

Septic Cerebral Embolisation in Fulminant Mitral Valve Infective Endocarditis

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Key Words

Cerebral emboli · Mitral valve · Infective endocarditis · *Staphylococcus aureus*

Abstract

A 37-year-old male with known intravenous drug use was admitted with an acute onset of worsening confusion and speech impairment. His vitals and biochemical profile demonstrated severe sepsis, with a brain CT showing several lesions suspicious for cerebral emboli. He then went on to have a bedside transthoracic echocardiogram that was positive for vegetation on the mitral valve, with associated severe mitral regurgitation. Unfortunately, before he was stable enough to be transferred for valve surgery, he suffered an episode of acute pulmonary oedema requiring intubation and ventilation on intensive care unit.

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Case Presentation

A 37-year-old Caucasian male was admitted in extremis to our emergency department with a precipitated history of acute confusion and incoherent speech developing over the course of 48 h. He had no previous medical history, was taking no medications, but was known to be an active intravenous drug user.

On examination, it became evident that this patient was floridly septic, with fever, tachycardia, and hypotension. He was disorientated in space and time, with a Glasgow Coma Scale (GCS) evaluated at 10 (E3 V3 M4). In addition, he was found to have an element of receptive dysphasia. On closer inspection, he was also noted to have a widespread purpuric rash all over his trunk and arms. An initial working diagnosis of meningo-encephalitis was made, and a brain CT was obtained, which demonstrated areas of low attenuation in the left cere-

bellar and cerebral hemispheres that were highly suspicious for septic emboli. Further evaluation with MRI with DWI confirmed multiple ring-enhancing areas within the left cerebral and cerebellar hemispheres, in keeping with infarcts in multiple vascular territories due to septic emboli.

Investigations

At that stage, haematological and biochemical tests were reported, confirming severe sepsis, accompanied by a degree of disseminated intravascular coagulation as well as acute renal impairment (table 1).

In view of the brain imaging findings (fig. 1, fig. 2), an urgent bedside transthoracic echocardiogram was performed, which showed a 1.1 × 1.2 cm fleshy, mobile mass on the anterior mitral valve leaflet, suspicious for vegetation. This was associated with the presence of severe mitral regurgitation. There was no tricuspid valve involvement, and left ventricular systolic function seemed preserved (fig. 3, fig. 4).

Diagnosis and Management

The diagnosis made was severe mitral valve endocarditis with subsequent multiple septic emboli. After prompt discussion with microbiology, he was started on a panoply of intravenous antibiotics and antifungals. He was also discussed with the nearest cardiothoracic centre, and the consensus was that he should be stabilised first and then transferred 48–72 h later, as the operative risks of causing a haemorrhagic transformation at the site of the cerebral emboli was deemed high in the initial stages.

He was therefore transferred to our Coronary Care Unit, where he was monitored for signs of fluid overload, as well as deterioration in GCS, in which case the plan was to repeat the brain CT to rule out further embolisation, as per neurosurgical advice.

Outcomes

Blood cultures, which were back the following day, grew Gram-positive cocci. Unfortunately, before he could be transferred for mitral valve surgery, this patient developed acute pulmonary oedema requiring intensive therapy unit (ITU) admission for intubation, ventilation, and inotropic support. After a prolonged stay on ITU, he eventually became stable enough for transfer to the nearest cardiothoracic unit, where he underwent prosthetic valve surgery, with a good outcome.

Infective Endocarditis – Discussion

Epidemiology

The annual incidence of infective endocarditis in developed countries is reported to be between 1.7 and 6.2 per 100,000 individuals [1]. Women seem to be less affected than men, with a male-to-female ratio of 2.5:1. The incidence of the condition tends to increase after 30 years of age, with the number of cases per 100,000 of people aged 50 and above exceeding 10 [1]. Although we have witnessed a significant reduction in rheumatic disease over the last few decades, the overall prevalence of infective endocarditis has remained stable due to the following reasons [1]:

- The rising frequency of degenerative and prosthetic heart valve disease
- The increase in intravenous drug user population worldwide
- An ageing population prone to nosocomial infections

- The higher pickup rate of infective endocarditis, with improved ultrasonographic methods

The overall mortality rate from infective endocarditis is estimated at 14.5% [2]. Mortality rates depend on the infecting organism. For instance, mortality rates associated with *Staphylococcus aureus* are extremely high (30–40%), except when in the context of intravenous drug use [3, 4].

