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Treatment of Late Infective Prosthetic Endocarditis Complicated by Cerebral Infarction with Vegetations: Pharmacotherapeutic Approach (Case Report)

Abstract. Prosthetic endocarditis is a serious complication in a long term. Vegetation as a thromboembolic complication leads to neurologic deficit varying in severity.

Case description. A 35-year-old female patient F. underwent surgical treatment at the Department of Surgical Treatment of Acquired Heart Diseases of the National Amosov Institute of Cardiovascular Surgery on September 07, 2016: aortic valve replacement with wrapping tape operation II. The patient was discharged from the hospital on the 9th day after surgery in a satisfactory condition.

On November 20, 2019, the patient was admitted to the Institute with the diagnosis of late infective prosthetic aortic valve endocarditis, status post aortic valve replacement and wrapping tape operation in 2016, first-degree atrioventricular block, cerebral infarctions in multiple locations with hemorrhagic transformation, with aphasia elements, ataxia, right-sided pyramidal insufficiency and suspected meningitis. After 21 days of drug therapy, the patient responded to treatment successfully and was discharged from the hospital in a satisfactory condition without surgical treatment.

Conclusions. Taking into consideration the serious condition of the patient, timely and carefully selected drug therapy can be the correct solution for the treatment of patients with late infective endocarditis. Thus, surgery is not always the treatment of choice.

Keywords: *secondary infective endocarditis of a prosthetic aortic valve, successful drug therapy, neurologic deficit, long-term complications, condition after prosthetic aortic valve, progressive neurologic failure, medical treatment of prosthetic aortic valve endocarditis.*

Introduction. Late infective endocarditis is associated with high mortality and frequent development of serious complications, despite the progress in its diagnosis and treatment.

Clinical case. On September 05, 2016, a 35-year-old female patient F. was admitted to the Department of Surgical Treatment of Acquired Heart Diseases of the National Amosov Institute of Cardiovascular Surgery with a diagnosis of congenital heart disease, bicuspid valve, stage 4 aortic stenosis with calcinosis score 3+, mitralization, post-stenotic distensibility of ascending aorta, type IIA heart insufficiency.

The surgery was performed on September 07, 2016: aortic valve replacement with wrapping tape operation II. The patient was discharged from the hospital on the 9th day after surgery in a satisfactory condition.

At the age of 38, the patient F. with suspected meningitis underwent inpatient treatment at the Sumy Regional Infectious Diseases Clinical Hospital, where she stayed from November 10, 2019 until November 14, 2019. After additional examination, she was transferred to the neurological department, where the state of health deteriorated in the course of antibiotic treatment. Additional examinations helped to establish a diagnosis: late active infective prosthetic aortic valve endocarditis, first-degree atrioventricular block, cerebral infarctions in multiple locations with hemorrhagic transformation with sensor aphasia elements, ataxia and right-sided pyramidal insufficiency.

The patient was transferred for further treatment to the Department of Surgical Treatment of Acquired Heart Diseases of the National Amosov Institute of Cardiovascular Surgery.

The patient was admitted to the National Amosov Institute of Cardiovascular Surgery on November 20, 2019 with the diagnosis: status post aortic valve replacement and ascending aorta wrapping tape operation in 2016, late infective prosthetic aortic valve endocarditis with the complaints about sudden fever up to 40 °C (November 10, 2019), limited physical activity, weakness and temporal orientation disorder. Chest X-ray did not show any abnormalities (Fig. 1).

Echocardiography performed on November 20, 2019 revealed sinus rhythm with a heart rate of 96 per minute, first-degree atrioventricular block and myocardial hypoxia of left ventricular anterior wall.

There were additional thread-like formations with a length of 0.9 to 1.5 cm on aortic valve prosthesis from the left ventricle side, which correspond to vegetations (Fig. 2, Table 1). There was a threat of fragment detachment. Aortic valve prosthetic cusps movement was not disturbed.

Lumbar puncture was performed on November 10, 2019, and *S. aureus* pathogen was revealed. Susceptibility to various antibiotics is outlined in Table 2.



