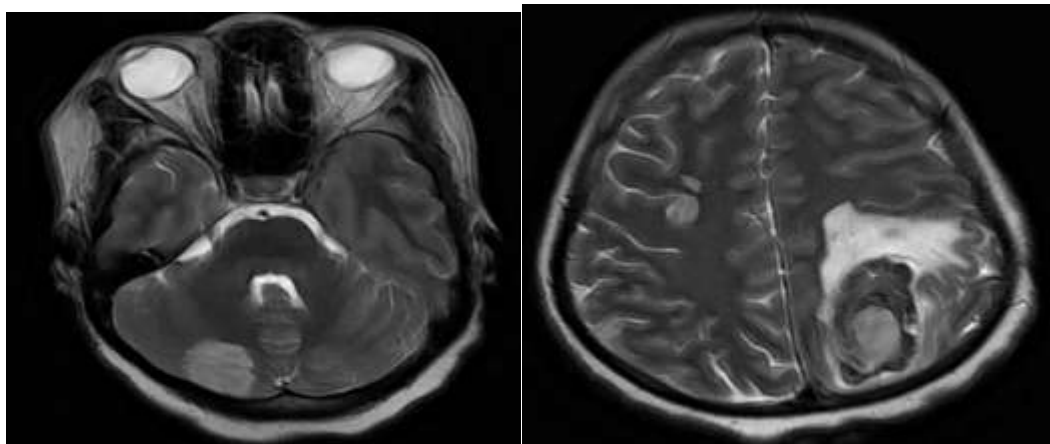
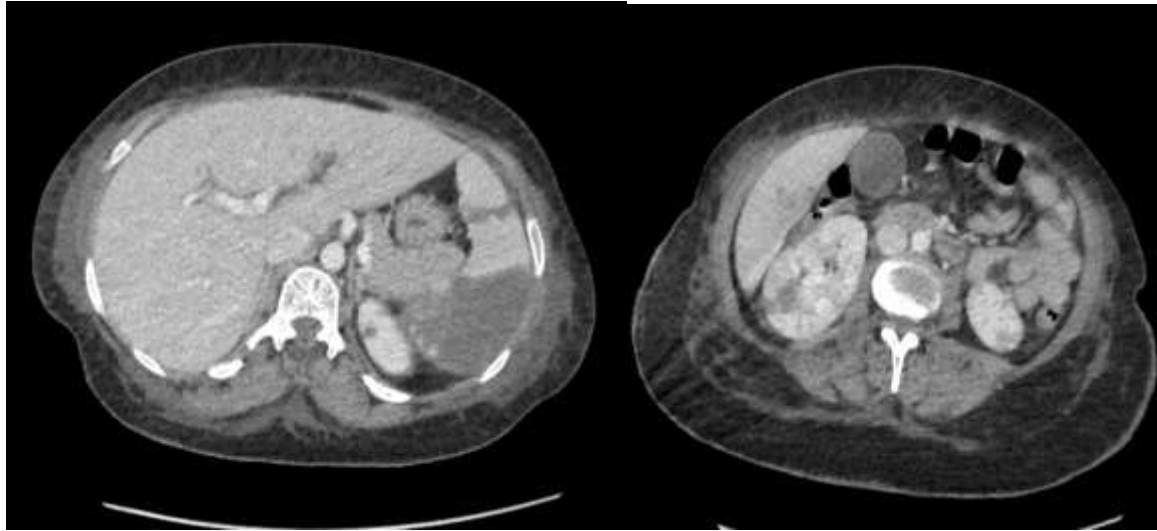


Figure 8&9 :MRI brain Acute hemorrhagic infarcts involving the left frontal, right frontoparietal, bilateral occipital lobes, and right cerebellum, Acute/subacute left posterior high convexity parietal hematomas with associated subarachnoid hemorrhage, vasogenic edema, and mild mass effect causing a 10 mm midline shift. Normal MRV with no evidence of cerebral venous sinus thrombosis.

