



INFECTIVE ENDOCARDITIS WITH NEGATIVE BLOOD CULTURES IN PATIENT WITH END-STAGE RENAL DISEASE TREATED WITH PERITONEAL DIALYSIS



Katarzyna Romejko, Magdalena Markowska, Agnieszka Ślepowrońska, Katarzyna Śliwakowska, Stanisław Niemczyk

Wojskowy Instytut Medyczny – Państwowy Instytut Badawczy, Klinika Chorób Wewnętrznych, Nefrologii i Dializoterapii, Polska

Abstract: Infective endocarditis (IE) is an inflammatory disease involving a proliferative-destructive processes, usually of streptococcal or staphylococcal etiology. It may also be caused by the physiological flora of the oral cavity, mainly gram-negative bacteria from the HACEK group. IE typically develops in damaged areas of the endocardium. Bacterial vegetations are found in majority on valves but they may be as well visualised in blood vessels, ventricles, on mechanical valves, electrodes and intracardiac catheters. Risk factors for endocarditis concern the growing population of adults with congenital heart disease and patients with frequent healthcare contact for other comorbidities, also patients who are immunocompromised, treated with hemodialysis or use intravenous drugs. The diagnosis of IE is made by the use of transthoracic or transesophageal echocardiography, also other imaging techniques are used. Blood cultures also should be taken. However, it was estimated that approximately 10% of patients have cultures and serologic tests negative for IE. In our study we present a case of a 51-year-old man with end-stage renal disease treated with peritoneal dialysis for 3 weeks prior to hospital admission with an acute infection of unknown origin. Infective endocarditis was suspected based on echocardiography examination. In this case PET-CT (positron emission tomography/computed tomography) was performed for verification. Its result as well as sterile blood cultures did not fully confirm the diagnosis of IE. Despite the access to highly specialized diagnostic methods and broad spectrum antibiotics the diagnosis and treatment were not easy. This story of patient's disease can be the confirmation that IE is heterogeneous in etiology, clinical manifestations, and course.

Keywords: peritoneal dialysis, echocardiography, infective endocarditis, blood cultures.

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Corresponding author:

Katarzyna Romejko
Wojskowy Instytut Medyczny – Państwowy Instytut
Badawczy, Klinika Chorób Wewnętrznych, Nefrologii
i Dializoterapii, Warszawa
e-mail: kromejko@wim.mil.pl

Introduction

Infective endocarditis develops as a result of an endocardial infection, most often of bacterial - staphylococcal etiology [1]. Risk factors include heart defects, previous endocarditis, medical procedures that disturb the continuity of heart tissue and frequent contact with health care [2, 3]. Despite the use of antibiotic prophylaxis in the highest-risk patients, preventive procedures and improvement of diagnostic methods it is still a disease that not only is a diagnostic challenge but is also associated with mortality up to 30% and serious complications [4, 5]. It can have a different course, from a mild infection to septic shock and multiorgan failure [6]. Early clinical suspicion and a rapid diagnosis are essential to enable the correct treatment pathways to be accessed and to reduce complication and mortality rates [7]. The clinical indications of IE relies on the Duke criteria which are presented in Table 1.

Case report

A 51-year-old man with a history of type 2 diabetes complicated by end-stage renal disease, diabetic retinopathy, bilateral diabetic foot syndrome, peripheral polyneuropathy, hypertension, atherosclerosis, after implantation of stents into the left femoral superficial artery, secondary hyperparathyroidism, hyperuricaemia, history of nicotine addiction, qualified to renal replacement therapy that started 3 weeks earlier with peritoneal dialysis, after implantation of the Tenckhoff catheter 1.5 months earlier, was applied to the Hospital Emergency Department because of worsening of his general condition and intensification of pain of the lumbosacral and thoracic spine. These symptoms were accompanied by a low-grade fever and a decrease of blood pressure. Symptoms began four days prior to hospitalization. Patient was admitted to the Department of Nephrology.

On admission to the Department of Nephrology detailed medical history was taken. Patient denied typical

Table 1. Modified Duke Clinical Diagnostic Criteria for Infective Endocarditis [13]

Major criteria	Positive blood cultures for infective endocarditis Typical microorganisms consistent with IE from 2 separate blood cultures: <ul style="list-style-type: none"> • Viridans streptococci, Streptococcus bovis, HACEK group (Haemophilus spp, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella spp, and Kingella kingae), S. aureus; or community-acquired enterococci, in the absence of a primary focus; or • Microorganisms consistent with IE from persistently positive blood culture results, defined as follows: <ul style="list-style-type: none"> • At least 2 positive culture results of blood samples drawn 12 h apart; or • All of 3 or most of ≥ 4 separate culture samples of blood (with first and last samples drawn at least 1 h apart) • Single positive blood culture result for Coxiella burnetii or antiphase I IgG antibody titer $> 1:800$
	Evidence of endocardial involvement <ul style="list-style-type: none"> • positive echocardiogram for infective endocarditis: oscillating intracardiac mass on valve or supporting structures or in the path of regurgitant jets or on implanted material in the absence of an alternative anatomical explanation or abscess or new partial dehiscence of prosthetic valve • new valvular regurgitation
Minor criteria	Predisposition , predisposing heart disorder, or IV illicit drug use
	Fever $\geq 38.0^{\circ}$ C
	Vascular phenomena: arterial embolism, septic pulmonary embolism, mycotic aneurysm, intracranial hemorrhage, conjunctival petechiae, Janeway lesions
	Immunologic phenomena: glomerulonephritis, Osler nodes, Roth spots, Rheumatoid factor
	Microbiologic evidence of infection consistent with but not meeting major criteria
	Serologic evidence of infection with organisms consistent with endocarditis

