

Anaemia and neurologic complications – the dominating manifestations of infective endocarditis – case report

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Abstract

Infective endocarditis (IE) is an infection of the endocardium, which most commonly involves the mitral and aortic valve. The estimated incidence of IE in patients with heart defects is 1–2%. One of the predisposing factor is mitral valve leaflet prolapse accompanied by incompetence. The diagnosis of IE can prove difficult due to the possible occurrence of symptoms from multiple organs. A multidisciplinary approach, and taking into consideration possible numerous complications is essential during diagnostic procedures. The clinical picture of IE includes embolic complications. The presented study describes the case of a 58-year-old male patient with a mitral defect diagnosed due to multi-cause anaemia, which delayed the diagnosis of IE. Besides anaemia, the clinical picture was dominated by numerous embolic brain lesions, being complications of IE, which caused disorientation and confusion.

Key words

stroke, anaemia, infective endocarditis, cerebral embolism, cerebral complications, neurologic complications

INTRODUCTION

Infective endocarditis (IE) is a life-threatening disease defined as an infection of the endocardium, most commonly involving the mitral and aortic valves. The estimated incidence of IE in patients with heart defects is 1–2%. The disease predominantly affects males aged 50–70 years. The predisposing factors include a history of rheumatic disease, congenital heart defects, mitral valve leaflet prolapse accompanied by incompetence, and valvular prostheses. The diagnosis of IE is extremely difficult and exacting due to the possible occurrence of non-specific symptoms, such as anaemia. IE leads to local endocardial and valvular apparatus destruction, peripheral emboli, and immune reactions leading to tissue damage. Peripheral emboli cause infarcts, multiple remote abscesses or remote site infections [1, 2, 3]. In each case, possible embolic complications should be considered, including cerebral complications, which are a poor prognostic factor [1, 3, 4].

CASE REPORT

A 58-year-old male patient presented to the Department of Internal Diseases with a long-standing history of arterial hypertension and chronic heart failure. In April 2017, he was diagnosed with a mitral defect, i.e. mitral valve leaflet prolapse accompanied by severe incompetence; moreover, he had periodic episodes of atrial fibrillation. To prevent the thrombotic complications, the patient received dabigatran in a dose of 150mg 2x daily.

From February 2017, the patient had been hospitalised multiple times, mainly due to atrial fibrillation. During the treatment with dabigatran, the patient was diagnosed with anaemia – the iron level – 26 µg/dl; the absorption curve was flat, the values of neoplastic markers were normal, endoscopy of the colon demonstrated bleeding from polyps. During colonoscopy, polypectomy was performed and the bleeding stopped.

In September 2017, the patient was re-admitted to our Department due to clinical symptoms of anaemia, weight loss of 15 kg during the period of 6 months, but without fever. Physical examination demonstrated deterioration of his general condition; the supra-mitral and supra-tricuspid valve murmur was found to be louder, compared to the previous hospitalisations. Abdominal CT revealed hepato- and splenomegaly. There were no clinical or laboratory signs of gastrointestinal haemorrhage (faecal occult blood test and gastrointestinal tract GI scintigraphy). The laboratory findings disclosed aggravated normocytic and normochromic anaemia, compared to the previous tests (Hb – 5.8 g/dl), haematuria with slight albuminuria, leukocytosis with a predominance of neutrophils, C-reactive protein elevated to 82 mg/l and impaired kidney function. Moreover, during the observation period, the patient developed neurologic symptoms, such as confusion and disorders of consciousness. Infective endocarditis was suspected.

Considering the patient's mitral defect, his deteriorating condition, persistence and aggravation of anaemia (which was a long-standing dominating clinical symptom) despite substitutive compensation (transfusions of RBC concentrates), and only slightly increased inflammatory markers and neurologic symptoms, the patient was scheduled to undergo echocardiography to confirm infective endocarditis.

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The echocardiographic findings demonstrated large balloting vegetations on both leaflets of the mitral valve (2.9cmx0.5cm on the posterior leaflet) (Fig. 1), small vegetations on the interventricular septum on the side of the left atrium, and severe mitral valve incompetence (Fig. 2). Moreover, the echocardiographic image was typical of mitral valve IE; the risk of pulmonary hypertension was high.