Fig. 1. Chest X-ray

Head magnetic resonance imaging (MRI) dated April 25, 2019 showed most certain MR picture of circulation disturbance in the left middle cerebral artery system and front bottom cerebellar artery which resulted into gliosis area and cystic lesions, cyst of the left maxillary sinus.

Head MRI dated November 13, 2019: multiple cerebral infarctions in right and left middle cerebral artery system, vertebrobasilar system with hemorrhagic permeation ("cardioembolic shower"). Residual effects of cerebral in-



Fig. 2. Aortic valve prosthesis echocardiography with the signs of endocarditis. The arrow shows vegetations on the cusps of prostheses

Table 1

Echocardiographic parameters

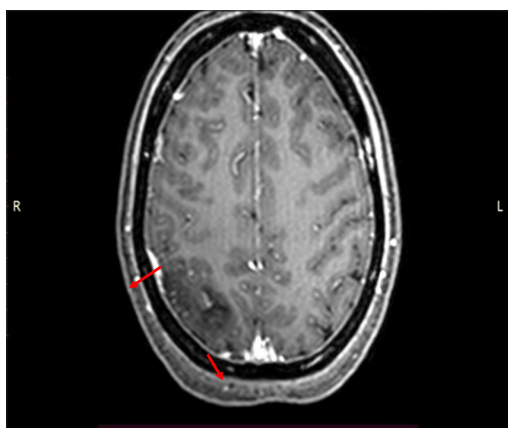
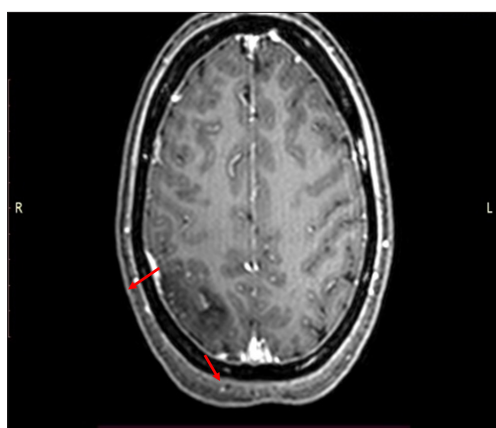
Parameters (units)	Values
Body surface area (m ²)	2.0
LV EDV/S (ml/m ²)	63.0
LV EDV (ml)	126.0
LV SV/S (ml/m ²)	38.5
LV SV (ml)	77.0
LVEF	0.6
Diameter of left atrium (cm)	2.8
Pulmonary artery systolic pressure (mm Hg)	30
Mitral valve	Insignificant regurgitation
Tricuspid valve	Insignificant regurgitation
Aortic valve prosthesis	Δ aortic valve = 33 mm Hg

LV EDV/S, left ventricular end-diastolic volume index; LV EDV, left ventricular end-diastolic volume; LV SV/S, left ventricular stroke volume index; LV SV, left ventricular stroke volume; LVEF, left ventricular ejection fraction.

Table 2*Antimicrobial susceptibility*

Antibiotics	Sensitivity
Vancomycin	+
Oxacillin	+
Amoxicillin	-
Ceftriaxone	+
Cefatoxime	+
Cefuroxime	+
Meropenem	+
Amikacin	+
Levofloxacin	+
Sulbactamax	+

farction in vertebrobasilar system with the damage of the cerebellum right hemisphere. Neurovasculitis complicated by cerebral infarctions cannot be excluded (Fig. 3, 4, 5). No signs of formed cerebrum abscess and pachymeninx reactions were observed during examination.

**Fig. 3.** Cerebral embolism due to vegetations**Fig. 4.** Cerebrum structures embolism due to vegetations

Head MRI dated November 27, 2019: MR lesions in the brain should be differentiated between encephalitis and abscess, which are formed in the left and right cerebrum hemispheres in the presence of cerebral blood supply disorder by ischemic type in subacute phase (Fig. 6).

Laboratory examination results on admission on November 21, 2019 are shown in Table 3.