Anatomy and Pathology

The valvular system is usually affected. Approximately 85% of all cases of infective endocarditis are left sided; of these, two thirds are aortic cases, a quarter mitral, and the remainder being mixed. Right-sided infective endocarditis tends to most frequently involve the tricuspid valve [1].

Endocarditic lesions are made up of vegetations and cause valvular destruction. Thrombi can also be associated with vegetations. Vegetations are found on valves and occasionally invade the atrial or ventricular endocardium. They start spreading along the valve closure line, at first appearing as pinkish-reddish masses, which could be sessile or pedunculated, and which represent an embolisation risk. Histologically, they consist of fibrin, platelets as well as bacterial debris [1].

Valvular destruction can take the form of tear, ulceration, perforation, and rupture of the valvular chordae tendineae. The extent of valvular destruction depends in part on the type of endocarditis, the location, and the duration of the disease process.

Pathogenesis

Endocarditis arises from the colonisation of the endocardium by microorganisms during episodes of bacteraemia [1]. In two thirds of cases of infective endocarditis, a portal of entry can be determined, and this can take various forms:

- Dental procedures
- Respiratory tract infections
- Surgery of the oropharynx
- Gastrointestinal and urinary tract infections
- Gastrointestinal tumours
- Urological and gynaecological interventions

Two factors are required in order to cause endocarditis. The first is an aseptic fibrinoplatelet thrombus that develops within damaged endothelium [1]. The second is the presence of microorganisms.

Of all the pathogens causing infective endocarditis, the most common are the *Streptococcus* species, with 25% being viridans streptococci such as *S. sanguis*, *S. salivarius*, *S. mitis*, and *S. mutans*, and 25% being of the group D variety, such as *S. bovis*, which is prevalent among the elderly population and correlates with colonic lesions. 5% of pathogens are group A, B, C, G *Streptococcus* and are particularly virulent. In patients known to be intravenous drug users or those who have indwelling long-term catheters, the most commonly seen pathogen is coagulase-positive *S. aureus*. HACEK organisms, which are known to be slow-developing, consist of Gram-negative bacilli such as *Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella corrodens*, and *Kingella kingae*. Even less commonly are organisms such as *Bartonella*, *Coxiella*, *Chlamydia*, *Pseudomonas*, and fungi such as *Aspergillus* and *Candida* [1].

Prior to colonisation of the thrombus and the damaged endothelium can take place, various factors [1] must prevail:

- Clusters of pathogens that enable endothelial invasion
- Weakened cellular immunity

- Adhesive capacity of microorganisms, enhanced by the production of dextran or glycocalyx

Pathophysiology

Clinical signs of infective endocarditis arise from five main processes [1]:

- Local intracardiac infections, with valvular destruction and acute regurgitations, and subsequent aneurysms of sinus of Valsalva, conduction defects, and pericarditis
- Embolisation from vegetations and thrombi, more frequently seen in large vegetations caused by *Candida*, *S. aureus*, and HACEK pathogens
- Metastatic infective process to distant locations
- Prompting of the immune system with activation of macrophages and splenomegaly
- Activation of the coagulation cascade with an increase in thromboembolic events

Clinical Manifestations

Signs of infective endocarditis include:

- Fever
- Pallor (anaemia-related)
- New regurgitant heart murmur
- Petechiae
- Splinter haemorrhages – dark red, linear streaks in the nail-beds
- Osler’s nodes – tender red-bluish lesions predominantly found on the finger pads
- Janeway lesions – erythematous painless lesions on palms and soles
- Roth spots – oval retinal micro-bleeds
- Embolic stroke with new neurological deficits
- Congestive heart failure with pulmonary oedema and raised jugular venous pressure
- Splenomegaly

Complications of Infective Endocarditis

Heart Failure

Heart failure is an ominous sign in infective endocarditis, and, as in our patient’s case, its presence usually mandates rapid surgery. Heart failure is triggered by valvular destruction, resulting in acute aortic or mitral regurgitation.