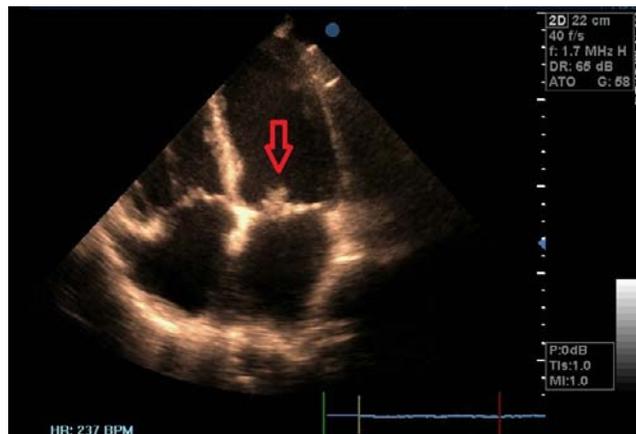


Figure 1. Echocardiographic imaging of mitral valve vegetations.

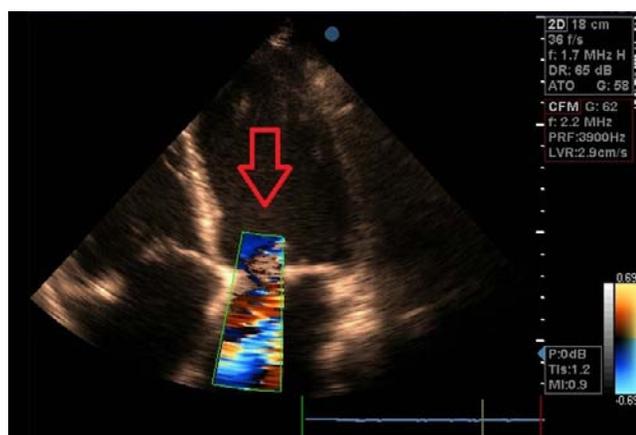


Figure 2. Echocardiographic imaging of severe mitral valve incompetence with vegetations

Empiric antibiotic therapy was instituted preceded by blood sampling for cultures. Considering the exacerbating disorders of consciousness and disorientation as to time and place, the head MRI was performed. The MRI findings demonstrated a wedge-shaped subcortical area of a low signal intensity on GRE T2* sequence and T2-weighted images – about 13x8 mm in size with a small zone of surrounding oedema in the anterior pole of the right frontal lobe. The image was suggestive of a haemorrhagic stroke focus, most likely of 2–3-day duration in the acute phase and early sub-acute phase (Fig.3). Moreover, numerous slight (up to 7 mm), disseminated foci were visualised in the white matter of cerebral hemispheres (predominantly in the frontal and parietal lobes), partly fusing into larger areas in the centrum semiovale and in the region of the trigone of the left lateral ventricle of a high signal intensity on the FLAIR sequence and T2-weighted images. The largest area was visible in the peripheral part of the temporal lobe and involved the cortical layer and the subcortical white matter, with constricted adjacent cortical sulci. The above changes showed the

features of diffusion restriction, most of them were contrast-enhanced, partially along the gyri; small petechiae were visible inside them (of a low signal intensity on GRE T2). The MRI image was suggestive of the ischaemic regions in the early sub-acute phase with the features of petechial haemorrhaging (Fig. 4). Additionally, a segmentally increased signal intensity on FLAIR, DWI and T2-weighted images was found in the anterior longitudinal fissure of the brain, in the pericommisural artery, about 10 mm long, which suggested occlusion (Fig. 5).