Other examination results were within normal levels.

The opinion of infectious disease specialist, candidate of medical sciences from L.V. Gromashevsky Institute of Epidemiology and Infectious Diseases of the National Academy of Medical Sciences of Ukraine, provided on November 21, 2019 at 15:30: "Taking into consideration multiple lesions in the cerebrum, surgery bears extremely high risk".

During the discussion of the case at scientific board on November 22, 2019, it was decided to postpone the surgery.

Starting from November 20, 2019, drug therapy was prescribed to the patient: Warfarin 5 mg once a day, Rifampicin 0.3 g twice a day, Vancomycin 1 g twice a day, Fluconazole Teva, Nexium 40 mg once a day, Quamatel 20 mg twice a day, Ascorutin 1 tablet three times daily.

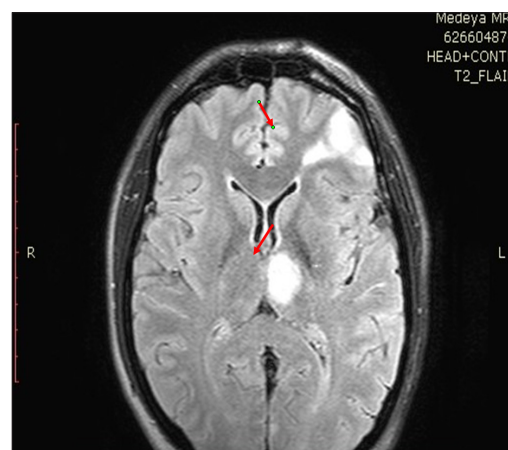
After three weeks of drug therapy, the patient felt significant gain in health.

According to the data of transesophageal echocardiography dated December 18, 2019, no moving vegetation was observed on aortic valve prosthesis and mitral valve structures (Fig. 7).

No pathologic changes in aortic valve prosthesis were observed according to the chest computed tomography (Fig. 8).

At the time of hospital discharge, the improvement of laboratory examination results was observed (Table 4).

The patient F. was discharged from the hospital in a satisfactory condition on December 21, 2019 (after 21 days of

**Fig. 5.** Cerebrum structures embolism due to vegetations

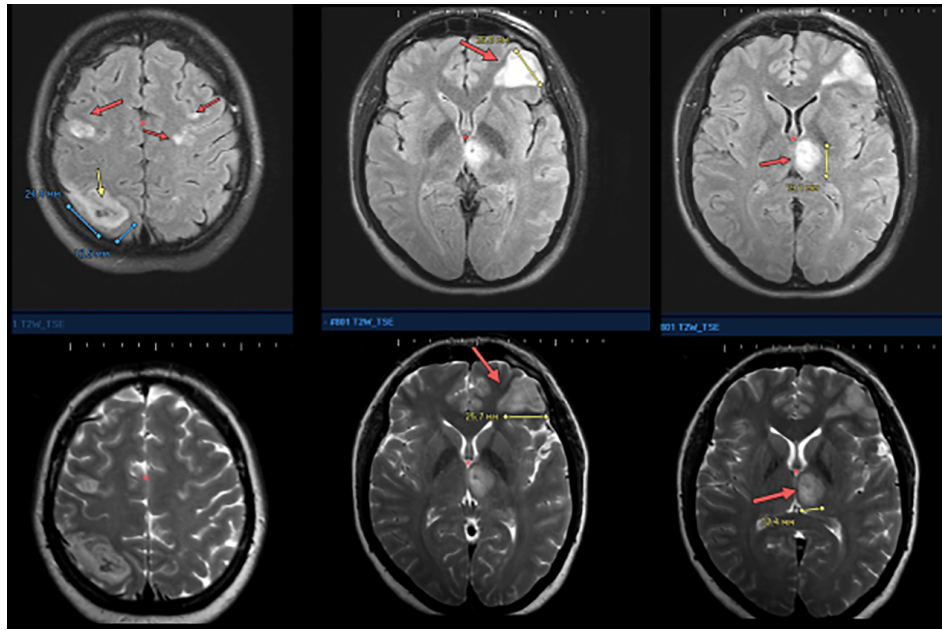


Fig. 6. Cerebrum structures embolism due to vegetations in T2 FLAIR and T2WI modes: multiple hyperintense subcortical lesions in both cerebral hemispheres, in left frontal cortex and left thalamus