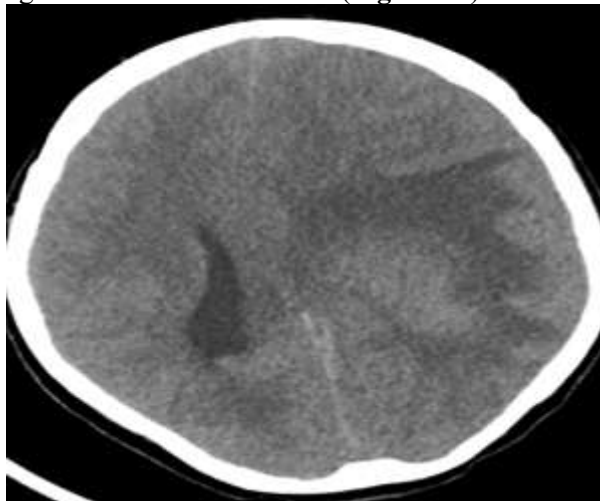
During this time, the patient required high-dose vasopressor support, including noradrenaline at 70 mcg/min and vasopressin at 3 U/hr. An ultrasound of the right breast revealed an early abscess, which was surgically drained. A CT scan of the abdomen and thorax showed splenic, renal, and hepatic infarcts, confirming systemic septic embolization (**Figure 10&11**). Given persistent thrombocytopenia, platelet transfusions were required, and DVT prophylaxis with enoxaparin was started.



(**Figure 10&11**). Spleen, kidneys, and liver show areas of subacute/acute infarcts, the largest involving the spleen..Suspected infarcts in antimesenteric walls of ileal and jejunal loops.

By Day 13, the patient's Glasgow Coma Scale (GCS) had declined to 2/10, and she required intubation. Her intracranial pressure (ICP) worsened, necessitating continued hypertonic saline therapy. Despite these measures, the patient's condition continued to deteriorate.

On Day 14, the patient developed fixed, dilated pupils, a sign of brain herniation, and remained on mechanical ventilation. She progressed to refractory septic shock and multi-organ failure. CT brain repeated and reported as no significant changes in the size or density of the previously observed left parietal hematoma. However, there is an increased severity of mass effect and a right-sided midline shift. Newly developed left transtentorial and cerebellar tonsillar herniation is noted. Additionally, there is a mildly progressive obstructive hydrocephalus, along with diffuse brain edema. Right cerebellar hypodensity is again noted of stable course (**Figure 12**).



(**Figure 12**). Newly developed left transtentorial and cerebellar tonsillar herniation

On Day 15, she developed ventricular tachycardia, followed by asystole. Resuscitation efforts were unsuccessful, and she was pronounced dead.

The final diagnoses included MRSA infective endocarditis with persistent bacteremia, septic embolization to multiple organs (brain, spleen, kidneys, and liver), right breast abscess, septic shock, multi-organ failure, and severe thrombocytopenia. This case underscores the aggressive nature of MRSA infective endocarditis, particularly in the setting of septic embolization and multi-organ dysfunction, and highlights the high mortality rate associated with such complications despite intensive care management.

Case3-A 60-year-old female with a history of diabetes, hypertension, ischemic heart disease, and end-stage renal disease was brought to the hospital by national ambulance. She had a long-standing medical history of being on Gliclazide 60 mg for diabetes, Amlodipine 10 mg for hypertension, and a combination of Bisoprolol 5 mg, Aspirin 100 mg, Clopidogrel 75 mg, and Atorvastatin 40 mg for ischemic heart disease. Additionally, she had a history of eczema and was diagnosed with exfoliative dermatitis five days prior, for which she had been started on Loratadine and emollient cream. She also had end-stage renal disease, requiring regular hemodialysis twice a week, which was often not done due to financial constraints. A right chest PermCath was inserted for dialysis on 6-month prior admission. She also had a prior history of a cerebrovascular accident and was bedridden.

