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## Tricuspid valve enterococcal endocarditis in the frail older woman — diagnostic and therapeutic difficulties — case study

### Trudności diagnostyczne i terapeutyczne w enterokokowym zapaleniu wsierdza na zastawce trójdzielnej u starszej pacjentki — opis przypadku

#### Abstract

Infective endocarditis continues to be a medical problem despite significant strides in diagnosis and treatment. In recent years, the epidemiological profile of the disease has changed — formerly, it mostly occurred in young people with rheumatic heart disease and is now found more frequently in elderly patients, frequently undergoing medical procedures, with a valve prosthesis or artificial pacemaker. We present a difficult case of enterococcus endocarditis of the tricuspid valve in a frail 76-year-old patient, successfully treated with linezolid and gentamicin and subsequent valve replacement.

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**key words:** infective endocarditis; *Enterococcus faecium*; tricuspid valve; diagnostic and therapeutic difficulties in old age

#### Introduction

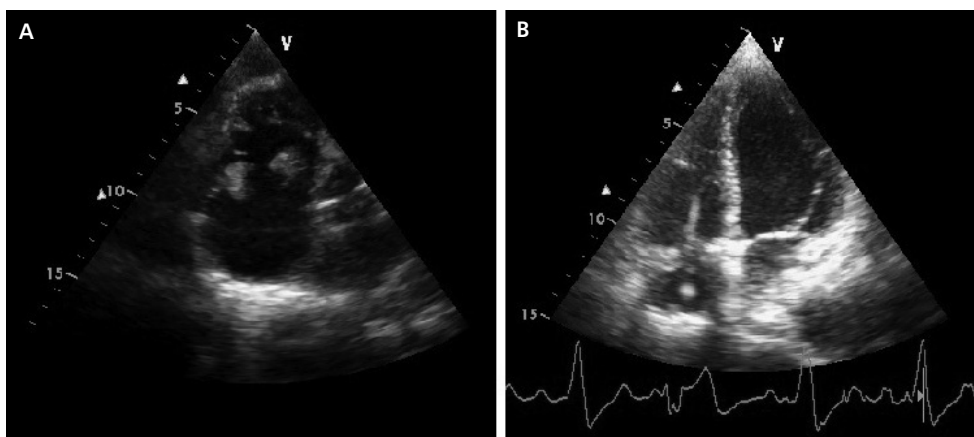
The annual incidence of infective endocarditis (IE) has not decreased over the last 30 years and ranges from 3 to 10 per 100 thousand people with the peak incidence rate of 14.5 per 100 thousand in people aged 70–80 [1–5]. This is caused by frequent invasive procedures, including cardiac surgery (pacemakers, cardioverters-defibrillators), central insertions, and dialysis shunts. Hence, the etiological profile of the

disease has changed — *Staphylococcus aureus* has become the most common pathogenic factor, moving streptococci into the second place [6]. Some studies show a higher occurrence rate in the elderly of IE caused by *Enterococcus spp.* and *Streptococcus bovis*, which have been associated with diseases of the large intestine. More frequent occurrences of IE pathogens of hospital origin and opportunistic pathogens from the urinary tract and digestive system have been noted [7–9]. We present an example of the latter as a difficult case to diagnose and treat.

#### Case report

A 76-year-old woman was admitted to the Department of Geriatrics because of weakness, weight

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**Figure 1.** A. Transthoracic echocardiography — large vegetations (20 × 25 mm) on tricuspid valve; B. transthoracic echocardiography 3 months after treatment — tricuspid bioprosthesis and electrodes of pacemaker

Rycina 1. A. Echokardiografia przezklatkowa — duże wegetacje (20 × 25 mm) na zastawce trójdzielnej; B. echokardiografia przezklatkowa 3 miesiące po zakończeniu terapii — biologiczna proteza zastawki trójdzielnej i elektrody stymulatora serca

loss, and recurring septic fivers occurring for about 8 months. During this time, she was given antibiotics for recurrent pneumonia and was diagnosed with liver neoplasm (the computed tomography (CT) of the abdominal cavity was inconclusive with possible inflammatory changes). She underwent an endoscopic examination a year earlier due to bleeding of the lower part of the digestive tract. In the past medical history she reported pulmonary tuberculosis, hepatitis B, chronic obstructive pulmonary disease (COPD), chronic colitis, renal stones, and cholecystectomy.