Paravalvular Abscesses

Unless small and uncomplicated, most paravalvular abscesses need surgery, because they may develop into fistula tracks leading to intracardiac shunts or pseudoaneurysms [1].

Arterial Emboli

Systemic emboli can occur in up to 50% of cases of infective endocarditis. The most commonly seen emboli are to the brain, especially in the middle cerebral artery distribution. Less frequently seen are emboli to the spleen, kidneys, limbs, hepatic system or coronary circulation [1].

Extracardiac Abscesses

These result from propagation of bacteria, and can affect the spleen, kidneys or central nervous system; with infection of the latter resulting in brain abscess or meningoen- cephalitis, such as was the case with our patient [1].

Renal Complications

Renal injury in infective endocarditis, in the form of either embolisation or immune- mediated glomerulonephritis, is a poor prognostic indicator [1].

Diagnosis

Duke's Criteria [5]

Major criteria:

- At least 2 positive blood cultures drawn >12 h apart
- Evidence of endocardial involvement with new valvular regurgitation, or positive echocardiographic evidence of mobile intracardiac valvular mass, abscess or dehiscence of prosthetic valve

Minor criteria:

- Predisposing cardiac condition or intravenous drug user
- Temperature >38°C
- Vascular phenomena: septic emboli, septic pulmonary infarcts, and mycotic aneurysms
- Immunological phenomena: glomerulonephritis, Osler's nodes, Roth spots
- Microbiological evidence: positive blood culture not meeting major criteria
- Echocardiographic findings not meeting major criteria

Criteria for infective endocarditis are:

- 2 major criteria or
- 1 major criterion and 3 minor criteria, or
- 5 minor criteria

Echocardiography

Transoesophageal echocardiography (TOE) is superior compared to transthoracic echocardiography (TTE) when it comes to sensitivity, and is recommended whenever TTE is normal in the context of strong clinical suspicion. In particular, TOE proves extremely helpful in diagnosing prosthetic endocarditis, pulmonary valve endocarditis, and endocarditis at unusual sites. It is also more reliable in picking up paravalvular abscesses and fistulae, as well as assessing the mechanism in mitral regurgitation.

Management

Antimicrobial Therapy

Once serial blood cultures have been sent to the laboratory, empirical antibiotics are started according to trust protocols available. The intravenous route is preferred due to maximal bioavailability [1]. Once sensitivities are defined according to the blood culture results, the antimicrobial therapy can be switched to antibiotics specific to the organism.

Surgery

Surgical intervention for infective endocarditis is indicated in the following circumstances [1]:

- Heart failure due to acute valvular regurgitation
- Evidence of para-valvular extension manifesting as heart block, aortic abscess or fistulae
- Persistent infection and spiking temperatures despite appropriate antibiotic therapy for 7–10 days
- Recurrent embolism and persistent vegetation despite adequate antibiotic therapy
- Prosthetic valve with relapsing infection

Timing of Surgery

Timing of valve surgery in patients admitted with virulent infective endocarditis can prove to be extremely tricky, and in this case even more challenging in view of the ongoing cerebritis involved. It is vital to strike the right balance between giving the patient time to be stabilised so as to prevent surgical complications (in this case haemorrhagic transformation) and getting the patient operated on before the development of new cardiac or extra-cardiac complications or further septic emboli.