On admission, she presented with a one-day history of shortness of breath, nausea and vomiting, anorexia, decreased urine output, fatigability, and abdominal pain. Clinically, her Glasgow Coma Scale indicated spontaneous eye opening, responding to pain with sound, and spontaneous movement. She was febrile, with a temperature of 39°C, and had signs of dehydration. Her blood pressure was 170/110 mmHg, her pulse was 114 bpm, and her respiratory rate was 27 breaths per minute. Examination revealed no neck swelling or congested neck veins, bilateral basal crepitations on chest examination, and a normal heart rhythm pan systolic murmur at the apex radiating to the axilla. Her abdomen was lax, non-tender, and not distended. There was no lower limb edema, with right-sided weakness from a previous cerebrovascular event. A dry pus discharge was noted from the PermCath site.

Investigations revealed significant abnormalities, including a white blood cell count of 25.9, hemoglobin of 8.9, potassium of 5.89, creatinine of 833, urea of 32, and hydrogen ion concentration (pH) of 7.1 with a bicarbonate level of 10.8. C-reactive protein 90 and procalcitonin 9.4 both were elevated. Three blood cultures were sent, all of which grew *Staphylococcus aureus*, and wound cultures from the PermCath site were also positive for *Staphylococcus aureus*.

The intensive care unit (ICU) team was contacted, and Biphasic Positive Airway Pressure (BiPAP) was applied. A transthoracic echocardiogram (ECHO) showed normal chamber dimensions and no regional wall motion abnormalities. and a large vegetation was noted on the anterior mitral valve leaflet, measuring 1.1 x 1.2 cm. This vegetation was associated with moderate to severe mitral regurgitation (MR). Mild tricuspid regurgitation (TR) (Figure 13). Surgical intervention for the mitral valve was discussed with the cardiothoracic surgeon, who recommended continuing medical treatment and stabilizing the patient before proceeding to surgery.



Figure 13. Modified 2 chamber view showed mitral valve Vegetation

Regrettably, the patient remained unstable, requiring inotropic support and noninvasive mechanical ventilation. Serial blood cultures repeatedly tested positive for *Staphylococcus aureus*. A repeat transthoracic echocardiogram indicated a reduction in mitral valve vegetation to 0.8 x 0.8 cm.

By Day 40, her condition had further deteriorated, necessitating high doses of inotropic support and laboratory findings consistent with multiorgan failure. Simultaneously, the patient's level of consciousness declined, leading to the need for intubation. A CT scan of the brain revealed a right cerebellar and posterior parietal bleed with surrounding edema, as well as bilateral cerebral subarachnoid hemorrhage (Figure 14). On Day 43, she went into asystole. Despite attempts at resuscitation, these efforts were ultimately unsuccessful, and she was pronounced dead.