On admission to the Department, the patient was emaciated [body mass index (BMI) — 15.8], had severe dyspnoea, a fever (38.4°C), and features of right ventricular failure. She scored 75 points on the Barthel scale. Laboratory test results — C-reactive protein (CRP) — 33.4 mg/l, anaemia with low iron-binding capacity: haemoglobin (Hb) — 10.7g/dl (107 g/l), plasma iron (Fe) — 9 ug/dl (1,61 umol/l), total iron binding capacity (TIBC) — 237 ug/dl (42,4 umol/l), hypoalbuminemia (31 g/l). Imaging examinations revealed small amount of fluid in the right pleural cavity and hypodense foci in the liver and spleen. Empirical antibiotic treatment was begun using ciprofloxacin 2 × 100 mg by i.v., and normal body temperature was attained. On the 7th day of hospitalization, a deterioration in the general condition was observed, with a fever recurrence and an increase in the inflammatory parameters, symptoms of amnesia, a significant stasis in the airways, as well as hypotonia and an increasing swelling of the lower limbs (without increase in the myocardial necrosis markers, without focal lesions in the CT of the central nervous system). Antibiotic treatment was modified — ceftriaxone (1 × 1.0 g i.v.) was started. An echocardiogram re-

vealed the presence of vegetation on the tricuspid valve cusps (20 × 25 mm) (Fig. 1A). Despite the maintained empirical ceftriaxone therapy, the patient's condition remained critical. The *Enterococcus faecium* grown from the hemocultures was sensitive to gentamicin, vancomycin, linezolid, and was resistant to ampicillin and streptomycin. In accordance with the antibiogram, associated therapy with vancomycin (3 × 500 mg i.v.) and gentamicin (2 × 40 mg i.v.) was begun, as well as antifungal prophylaxis (fluconazole 1 × 100 mg i.v.). An improvement in the clinical condition and a reduction of CRP to 5.7 mg/l were observed. On the 12th day of antibiotic treatment, there once again was an increase in body temperature to 38.5 degrees Celsius and the inflammatory parameters (CRP — 96 mg/l). Hemocultures were collected — sterile. The control imaging examinations (chest x-ray, abdominal ultrasonography, heart echography) did not reveal new changes. After microbiological consultation, linezolid was administered this time (2 × 600 mg i.v.), in combination with gentamicin (1 × 60 mg i.v. — due to the creatinine clearance 40 ml/min), and in order to prevent superinfection piperacillin-tazobactam (2 × 4,5 g i.v.) was added and fluconazole was maintained. An improvement in the patient's condition was achieved. However, a check-up echocardiography showed no reduction in the vegetation size. After normalization of the inflammatory parameters, the patient was sent to the Cardiosurgery Clinic for surgical treatment. At the time, the patient weighed 36 kg (BMI — 14.1) in spite of oral nutritional intervention and partially parenteral (3.5% amino acid solution with electrolytes and glucose) — the patient did not consent to enteric nutritional treatment.

Despite a high operational risk, on the 15th day of antibiotic treatment, the implantation of biological tricuspid valve prosthesis was performed. Cultures from the patient's tricuspid valve were sterile. The post-operative course was complicated by a complete atrio-ventricular block. The patient was transferred to the Department of Cardiology, where a DDD type cardiac pacemaker was implanted. Linezolid antibiotic treatment was continued for 15 days and gentamicin for 11 days after surgery (then changed to amikacin, because of positive urine cultures — in accordance with the antibiogram), as well as piperacillin-tazobactam up to 27 days after surgery, and also an antidepressant treatment (sertraline) was implemented. Control hemocultures did not show any bacterial growth. The patient was discharged home in an improving state. During a control visit in the Geriatric Out-Patients Clinic 2 months after hospitalization, the patient was in general good condition, with normal verbal contact, 100 points on the Barthel scale, BMI — 19.2. In laboratory tests: CRP — 1.4 mg/l, Hb — 13g/dl (130 g/l), Fe — 83 ug/dl (14,9 umol/l), creatinine — 0.81 mg/dl (71,6 umol/l). In the electrocardiogram sinus rhythm 80/min and effective stimulation of VDD were observed. The echocardiography showed biological tricuspid valve prosthesis, with no features of pulmonary hypertension, ejection fraction (EF) — 60% (Fig. 1b). Drugs taken systematically by the patient: metoprolol (2 × 50 mg), simvastatin, acenocoumarol, salmeterol (2 × 25 ug), budesonide (2 × 250 ug), mianserin (1 × 15 mg), sertraline (1 × 50 mg) (pantoprazole 1 × 20 mg). However, the sinus tachycardia 92–96/min persisted, despite the use of a beta-blocker. Increasing the dose was difficult because of the tendency of hypotonia — a short-acting beta-blocker was replaced by a long-acting type of drug with relatively good tolerance by the patient.

### Discussion

The seizure of the right heart constitutes approximately 10% of all IE cases [2] and occurs primarily in intravenous drug users, but also in patients with central insertions, implanted pacemakers, cardioverters-defibrillators, and those undergoing dialysis. Our patient lacked the above mentioned risk factors in the history; however, she was hospitalized 1.5 years earlier and underwent diagnostic gastrointestinal endoscopy, which we consider a potential source of the opportunistic infection.

