



# Infective endocarditis diagnosed by embolic complication: reports of two cases

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## ABSTRACT

Infective endocarditis (IE) is an acute, subacute, and chronic infectious disease affecting the heart valves and endocardium. Although IE is a rare disease, it is still important because of the morbidity and mortality it causes. Because of non-specific clinical manifestations of IE such as fever, malaise, anemia, and embolic complications, the disease may be confused with many disease manifestations and the diagnosis may be delayed. This article reported two cases with an initial diagnosis of meningitis and cellulitis as a result of embolic complications of IE.

**Keywords:** Infective endocarditis, embolism, *S. aureus*

## INTRODUCTION

Infective endocarditis (IE) is an infectious disease caused mostly by bacteria and characterized by the involvement of heart valve endocardium, congenital cardiovascular lesions, or prosthetic valves.<sup>1</sup> The prevalence of IE in developed countries is approximately 6/100 000 people. Epidemiological studies have shown that the frequency of IE has increased in recent years and this increase has occurred especially in the elderly and the rate of IE in people over 70 years of age has been determined as 11.7-19/100 000. There is no incidence study on IE in our country. However, when compared with developed countries, it is possible that the prevalence of IE is higher in our country due to the high prevalence of conditions that increase the risk of IE such as acute rheumatic fever (ARF) and rheumatic heart disease (RHD, and nosocomial bacteraemia.<sup>2</sup>

Although IE is rare, it still maintains its importance because of the high morbidity and mortality it causes. Clinical signs and symptoms of IE are highly variable and findings including fever, new cardiac murmur, anemia, and splenomegaly may not always be present in most patients.<sup>3</sup> Embolic events are common and life-threatening complications in patients with IE. Since embolic presentation may be confused with clinical findings of many diseases, it may cause difficulties in diagnosis. In this article, two cases of IE presenting with embolic presentation and different diagnoses are presented.

## CASE

### Case 1

A 36-year-old female patient with no medical history was admitted to the emergency department with a headache and confusion. On physical examination, the patient

was unconscious and wasn't oriented and cooperative, there was 2-3/6 systolic murmur in the mitral focus, and hepatosplenomegaly. The general examination was normal. Her parameters were fever: 39°C, heart rate 110/min, arterial blood pressure 110/80 mmHg, and respiratory rate 26/min. Laboratory investigation showed white blood cells (WBC): 17400/mm<sup>3</sup> (75% neutrophils), hemoglobin: 8.3 g/dL, platelets (PLT): 282000/mm<sup>3</sup>, urea: 38.5 mg/dL, serum creatinine: 0.51 mg/dL, aspartate transaminase (AST): 183 IU/L, alanine transaminase (ALT): 91.4 IU/L, serum albumin 2.3 g/dL, prothrombin time (PT) 16.3 min., international normalised ratio (INR): 1.48, C-reactive protein (CRP): 24.4 mg/dL (N:0-0.5), erythrocyte sedimentation rate (ESR): 68 mm/h. A lumbar puncture and blood cultures were performed. The cerebrospinal fluid (CSF) contained 10 leukocytes/mm<sup>3</sup> cell count and Gram staining showed no microorganisms. The patient was hospitalised in the infectious diseases unit. An antibiotic therapy with ceftriaxone 2 gram IV bid and vancomycin 1 gram IV bid was started for presumptive diagnosis of acute meningitis. On cranial magnetic resonance imaging (MRI), there was a 5×6 mm nodular hemorrhage area on the cortical surface at the junction of the frontoparietal lobe on the left (**Figure 1**) (This appearance was interpreted as a septic embolism by the radiologist.). All blood cultures were positive for Methicillin-susceptible *Staphylococcus aureus* (MSSA) growth. On transthoracic echocardiography (TTE), 1x1 cm vegetation was detected on the aortic valve. Ceftriaxone and vancomycin treatments were stopped. Considering infective endocarditis, cefazolin 3 gram IV bid and gentamicin 3 mg/kg/day IV were started. The patient's confusion and fever regressed during the follow-up. There was no need for surgery in terms of IE. The patient was discharged after 6 weeks of treatment.