References

- 1 Crawford MH, DiMarco JP, Paulus WJ: Cardiology, ed 3. Philadelphia, Elsevier, 2010.
- 2 Bor DH, Woolhandler S, Nardin R, Brusch J, Himmelstein DU: Infective endocarditis in the U.S., 1998–2009: a nationwide study. *PLoS One* 2013;8:e60033.
- 3 Wang A, Athan E, Pappas PA, Fowler VG Jr, Olaison L, Paré C, et al: Contemporary clinical profile and outcome of prosthetic valve endocarditis. *JAMA* 2007;297:1354–1361.
- 4 Chu VH, Cabell CH, Benjamin DK Jr, Kuniholm EF, Fowler VG Jr, Engemann J, et al: Early predictors of in-hospital death in infective endocarditis. *Circulation* 2004;109:1745–1749.
- 5 Durack DT, Lukes AS, Bright DK: New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service. *Am J Med* 1994;96:200–209.

Table 1. Blood tests on admission

Blood test	Result
Haemoglobin, g/dl	13.0
White cell count, 10 ⁹ /l	24
Neutrophil count, 10 ⁹ /l	22
Platelets, 10 ⁹ /l	69
Sodium, mmol/l	132
Potassium, mmol/l	3.7
Urea, mmol/l	25
Creatinine, mmol/l	194
Albumin, IU/l	22
Alanine aminotransferase, IU/l	49
Alkaline phosphatase, IU/l	110
Bilirubin, IU/l	28
CRP	308



Fig. 1. CT brain demonstrating areas of low attenuation in the left cerebellar and cerebral hemispheres suspicious for septic emboli.