Table 3

Laboratory examination findings

Parameters	Values
WBC	12.8 x 10 ⁹ /l
ESR	43 mm/h
EIA Procalcitonin	0.24 ng/ml
C-reactive protein	60.13 mg/l
Blood sterility	Blood is sterile

WBC, white blood cells; ESR, erythrocyte sedimentation rate; EIA procalcitonin, enzyme immunoassay procalcitonin.

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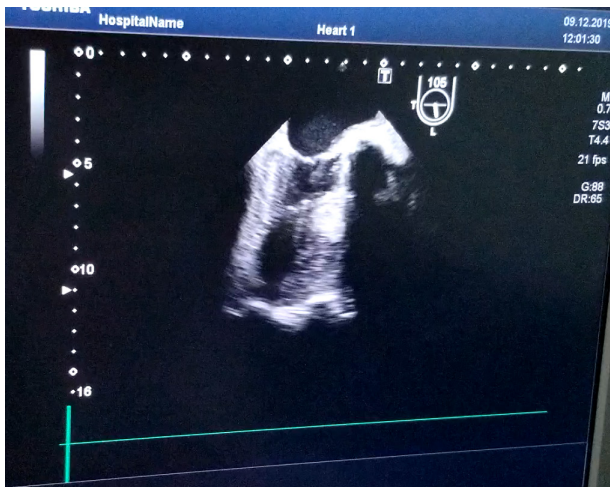


Fig. 7. Transesophageal echocardiography

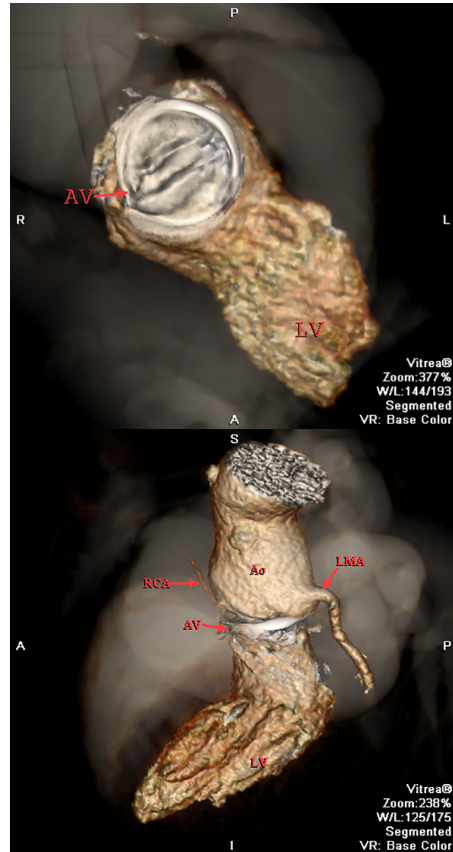


Fig. 8. Chest computed tomography scan. A. Absence of vegetations at the leaflets of prostheses. B. Absence of vegetations at the ascending aorta and the basement of aorta

Table 4

Comparison of laboratory examination findings on admission and at discharge

Parameters	Values	
	On admission	At discharge
WBC	12.8 x 10 ⁹ /l	10.8 x 10 ⁹ /l
ESR	43 mm/h	18 mm/h
EIA Procalcitonin	0.24 ng/ml	0.01 ng/ml
C-reactive protein	60.13 mg/l	20.56 mg/l
Blood sterility	Sterile	Sterile

treatment) in order to continue the treatment in the cardiologic hospital in her residence area.

After 6 months, the patient arrived for scheduled follow-up visit. Echocardiography and laboratory examination did not show any abnormalities. Only moderate neurologic symptoms were present (concentration and memory disorders).