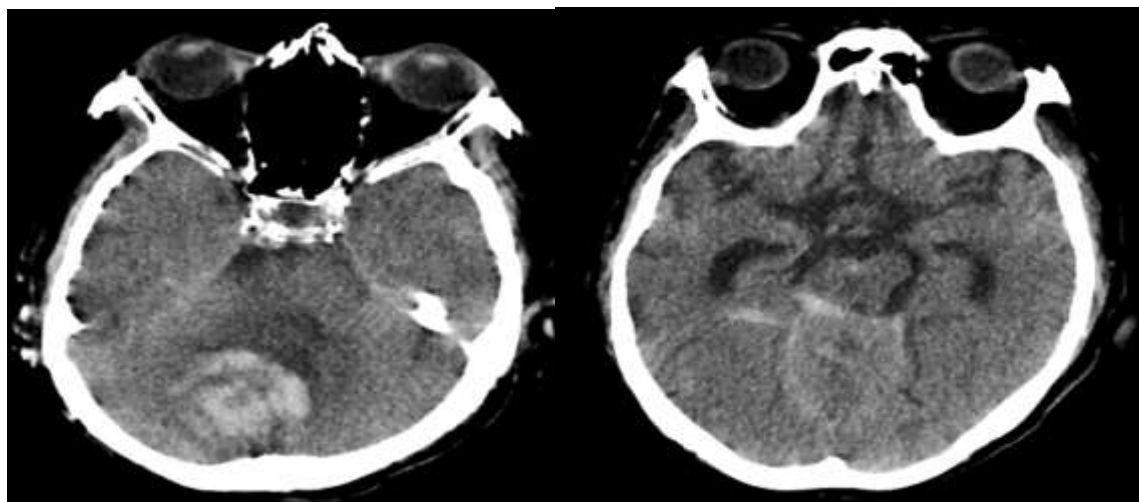


Figure 14. Right cerebellar area of fresh blood density with surrounding oedema, right posterior parietal small area of hyperdensity with surrounding edema and bilateral cerebral subarachnoid haemorrhage. This patient was diagnosed with infective endocarditis complicated by septicemia and a PermCath-related infection, with ongoing renal failure, electrolyte disturbances, and respiratory distress. Management included aggressive antibiotic therapy, respiratory support, and continuous monitoring in the intensive care unit.

Discussion:

Our patients had definite infective endocarditis according to the Duke Criteria, which were based on two major criteria: the typical endocarditis pathogen *Staphylococcus aureus* grown on multiple positive blood cultures and evidence of valvular vegetation with severe eccentric mitral regurgitation on initial transthoracic echocardiography (9). TTE is a quick, non-invasive, and first suggested diagnostic imaging method for evaluating suspected native valve endocarditis, with reported sensitivity of up to 75% and specificity of more than 90% (10). TTE imaging scans are classified as Class 1 in the management of infective endocarditis by the American Heart Association/American College of Cardiology guidelines, both for initial diagnosis and subsequent monitoring. Our patients show the characteristic mobile valvular vegetations found on mitral leaflets in early TTE pictures.

Tricuspid valve vegetation from right-sided endocarditis predominates in the intravenous drug user community due to its proclivity for venous endothelial injury. However, left ventricular involvement accounts for 20-35% of the high frequency of transitory bacteremia and typically affects structurally normal mitral valves, as demonstrated in our patient (11). Overall, patients with injectable drug-related infective endocarditis are up to 60% more likely to undergo systemic septic embolization than non-addicts (12).

While left-sided endocarditis is more common, long-term central venous catheters pose a high risk for right-sided infective endocarditis (13). Approximately 20%-50% of patients experience embolic events induced by the displacement of infectious material into the arterial circulation (14). A vegetation size of more than 10 mm, as shown in our patients, is frequently regarded a crucial signal for measuring embolic event risk, as highlighted in the American Heart Association's infective endocarditis recommendations (15,16). This threshold is also very important in major clinical trial protocols. However, the foundation for this threshold is mostly based on observational data from tiny studies, which may contain selection bias and differing methodology. Some studies show that larger vegetations do not always correlate with increased embolic risk (17,18), whilst others show that vegetations larger than 10 mm have a significantly higher risk of systemic embolization (18,19). Given the high risk of complications such as heart failure, uncontrolled infection, and embolic phenomena, current American Heart Association guidelines recommend early surgical evaluation and a lower threshold for operative intervention in patients with injection drug-related endocarditis compared to non-addicts (20). Patients with consistently positive blood cultures after 7 days of antibiotic therapy, new heart block, annular or aortic abscess, or new-onset heart failure (Class 1) should be surgically treated. Emergent surgery is recommended in the situation of valve perforation or dehiscence, mycotic aneurysm at danger of rupture, or massive cerebral infarctions with mass effect. (20)

Embolic events occur in 20%-50% of patients with infective endocarditis (IE), resulting from the arterial spread of infected material [21]. The central nervous system is especially vulnerable, and cerebral embolisms frequently complicate treatment. A large number of these emboli are clinically quiet, demonstrating the diagnostic utility of brain MRI [22]. Neurological consequences, such as ischemic stroke and transient ischemic episodes caused by cerebral artery occlusion, account for 40%-50% of cases, outnumbering other manifestations such as meningitis, brain abscess, mycotic aneurysm, and intracranial hemorrhage.

