

Cardioembolic Stroke at Prosthetic Valve Endocarditis _____

Eneida HOXHA, MD _____

DEPARTMENT OF INTERNAL MEDICINE,
UNIVERSITY HOSPITAL CENTER MOTHER TERESA, TIRANA, ALBANIA
CORRESPONDING AUTHOR
E-MAIL: ENEIDA_HOXHA@YAHOO.COM

Somida KUKA, MD _____

DEPARTMENT OF INTERNAL MEDICINE,
UNIVERSITY HOSPITAL CENTER MOTHER TERESA, TIRANA, ALBANIA

Ledio COLLAKU, MD, Dr. Sc. _____

DEPARTMENT OF INTERNAL MEDICINE,
UNIVERSITY HOSPITAL CENTER MOTHER TERESA, TIRANA, ALBANIA

Elvana RISTA, MD, Dr. Sc. _____

HYGEIA HOSPITAL, TIRANA, ALBANIA

Jorida DJAMANDI, MD _____

HYGEIA HOSPITAL, TIRANA, ALBANIA

Jona MUSABELLIU, MD _____

DEPARTMENT OF INTERNAL MEDICINE,
UNIVERSITY HOSPITAL CENTER MOTHER TERESA, TIRANA, ALBANIA

Margarita GJATA, MD, Prof. Dr. _____

HYGEIA HOSPITAL, TIRANA, ALBANIA

Abstract¹

Background: Embolic events are frequent and life-threatening complications of infective endocarditis (IE), related to the migration of cardiac vegetations. The risk of embolism is very high in IE, with embolic events occurring in 20-50% of patients. The brain and spleen are the most common sites of embolism in left-sided IE. Stroke is a severe complication and is associated with increased morbidity and mortality rates.

Case presentation: A 73-year-old male presented to the Emergency Department, in May 2022 with right hemiparesis, aphasia and fever (38 °C). He reported a history of recurrent fever lasting two days. His pre-existing comorbidities included Diabetes Mellitus, Arterial Hypertension and Atrial Fibrillation on anticoagulation therapy with Acenocoumarole and INR levels within normal range. His past medical history was significant for an Aortic Valve Replacement, in September 2021 and a subsequent hospitalization in January 2022 with Prosthetic Valve Endocarditis. At the time, he presented with recurrent fever up to 38.8 °C, no significant findings in the transthoracic echocardiogram (TTE) and positive blood cultures for Enterococcus faecalis. It was started an antibiotic therapy. Laboratory and imaging studies in his latest admission revealed a cardioembolic stroke.

Conclusion: Infective endocarditis can present with a wide variety of symptoms and early diagnosis can be challenging. Establishing the diagnosis early in the course of the disease would enable a prompt implementation of empiric antibiotic therapy, potentially preventing serious complications. Keeping a high index of suspicion when evaluating patients at high risk for IE, might lead to more favorable outcomes of major complications associated with it.

Keywords: *Biological prosthetic aortal valve, bacterial endocarditis, stroke.*

Background

Endocarditis may be classified as native valve endocarditis, endocarditis in intravenous drug addicts and prosthetic valve endocarditis. The most severe form of Infective Endocarditis (IE) is Prosthetic Valve Endocarditis (PVE), which occurs in 1–6% of patients with valve prostheses.¹ 10–30% of IE cases belong to PVE and it is divided equally between mechanical and bioprosthetic valves. PVE is today still a challenge for internals with difficulties in diagnosis, therapeutic strategy and poor prognosis.

¹ This abstract is published from the authors in Cardiovascular Research, Volume 118, Issue Supplement_2, October 2022, cvac157.032.

The diagnosis of prosthetic valve Endocarditis is more difficult than in NVE (Native valve endocarditis). The base of diagnosis is echocardiography and blood cultures. Based on studies, it is frequent in a PVE to be found negative blood cultures and no significant echocardiographic findings.⁴

PVE needs immediate and aggressive treatment, especially antibiotic therapy, and reintervention when it is considered and valued with imaging.

Case presentation

A 73-year-old male presented to the Emergency Department, in May 2022 with right hemiparesis, aphasia and fever (38 °C). He reported a history of recurrent fever lasting two days.