Discussion. Prosthetic aortic valve endocarditis is a serious complication in the late period [1,2,3,4,5,6]. Vegetation appearance on the aortic mechanical prosthesis often causes embolization, especially in the brain, which limits the possibilities of the surgical treatment [5,6,7].

The patient sought for specialized medical help relatively late, which caused significant neurologic complications. Blood cultures were negative and didn't allow to identify flora on the prosthesis.

Random right choice of adequate antibacterial therapy allowed to eliminate the causative pathogen within almost a month and within further 2 months allowed to secure positive clinical result. Obligatory fungicide therapy was an important element of treatment.

Conclusions. Surgery is not always the only solution in the treatment of prosthetic aortic valve endocarditis, especially in the presence of concurrent serious neurologic deficit of cerebral structures, making cardiopulmonary bypass impossible. Long-term properly chosen antibacterial therapy combined with fungicide therapy provided reasonable positive results. Concurrent vegetation in the brain made the recovery more complicated, leaving irreversible moderate neurologic symptoms (concentration and memory disorder), but neurologic status gave positive effect in general and significantly improved within six months after treatment. The experience of our Institute showed a correct strategic solution in this very complicated and rare clinical case.

Early diagnosis of pathogen (including preventive echocardiography after any body temperature increase lasting for several days) and immediate dedicated medical

care are very important. Conservative therapy, which can be effective in prosthetic endocarditis, can be considered as an alternative to surgery in the absence of gross morphological changes in the aortic root and the preserved function of the prosthesis.

Patient consent. Obtained.

Conflict of interest. The authors have no conflicts of interest to declare.

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Лікування пізнього інфекційного протезного ендокардиту, ускладненого інфарктом мозку з вегетаціями: яка медикаментозна тактика?

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Резюме. Протезний ендокардит є проблемним ускладненням у довгостроковій перспективі. Вегетація, як тромбоемболічне ускладнення, призводить до різного ступеня неврологічного дефіциту.

Опис випадку. Хвора Ф., 35 років, госпіталізована 05.09.2016 р. у відділення хірургії набутих вад серця НІССХ ім. М. М. Амосова з діагнозом: двостулковий клапан, стеноз аорти 4-го ступеня з кальцинозом 3+, мітралізація, постстенотичне розширення висхідної аорти, серцева недостатність ІІА типу. Операція проведена 07.09.2016 р.: протезування аортального клапана за методикою тасьмового огортання висхідної аорти (модифікація ІІ). Хвору виписано зі стаціонару на 9-у добу після операції в задовільному стані. Пацієнтка Ф. була повторно госпіталізована в НІССХ ім. М. М. Амосова з діагнозом: пізній інфекційний ендокардит протезованого аортального клапана 20.11.2019 р. Стан після протезування аортального клапана та тасьмового огортання висхідної аорти в 2016 р., атріовентрикулярна блокада 1-го ступеня, інфаркти мозку множинної локалізації, з геморагічним перетворенням, елементами афазії, атаксією, правобічною пірамідною недостатністю та підозрою на менінгіт. Після тривалої терапії хвора успішно відповіла на лікування і була виписана зі стаціонару в задовільному стані без оперативного лікування. Через 6 місяців прийшла на перевірку. Ефект позитивний.

Висновки. Враховуючи тяжкий неврологічний стан хворої, своєчасне та правильне медикаментозне лікування може бути правильним рішенням для лікування хворих з пізнім інфекційним ендокардитом. Таким чином, повторна операція не завжди є вибором лікування. Консервативна терапія, яка може виявитися ефективною при протезному ендокардиті, розглядається як альтернатива хірургії за відсутності грубих морфологічних змін у корені аорти і за збереженої функції протеза.

Ключові слова: вторинний інфекційний ендокардит протезованого аортального клапана, успішне медикаментозне лікування, неврологічний дефіцит, ускладнення віддаленого періоду, стан після протезування аортального клапана, прогресуюча неврологічна недостатність, медикаментозне лікування протезного ендокардиту аортального клапана.

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