Intracerebral hemorrhage is the most deadly neurological consequence, occurring in approximately 7% to 27% of infective endocarditis patients (23). A ruptured mycotic aneurysm has a poor prognosis compared to bland infarctions, with a death rate approaching 60% (23). Early administration of bactericidal antibiotics (often dual) that penetrate the central nervous system is recommended, as is intracranial pressure monitoring, and neurosurgical evaluation for aneurysm clipping, drainage, or debridement, particularly in cases of large brain abscesses (24).

Conclusion:

These three instances demonstrate the devastating repercussions of infective endocarditis (IE) in various scenarios, stressing the significance of early identification and treatment. Transthoracic echocardiography (TTE) has proven to be an effective diagnostic tool, allowing for the quick and non-invasive diagnosis of valvular vegetations and evaluation of heart function. Furthermore, extensive vegetation (>10 mm) increases the risk of embolic events such as stroke and systemic embolization. Notably, neurological consequences are prevalent and catastrophic, accounting for up to 65% of left-sided IE cases and ranging from ischemic and hemorrhagic stroke to meningitis and brain abscesses. As a result, prompt and aggressive care is required, including early delivery of bactericidal antibiotics, consideration of intracranial pressure monitoring, and neurosurgical evaluation. Finally, detecting and controlling intracerebral hemorrhage, the most serious complication of IE, is important to lowering mortality.

References

1. Cahill TJ, Prendergast BD. Infective endocarditis. *Lancet*. 2016;387(10021):882-893.
2. Murdoch DR, Corey GR, Hoen B, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century. *Arch Intern Med*. 2009;169(5):463-473.
3. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications. *Circulation*. 2015;132(15):1435-1486.
4. Yallowitz AW, Decker LC. Infectious Endocarditis. 2023.