Inadequate IE symptomatology at an older age generally leads to delays in diagnosis. The IE symptoms are non-specific and are often attributed to other

diseases. At the forefront is weakness, sitophobia, anemia, weight loss, mental disorders. Fever may not occur. A murmur audible above the heart is associated with valve degeneration, frequently in elderly persons. Moreover, about 1/3 of patients with tricuspid valve seizure may not show audible changes above the heart — as it occurred in the described case. Some patients manifest aggravation of a congestive heart failure. Incidents of embolia and vascular symptoms are slightly less common in the elderly, mainly due to the smaller bacterial vegetation size and a reduced inflammatory response of the acute phase [8]. IE of the right heart — as in the presented patient — is dominated by symptoms of recurrent pneumonia, pleural effusion, and pulmonary embolisms. The empirical antibiotic treatment introduced for this reason was the cause of sterile hemocultures and rendered the diagnosis difficult. There were also difficulties in the correct interpretation of the echocardiography examination. The degenerative changes of heart valves, valve prostheses, and intracardiac devices reduce the sensitivity of the examination in detecting changes typical for endocarditis. However, similarly as in younger people, diagnosis is made based on modified Duke criteria [10].

Enterococci are responsible for approximately 6–10% of IE cases [7]. The main pathogens are *E. faecalis* (90%), *E. faecium*, *E. durans*, and recently reported cases are also caused by *E. raffinosus*. A more frequent occurrence of enterococci is observed in the elderly, at the same time a greater relationship with the source of infection from the gastrointestinal tract or urinary tract has been proved [7–9].

In clinical practice, two main problems associated with this IE etiology should be taken into account. Firstly, both beta-lactams and vancomycin are only bacteriostatic against enterococci. Their administration along with aminoglycosides ensures their bactericidal activity, but it requires prolonged combined treatment (up to 6 weeks). Experimental studies have shown that aminoglycoside should be administered in 2–3 divided doses in order to ensure therapeutic drug concentration in the blood [11]. In the elderly, the possibility of long-term antibiotic treatment is often limited due to impairment of kidney function and the side effects of the drugs. Secondly, enterococci may be resistant to many drugs, including aminoglycosides, beta-lactams and vancomycin. In the case of poly-resistant strains, treatment with new antibiotics, such as quinopristina/dalfopristina or linezolid, is attempted. Linezolid is a representative of oxazolidinones and is bacteriostatic against vancomycin-resistant Gram-

-positive strains. Its effectiveness has been evaluated in few studies, but there have been recorded cases of successful treatment of *enterococcus endocarditis* [12, 13]. Unfortunately, recently, there have been isolated cases of *E. faecium* resistance to linezolid [14].

Surgical treatment of IE is applied less frequently in elderly persons, mainly because of the higher risk of perioperative complications and more frequent coexisting diseases [8, 15]. Thus, this contributes to a worse prognosis compared with younger patients [9]. However, the indications for surgical treatment are the same for each age group. IE of the right heart should be considered in the case of right ventricular failure resistant to diuretic treatment, ineffective antibiotic treatment (positive hemoculture sustained > 7 despite adequate treatment), or *a priori* pathogens resistant to conservative treatment (e.g. fungi), as well as large

(> 20 mm) vegetation on the tricuspid valve with accompanying embolism [15, 16].

### Conclusions

Infective endocarditis in elderly persons is connected with a worse prognosis and more frequent complications. Little and non-specific symptomatology leads to delays in diagnosis, and higher perioperative risk and numerous coexisting diseases cause that the decision for operative treatment is made less often. The possibility of IE should always be considered in the case of a persistent fever of unclear origin or unintentional weight loss in elderly persons, including after endoscopic examinations.

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### Streszczenie

*Infekcyjne zapalenie wsierdza wciąż stanowi problem medyczny, mimo znacznego postępu w jego diagnostyce i leczeniu. W ostatnich latach zmienił się profil epidemiologiczny choroby — kiedyś, występująca głównie u osób młodych, z chorobą reumatyczną serca, obecnie coraz częściej jest spotykana u chorych w starszym wieku, poddawanych często procedurom medycznym, z protezą zastawkową czy stymulatorem serca. W niniejszej pracy przedstawiono trudny przypadek enterokokowego zapalenia wsierdza na zastawce trójdzielnej u 76-letniej pacjentki, leczonego skutecznie linezolidem z gentamycyną, z następczą wymianą zastawki.*

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**słowa kluczowe: infekcyjne zapalenie wsierdza; Enterococcus faecium; zastawka trójdzielna; trudności diagnostyczne i terapeutyczne w starości**

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