symptoms of respiratory or urinary tract infections. Physical examination revealed regular heart rate, clear and correctly accentuated heart tones, correct blood pressure values. Lung fields were normal on auscultation. There was a skin lesion on the surface of the right heel. In biochemical tests normocytic anaemia (haemoglobin 11,1g/dL, mean corpuscular volume of red cells 93 fl), leukocytosis ($10,54 \times 10^9/L$) with neutrophilia (75,7%), increased inflammatory parameters – C-reactive protein (CRP) (2,7mg/dL) and procalcitonin (PCT) (0,9ng/L) were found. Slight leukocyturia was researched in the analysis of urine, but there were no bacteria in the sample. What is more no evidence of peritonitis was detected during assessment of dialysis fluid morphology. Blood and urine cultures also were tested. Considering the health state of patient (*weakness, fever*) empiric antibiotics were initiated (*ciprofloxacin and ceftriaxone*). Despite wide range of examinations trigger of infection was not revealed. As part of the search a surgical consultation was made to assess the skin change on patient's right heel. A second-degree thermal burn was diagnosed. It was unlikely to be the source of suspected bacteremia. In connection with persistent pain of the lumbosacral and thoracic spine computed tomography and magnetic resonance were performed. Imaging showed degenerative changes of the spine and excluded the presence of abscesses in the thoracic and lumbosacral spine. The ultrasound examination of the abdomen apart from the increased echogenicity of both kidneys was correct. Blood and urine cultures were

sterile. Due to the persistently high values of inflammatory parameters and the lack of clinical improvement, antibiotic therapy was modified. Meropenem and vancomycin were started. In the course of further diagnostics the echocardiography examination was performed, which visualized the 6mm x 9 mm lesion connected to the edge of the non-coronary aortic valve cusp (Figure 1). Infective endocarditis was suspected. Firstly transesophageal echocardiography was made for verification. It revealed small degenerative changes in the coronary aortic valve cusp and also small, thin, airy threadlike echo, connected with coronary aortic valve cusp, 7 mm long, which was diagnosed as a Lambla thread for possible differentiation with bacteria vegetation in the course of IE. The patient was qualified for PET/CT examination and increased accumulation of 18-fluorodeoxyglucose in a delayed phase in left ventricle was shown. However, no definite diagnosis of IE was made after all this examinations. On completion the treatment the patient's condition improved significantly. Inflammatory markers were finally decreased (CRP 0,4mg/dL, PCT 0,21ng/mL). Peritoneal dialysis was correct, without peritonitis in clinical examination and in peritoneal effluent examination. Although the diagnosis was not clear, patient was discharged with the intention of another echocardiographic examination in two weeks during the planned visit at the Dialysis Center.

As recommended, the patient applied for a follow-up. In transthoracic echocardiography examination a hy-

poechogenic lesion associated with the margin of the non-coronal aortic valve cusp, measuring 12 mm x 4 mm, was visualised (Figure 2). Unfortunately second time the progressive weakening and a dynamic rise of inflammatory parameters (CRP 28mg/dL, PCT 0,9ng/dL) were noticed. Decision was made to use another empiric antibiotic therapy (*biseptol and fluconazole*) and to admit the patient to the hospital for further diagnostics.

On admission patient reported weakness, fatigue, dizziness and pain of the lumbar spine making it difficult to move. As previously, the physical examination found no significant pathologies. The heel area of the right foot showed no signs of inflammation, the burn was in the process of healing. Blood cultures were negative. During hospitalization an echocardiographic examination was performed. The reduction of the lesion associated with the edge of the non-coronary aortic valve cusp to 5 mm x 2 mm was noticed. More of the same diagnostics were performed to identify different sources of infection. Even skin and rectum swabs remain negative. Patient was consulted by otolaryngologist and dentist - no potential foci of infection were detected. As well as no inflammatory changes were visualized on the chest X-ray. Based on the overall clinical picture, echocardiography examination, PET-CT examination and by exclusion of other active foci of infection, the diagnosis of infectious endocarditis of the aortic valve was made. Empirical antibiotic therapy was started - ampicillin, cloxacillin and gentamicin. During further treatment, considering a slight decrease of inflammatory markers after 7 days of full antibiotherapy (CRP 28 -> 23,8mg/dL, PCT 0,9 -> 0,86ng/mL), a decision was made to replace cloxacillin with vancomycin. After this modification, the patient's condition improved quickly. Control laboratory tests showed the significant decrease of inflammatory markers (CRP 0.7 mg/dL and PCT 0,2ng/mL). The patient, in fairly good general condition, was discharged with instructions to continue antibiotic therapy during outpatient treatment.