5. Bor DH, Woolhandler S, Nardin R, Brusch J, Himmelstein DU. Infective Endocarditis in the U.S., 1998–2009: A Nationwide Study. *PLoS One*. 2013 Mar 20;8(3):e60033.
6. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Guyton RA, et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease. *Circulation*. 2014 Jun 10;129(23).
7. Baddour LM, Wilson WR, Bayer AS, Fowler VG, Tleyjeh IM, Rybak MJ, et al. Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications. *Circulation*. 2015 Oct 13;132(15):1435–86.
8. Tong SYC, Davis JS, Eichenberger E, Holland TL, Fowler VG. *Staphylococcus aureus* Infections: Epidemiology, Pathophysiology, Clinical Manifestations, and Management. *Clin Microbiol Rev*. 2015 Jul;28(3):603–61.
9. Cooper HLF, Brady JE, Ciccarone D, Tempalski B, Gostnell K, Friedman SR. Nationwide Increase in the Number of Hospitalizations for Illicit Injection Drug Use-Related Infective Endocarditis. *Clinical Infectious Diseases*. 2007 Nov 1;45(9):1200–3.
10. Holte E, Dweck MR, Marsan NA, D'Andrea A, Manka R, Stankovic I, et al. EACVI survey on the evaluation of infective endocarditis. *Eur Heart J Cardiovasc Imaging*. 2020 Aug 1;21(8):828–32.
11. Zornoff LAM, Skali H, Pfeffer MA, St. John Sutton M, Rouleau JL, Lamas GA, et al. Right ventricular dysfunction and risk of heart failure and mortality after myocardial infarction. *J Am Coll Cardiol*. 2002 May;39(9):1450–5.
12. Thakrar K, Rokas KE, Lucas FL, Powers S, Andrews E, DeMatteo C, et al. Mortality, morbidity, and cardiac surgery in Injection Drug Use (IDU)-associated versus non-IDU infective endocarditis: The need to expand substance use disorder treatment and harm reduction services. *PLoS One*. 2019 Nov 26;14(11):e0225460.
13. Delgado V, Ajmone Marsan N, de Waha S, et al.: 2023 ESC Guidelines for the management of endocarditis . *Eur Heart J*. 2023, 44:3948-4042. 10.1093/eurheartj/ehad193
14. Asopa S, Patel A, Khan OA, Sharma R, Ohri SK: Non-bacterial thrombotic endocarditis. *Eur J Cardiothorac Surg*. 2007, 32:696-701. 10.1016/j.ejcts.2007.07.029
15. Kang DH, Kim YJ, Kim SH, et al. Early surgery versus conventional treatment for infective endocarditis. *N Engl J Med*. 2012;366(26):2466-2473. PubMedGoogle ScholarCrossref
16. Baddour LM, Wilson WR, Bayer AS, et al; American Heart Association Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young; Council on Clinical Cardiology; Council on Cardiovascular Surgery and Anesthesia; Stroke Council. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American Heart Association. *Circulation*. 2015;132(15):1435-1486. PubMedGoogle ScholarCrossref
17. Thakrar K, Rokas KE, Lucas FL, Powers S, Andrews E, DeMatteo C, et al. Mortality, morbidity, and cardiac surgery in Injection Drug Use (IDU)-associated versus non-IDU infective endocarditis: The need to expand substance use disorder treatment and harm reduction services. *PLoS One*. 2019 Nov 26;14(11):e0225460.
- 17-Buda AJ, Zoltz RJ, LeMire MS, Bach DS. Prognostic significance of vegetations detected by two-dimensional echocardiography in infective endocarditis. *Am Heart J*. 1986;112(6):1291-1296. PubMedGoogle ScholarCrossref
18. Hwang JJ, Shyu KG, Chen JJ, Tseng YZ, Kuan P, Lien WP. Usefulness of transesophageal echocardiography in the treatment of critically ill patients. *Chest*. 1993;104(3):861-866. PubMedGoogle ScholarCrossref
19. Thuny F, Di Salvo G, Belliard O, et al. Risk of embolism and death in infective endocarditis: prognostic value of echocardiography: a prospective multicenter study. *Circulation*. 2005;112(1):69-75. PubMedGoogle ScholarCrossref
20. Habib G, Lancellotti P, Antunes MJ, Bongioanni MG, Casalta JP, Del Zotti F, et al. 2015 ESC Guidelines for the management of infective endocarditis. *Eur Heart J*. 2015 Nov 21;36(44):3075–128.

- 21-Asopa S, Patel A, Khan OA, Sharma R, Ohri SK: Non-bacterial thrombotic endocarditis. *Eur J Cardiothorac Surg.* 2007, 32:696-701. 10.1016/j.ejcts.2007.07.029
- 22-Grecu N, Tiu C, Terecoasa E, Bajenaru O: Endocarditis and stroke. *Maedica (Bucur).* 2014, 9:375-81.
- 23.Carneiro TS, Awtry E, Dobrilovic N, Fagan MA, Kimmel S, Weinstein ZM, Cervantes-Arslanian AM: Neurological complications of endocarditis: a multidisciplinary review with focus on surgical decision making. *Semin Neurol.* 2019, 39:495-506. 10.1055/s-0039-1688826
24. Kuo I, Long T, Nguyen N, Chaudry B, Karp M, Sanossian N. Ruptured Intracranial Mycotic Aneurysm in Infective Endocarditis: A Natural History. *Case Rep Med.* 2010;2010:1–7.