Medical history

Regarding the medical anamnesis we note that the patient had Diabetes Mellitus, Arterial Hypertension, Atrial Fibrillation on anticoagulation therapy with acenocoumarole and INR levels within the therapeutic ranges. In September 2021 the bioprosthetic aortic valve was replaced. The patient suffered biological prosthetic Valve Endocarditis in January 2022, followed with readmission in the hospital. At that time, he was presented with recurrent fever up to 38.8 °C, shivers, sweating, dyspnea, cough. There were positive blood cultures for *Enterococcus faecalis* but no significant findings in the transthoracic echocardiogram (TTE) and transesophageal echocardiogram (TEE). It was started an antibiotic therapy.

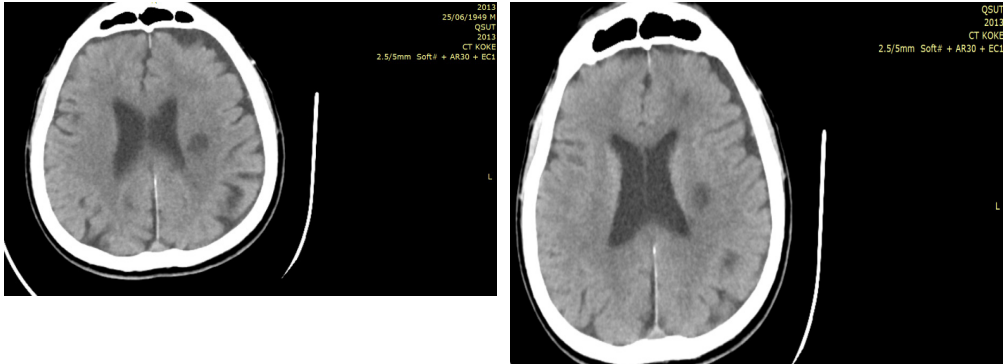
Family history: Arterial Hypertension and Diabetes Mellitus

Physical examination: Conscious. Pale. Pulmonary bilateral basal crepitations with RF 20/min and SpO₂ 91%. Tachycardic, arrhythmic with HR 121/min and BP 90/60 mmHg. No oedema.

Neurological examination: Alert, oriented. Normal communication. Preserved verbal fluency. Cranial nerves: Paralysis facial dexter. Reflexes: ROT 2+ Bilateral. No pyramidal signs. Normal sensitivity. No meningeal syndrome. Hemiparesis dexter with F/M 3/5. No extrapyramidal signs. Hemiparetic gait.

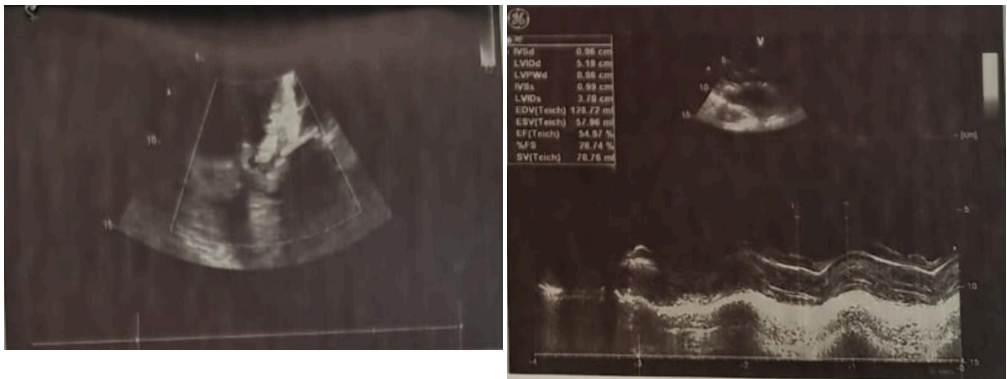
During hospitalization, the patient was examined with laboratory and imagery findings. The first imagery examinations of CT-Scan of head showed a subacute ischemic lesion in left basal ganglia (Fig. 1 &2).