Figure 3. MRI of the head visualising the area of haemorrhagic stroke focus in the acute / early sub-acute phase (T2* GRE sequence)

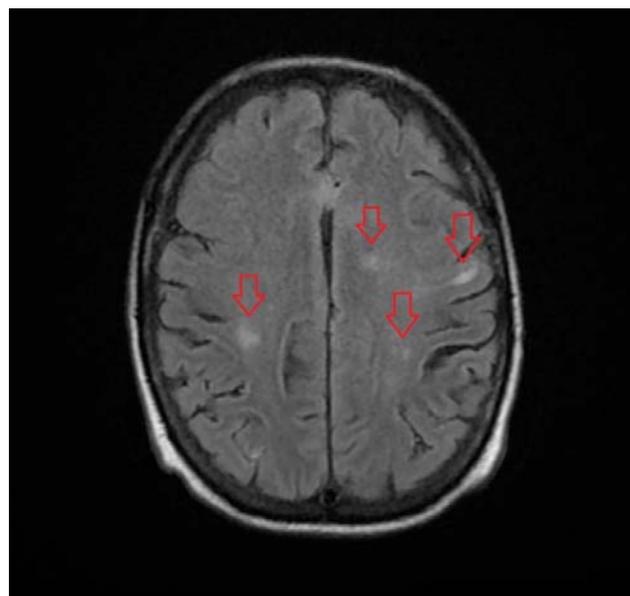


Figure 4. Numerous foci of ischaemic stroke in both cerebral hemispheres in the early sub-acute phase – FLAIR MRI

The patient was scheduled for urgent valve surgery due to extensive haemorrhagic cerebral infarct. Despite the treatment used, the symptoms of cardiac and renal failure, as well as neurologic symptoms exacerbated; moreover, the patient developed respiratory disorders. After several days, the patient died due to respiratory and cardiac arrest.

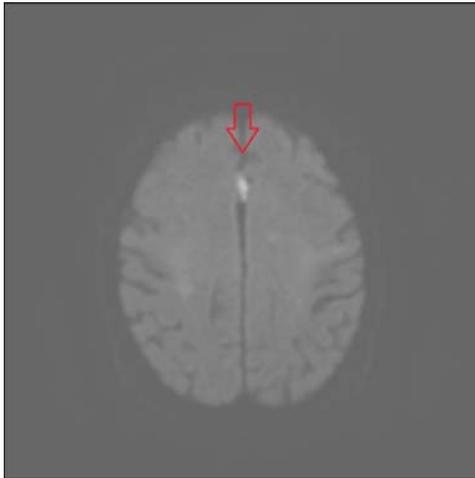


Figure 5. DW-MR imaging of pericommisural artery occlusion

DISCUSSION

Infective endocarditis (IE) is a severe disease with a high mortality rate [5]. In developed countries, the estimated prevalence of IE is 3 – 9 cases per 100,000 annually [6]. The hospital mortality of IE patients ranges from 15% – 20 % [2]. In recent years, the availability of antibiotic therapy, its widespread use and medical care accessibility have changed the clinical picture and the epidemiologic profile of the disease. Increasingly, elderly patients are affected, and the course and clinical picture of infective diseases have changed in which staphylococcus aureus is found to be an increasingly common aetiological factor of infective endocarditis [1, 4, 7]. The dominating symptoms developing in IE patients, such as anaemia, at slightly elevated CRP and leukocytosis, haematuria, and an enlarged spleen, are currently considered non-specific and are not reflected in the current diagnostic criteria of IE, although they are observed in a high proportion of patients [3].

Laboratory tests reveal anaemia, usually normocytic and normochromic, in 70 – 90% of IE patients [1]; haemolytic anaemia is observed less frequently [8]. In the presented case, anaemia recurred multiple times during hospital and out-patient treatment. The diagnostic difficulties resulted from the abnormalities found in additional examinations, which suggested a post-haemorrhagic cause of anaemia – bleeding from colonic polyps, with iron deficiencies and its impaired absorption during anti-thrombotic treatment with dabigatran, which could have increased the risk of bleeding [9]. Irrespective of its cause, the diagnosis of anaemia is difficult as well as time-consuming, and requires a multi-disciplinary approach.

The several-month hospital and outpatient observation most likely suggests that anaemia was one of the first symptoms of IE. Beside the causes of anaemia mentioned above, a significant pathogenetic factor of this anaemia was a chronic infection of the mitral valve.

In the current case, the multi-factorial causes of anaemia at the lack of fever and insignificantly elevated markers of inflammation resulted in diagnostic difficulties and delayed the diagnosis of IE.