Figure 1. Transthoracic echocardiography visualising lesion connected with aortic valve. Modified parasternal long-axis view.

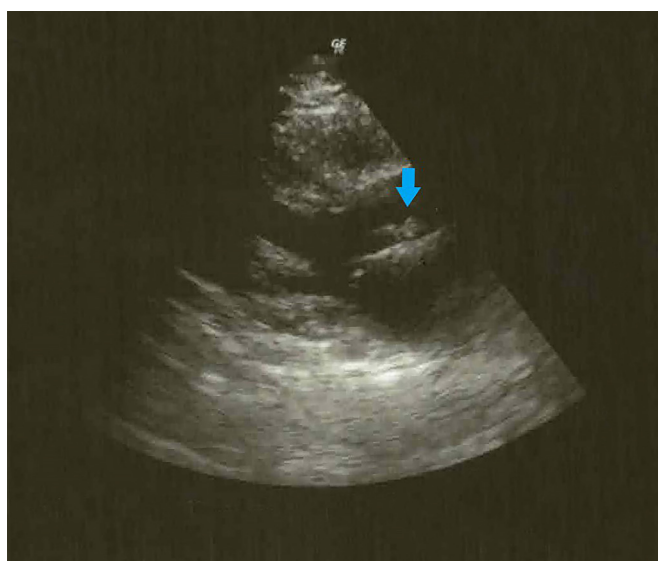
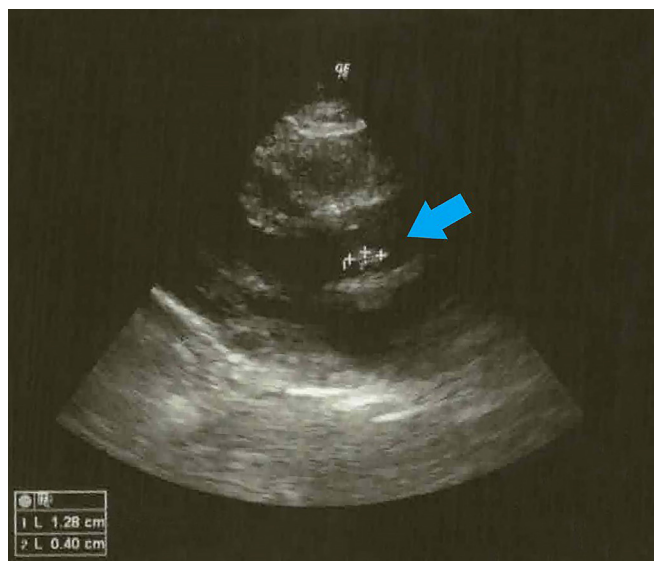


Figure 2. Transthoracic echocardiography visualising the dimensions of the lesion connected with aortic valve. Modified parasternal long-axis view.



Discussion

Infective endocarditis is a diagnostic challenge due to the numerous possibilities of clinical manifestation and the serious consequences of late diagnosis. The course may differ depending on the etiology and the presence of risk factors [9]. It is also quite rare disease so definitive studies of IE have been limited [10]. Because of a non-specific character of inflammatory parameters such as CRP and PCT they cannot be used as a basis for the diagnosis of infective endocarditis. It is recommended to use the algorithm according to the modified Duke criteria in which the result of transthoracic and transesophageal echocardiography, positive blood culture results, and the presence of clinical symptoms are crucial for the diagnosis [11]. In the discussed case numerous comorbidities including type 2 diabetes and end-stage renal disease treated with peritoneal dialysis program made the diagnosis of IE difficult and challenging. It was very important to find the solution quickly because infection is a significant cause of morbidity in patients with end-stage renal disease undergoing maintenance dialysis [12]. One of the most common localization of infection in this group of patients is peritonitis. New onset of abdominal pain, fever, or the appearance of cloudy peritoneal effluent need immediate response [13]. However also the incidence of IE is higher in dialysis patients compared to the general population [14]. The frequency of IE in patients treated with hemodialysis compared with those receiving peritoneal dialysis differ widely, but in both groups it is raised [15]. The difficulty in the case of described patient was that he did not present typical symptoms as well as examinations were incoherent. Fever, weakness, osteomuscular pains occur in almost every cold and lots of different infections. Thereupon sometimes they do not seem to be serious. Doctor's problem is to distinguish when fast diagnostic is needed. Based on this case we can also draw a conclusion that staying broadminded and searching for new, non-obvious solutions is very important.

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