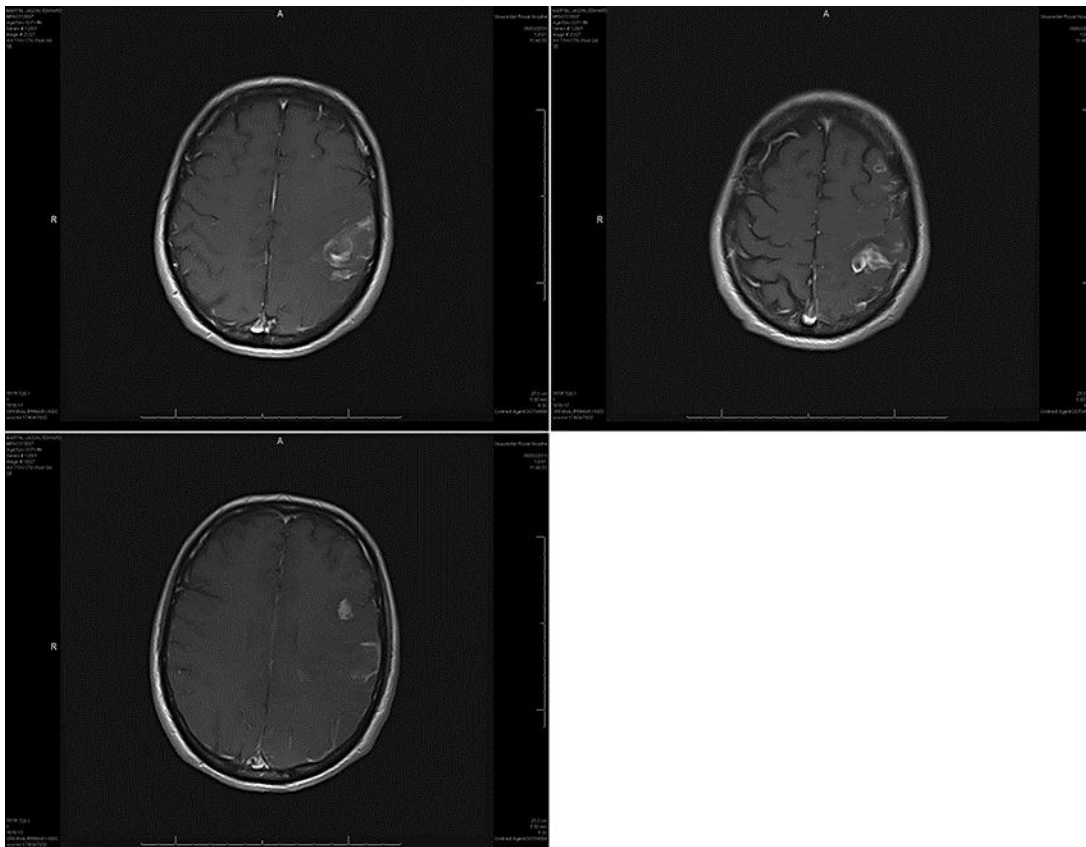


Fig. 2. Multiple septic emboli showing evidence of early- and late-phase cerebritis and evidence of early abscess formation in the left occipital and left parietal regions.

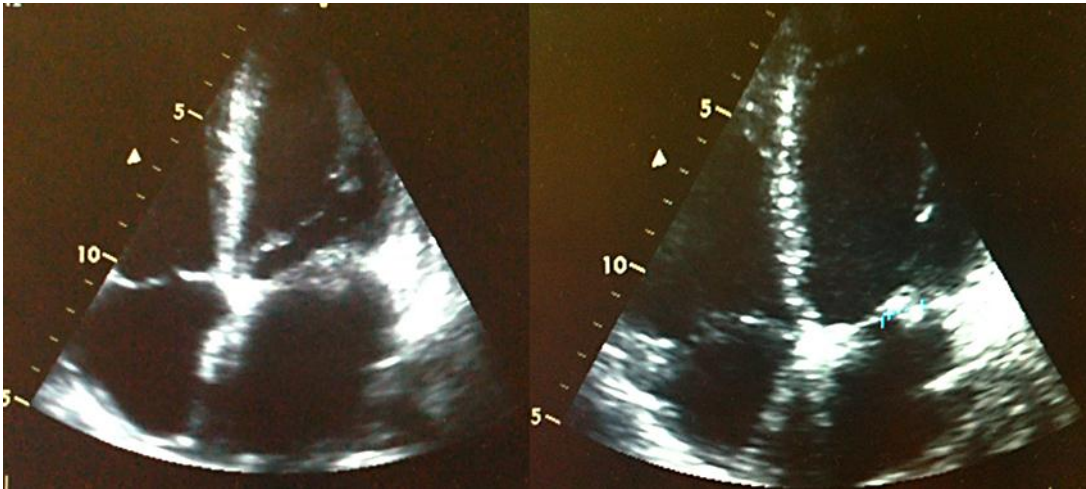


Fig. 3. Four-chamber apical view on echo showing vegetation on the mitral valve measuring 1.1 × 1.2 cm.

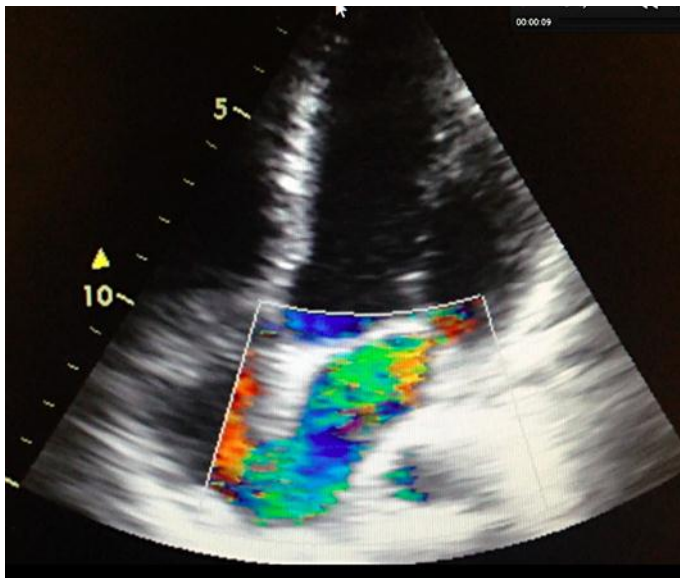


Fig. 4. Severe mitral regurgitation associated with mitral valve endocarditis.