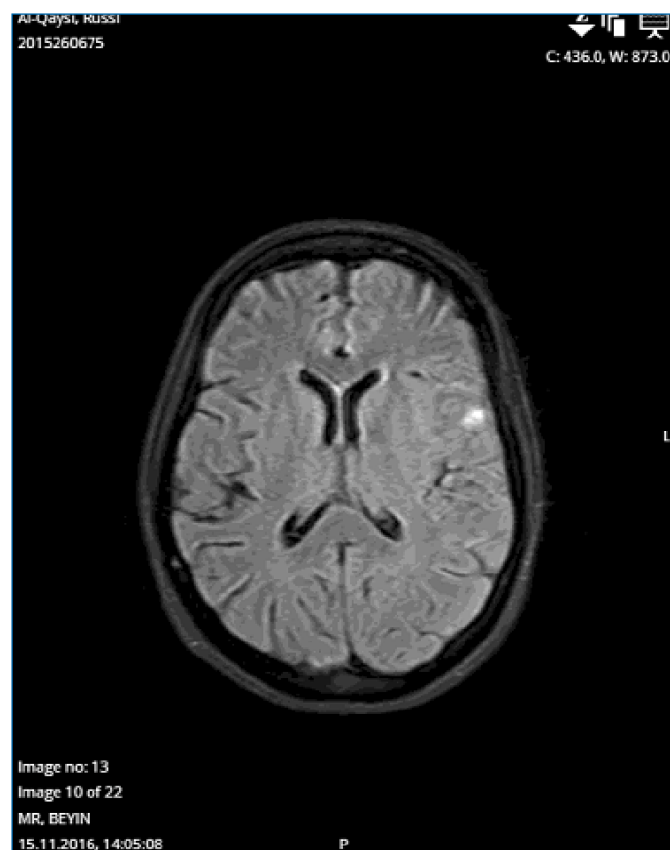


Figure 1. Cranial diffusion MRI: nodular hemorrhage area

### Case 2

A 60-year-old male patient was admitted to the emergency department with erythema in both upper extremities (Figure 2). On physical examination, his parameters were fever: 38°C, pulse rate: 100/min, blood pressure: 110/80 mmHg, and respiratory rate: 22/min. The patient reported a history of presenting to the emergency department 2 days ago with fever and malaise and was prescribed amok-clav 2 gram bid oral with the diagnosis of cellulitis. The tests performed in the emergency department revealed haemoglobin: 11 mg/dl, WBC: 14000/mm<sup>3</sup>, PLT: 196000/mm<sup>3</sup>, CRP: 36.2 mg/dl, ESR: 98 mm/h. Other examination findings were normal and the patient was hospitalised in the infectious diseases ward with a prediagnosis of cellulitis. Blood cultures were performed. Ampicillin-sulbactam 1.5 g 6 hourly treatment was started. During follow-up, the fever persisted and a detailed physical examination revealed painful red skin lesions on the soles of the feet and fingers. On the third hospital day, the blood cultures drawn on admission returned positive for MSSA. TTE was performed for infective endocarditis and 8 mm vegetation on the aortic valve and pericardial fluid were revealed. Extensive erythema around a small papule on both arms and lesions on the soles of the feet were evaluated as septic embolism. Ampicillin-sulbactam treatment was stopped and cefazolin 3×2 (6 weeks) and gentamicin 3 mg/kg/day (5 days) were started. Aortic valve insufficiency developed in the fourth week of treatment and the patient was transferred to cardiovascular surgery for valve replacement. Aortic valve replacement was performed and the patient was discharged without complications.



Figure 2. Erythema in both upper extremities

## DISCUSSION

In epidemiological studies conducted in developed countries, it has been observed that the incidence of IE, which is approximately 6/100,000, has increased in recent years and IE is the fourth most life-threatening infectious disease after sepsis, pneumonia and intraabdominal infections.<sup>1</sup> The frequency of IE, causative microorganisms, mortality and morbidity rates differ between countries. In developed countries, survival rates in IE are 80% in the hospital, 70% at the end of the 1st year after discharge and only 60% at the end of the 5th year.<sup>2</sup> In Turkey, mortality rates are higher and are 25-30% even during hospitalisation.<sup>3</sup> Acquired valvular diseases or congenital heart diseases and a history of previous IE are the most common predisposing conditions for the development of IE.<sup>3</sup> Endothelial damage is held responsible for the pathogenesis of IE. After mechanical damage or inflammation in the endocardium, small masses called vegetation are formed by bacteria settling in the region. As a result of the arrival of platelets in the region and formation of a fibrin network, the vegetation grows even more.