Analysis of the clinical course of the case described poses the question whether and to what extent the earlier hospitalisations

and interventions involving tissue discontinuity contributed to the development of IE. According to some authors, higher incidences of IE are associated with medical procedures, such as intravenous treatment administered to patients during earlier hospitalisations [1, 2, 7].

Neurological manifestations can be the first sign of IE [10], and are relatively common and potentially life-threatening [3, 6]. In cases of involvement of the left heart valves, as happened in the current case, the symptoms related to peripheral emboli predominate, which has also been reported by other authors [1, 4, 5]. In IE patients, especially when the left part of the heart is affected, the early detection of neurological complications can contribute to a better therapeutic outcome. At present, such complications are considered one of the essential prognostic factors [1, 3, 5, 6].

According to the available data, ischaemic stroke is the most common neurological complication in IE (occurring in 20 – 40% of patients); asymptomatic ischaemia develops in another 30 – 40% of patients. The second most common neurological complication is haemorrhagic stroke (4 – 27% of patients), while haemorrhagic microstrokes develop in up to 30 – 40% of patients. The remaining cerebral complications of IE are much rarer [6, 7].

Neurological complications can be relatively non-specific and result in focal deficits, headaches, confusion, mental disturbances, proptosis, paralysis of the eyeball muscles, epileptic seizures, fever due to cerebral abscesses, back pain, nuchal rigidity, photophobia, fever, psychoses, and stupor [1, 6, 11].

The symptoms of brain infarct and haemorrhage are determinants of mortality, as opposed to silent neurologic events [5, 7, 12]; therefore, a quick diagnosis is essential. Head MRI is more sensitive than computed tomography, particularly when performed according to standard protocols and sequences. [2, 3, 7]. Due to silent neurologic events in patients with IE who were not diagnosed using imaging methods, the total incidence of neurologic complications can be even higher and difficult to estimate [7].

Confusion observed in the patient in the presented case was the first neurological symptom, which can be a sign of cerebral stroke caused by embolism, and usually occurs in 10 – 20% of IE patients [1].

Peripheral emboli are most commonly located in the brain and spleen [4]. Their kind and severity significantly affect the decision about possible cardio- and neurosurgical treatment [3, 5, 6]; therefore, multi-disciplinary cooperation is required to optimise the treatment outcomes in IE patients [6]. Emboli are more common in patients with moveable and large vegetations (>10mm, the risk is 30 – 40%) or with vegetations located on the anterior leaflet of the mitral valve [1, 12]. In the presented case, the vegetations on the mitral valve fulfilled the criteria of a high risk of cerebral complications described in the above-mentioned studies. Cardiosurgical intervention was postponed due to detected extensive complications resulting from brain embolism in order to improve the patient's neurological status. According to the 2015 ESC guidelines, cardiosurgical interventions are contraindicated in patients with extensive brain damage or haemorrhage; otherwise, the patients with non-extensive lesions can undergo surgery [3].

The other factor increasing the risk of neurologic complications is anti-coagulant therapy during differential diagnosis of IE [10]. In this case, anti-coagulant therapy was

discontinued earlier due to suspected haemorrhage from the gastrointestinal tract and increasingly severe anaemia during diagnostic procedures. It is currently believed that IE is not an indication to start anti-platelet or anti-thrombotic treatment [1]. The available studies performed using anti-platelet drugs have shown neutral or negative results [6]. In cases of haemorrhagic stroke, anti-thrombotic and anti-platelet agents should be withdrawn [1, 7].

CONCLUSIONS

- 1) Infective endocarditis is a severe disease which can cause a wide array of relatively non-specific symptoms, e.g. anaemia.
- 2) The diagnosis of IE can prove difficult due to the occurrence of symptoms from multiple organs. A multidisciplinary approach, and taking into consideration possible numerous complications, are essential during diagnostic procedures.
- 3) The dominating and first symptoms of IE are neurological complications which usually occur as ischaemic or haemorrhagic cerebral stroke.
- 4) The first neurological symptoms are difficult to define; they can develop as confusion, disorientation, without focal symptoms.

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