In recent years, it has been found that the clinical features and common factors of IE have changed.<sup>4</sup> Today, the population at risk is different for several reasons: a decrease in rheumatic heart disease, haemodialysis patients, widespread prosthetic valves, intracardiac devices, intravenous drug use and an increase in healthcare-associated infections, *S. aureus* and coagulase-negative staphylococci (CNS) are more common causes, while the proportion of viridans streptococci has relatively decreased.<sup>5</sup> The most common pathogens in the etiology have shown a microbiological shift from streptococci to staphylococci.<sup>6</sup> *S. aureus*, *Streptococcus* spp. and CNS are the most common agents in cases of IE reported in Turkey. These are followed by enterococci and *Brucella* spp. HACEK group bacteria (*Haemophilus* spp., *Aggregatibacter*, *Cardiobacterium* spp., *Eikenella* spp., *Kingella* spp.), *Coxiella burnetii* and *Bartonella* spp., gram-negative rods and fungi (especially *Candida* spp.) are other IE agents.<sup>3</sup> In our cases, the causative microorganism was MSSA as in the literature. There were no underlying risk factors including congenital or acquired valvular disease, intracardiac foreign body or haemodialysis history in our patients. Although the initial clinical pictures of the patients suggested different diagnoses, MSSA grown in blood culture brought infective endocarditis to our mind in the differential diagnosis.

Although the most common clinical finding in IE is fever, it is a multisystem disease with highly variable clinical symptoms. Classical findings such as fever, anorexia, cardiac murmur and anaemia may not always be present. Various organ systems such as skin, mucosa, central nervous system and kidney may be affected due to embolic and immunological complications. The disease may be acute or chronic with subacute or subfebrile fever and silent findings. In a study conducted in Turkey, the most common examination findings in patients were found to be fever (94%) and newly developing murmur (45%).<sup>7</sup> In both cases, infective endocarditis was not initially considered. In the first case, meningitis was considered with a presentation of fever and confusion and in the second case, cellulitis was considered because of fever and erythema in the arms. In both cases, the clinical presentation was actually caused by embolic complications of IE, and the diagnosis of IE was initially missed.

Currently, echocardiography is the most commonly used imaging modality for diagnosis of IE and TTE should be the first investigation to be performed in a patient with suspected IE. Transesophageal echocardiography (TEE) should be performed in the presence of high clinical suspicion even if TTE is negative. On echocardiographic examination, endocardial vegetation, abscess, valve perforation or recent detachment of the prosthetic valve and newly developing valve insufficiency support the diagnosis of IE. Imaging modalities including cardiac CT/MRI and labelled leukocyte scintigraphy are other diagnostic modalities that may be helpful in demonstrating endocardial involvement and detecting cardiac or non-cardiac complications.<sup>8</sup> In both of our cases, the vegetations were quite large and were also seen on TTE and there was no need for TEE.

Embolic events are the most common non-cardiac complications of IE and frequently occur in the initial phase of IE. The diameter, mobility, structure and rapid growth of vegetation are important risk factors for embolism. The risk of embolism varies according to the causative microorganism. Endocarditis caused by staphylococci, *Candida* spp., *HACEK* and *Abiotrophia* is more risky in terms of septic embolism.<sup>9,10</sup> Septic emboli may affect many tissues and organ systems such as the brain, kidney, spleen, skin, and coronary arteries.<sup>11</sup> Various studies had reported septic embolies are frequently seen in the central nervous system.<sup>12</sup> Neurological involvement includes complications such as stroke, intracerebral haemorrhage, meningitis and abscess.<sup>13</sup> Neurological complications may be associated with poor prognosis. The most common neurological complication is cerebral ischaemia, which is associated with increased morbidity and mortality. Our first case initially presented with neurological findings and was diagnosed with meningitis because of findings compatible with bacterial meningitis on LP performed due to fever. A brain MRI that was performed because the patient's clinical findings did not improve revealed nodular haemorrhage and septic embolism. TTE was performed and the diagnosis of IE was thus made.

Initial treatment of IE is started empirically according to the patient's risk factors. However, once the causative microorganism is identified, treatment directed towards the causative agent constitutes the basis of IE treatment. However, surgery performed in appropriate indications has a very important role in the prognosis of IE.<sup>14</sup> Treatment of septic emboli is best performed with antimicrobial therapy, but anticoagulant therapies are also recommended.

## CONCLUSION

Infective endocarditis is a disease with high mortality and morbidity and is being seen more and more frequently today. Especially in cases with subacute courses and without fever, these patients may be misdiagnosed because IE does not come to mind in the initial diagnosis. These patients may present with systemic embolism complications before showing clinical findings specific to infective endocarditis. In case of bacteremia or fungemia of unknown cause or an embolic event, IE should be kept in mind in the differential diagnosis. Also, our cases are important in terms of drawing attention to the different presentations of infective endocarditis and the importance of physical examination in the diagnosis.

## ETHICAL DECLARATIONS

**Informed Consent:** All patients signed the free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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