FIG. 1&2 Non contrast computed tomography showed subacute ischemic lesion in left basal ganglia



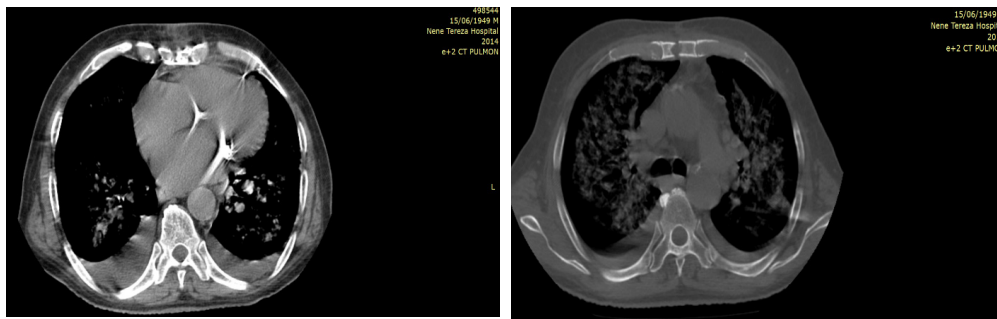
Based on his medical history (Bioprosthetic Aortic Valve Replacement, in September 2021), a subsequent transthoracic echocardiogram was accomplished. In transthoracic echocardiogram (TTE) resulted Aortal biological protheses with Vmax 3.2 m/s and moderated paravalvular jet. This data were compared to both TTE and TEE, made in January 2022, when he was presented with recurrent fever up to 38.8 grade Celsius, shivers, sweating, dyspnea, cough. (In January 2022 TTE and TEE resulted negative, even though the positive blood cultures for *Enterococcus faecalis*). TTE resulted with no significant findings. The hemoculture resulted again positive with *Enterococcus faecalis* (Vancomycin sensible, HLGR, HLSR)

FIG. 3&4. Transthoracicechocardiogram (TTE) resulted Aortal biological protheses with Vmax 3.2 m/s and moderated paravalvular jet.



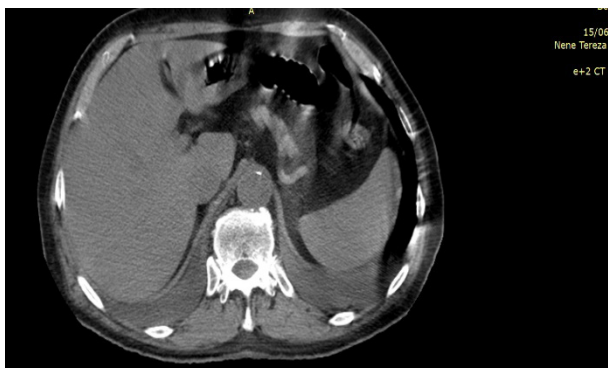
It was impossible for the patient, because of his medical condition, to be provided with TEE. He presented as cardiac decompensated too. This followed a Thorax-CT (Fig.5&6.), which showed cardiomegaly, bilaterally pleural effusion, and diffuse central bilateral ground glass opacifications.

FIG. 5&6 Non contrast computed tomography showed cardiomegaly, bilaterally pleural effusion and diffuse central bilateral ground glass opacifications



So the therapy with diuretics i.v. accompanied Vancomycin 1g i.v. bid. On the other side, the patient was under Acenocoumarole when he was admitted in hospital, which was substituted with Enoxaparin 0.6 ml SC. To exclude other focuses or ascites, was performed an Abdomen-CT in the same time as the Thorax one. Here resulted only Hepatomegaly.

FIG. 7. Non contrast computed tomography showed hepatomegaly



Other findings

The full Blood Count analysis showed: WBC 12100/mm³ (n.v 4000-10000), HGB 7.3 g/dl (n.v 11.0-16.5), RBC 2820000/mm³ (n.v 4.2-6.1 x 10⁶), HCT 23.1% (n.v 35.0-50.0), MCV 81.8 (n.v 80-97), MCH 25.7 (n.v 26.5-33.5), PLT 520x10³ (n.v 150-400); ESR 53 mm/h

Laboratory findings were as follows: prothrombin time (PT)— INR 4.63 (n.v. < 1.2), activated Partial Thromboplastin Time (aPTT) 15 (n.v. < 1.20), Alkaline Phosphatase 46 U/L (n.v. 40–150), Alanine aminotransferase ALT 6 U/L (n.v. 0–45), Aspartate aminotransferase AST 8 U/L (n.v. 0–35), GGT 18 U/L (n.v 12-

64), C-Reactive-Protein (CRP) 5.66 mg/L (<0.5), PCT 1.1 ng/ml (<0.1), Serum Urea 55.3 mg/dl (n.v 10-43), Creatinine 0.79 mg/dl (n.v 0.5-1.2), Total Protein 6.0 g/dl (5.8-7.6), Albumin 3.0 g/dl (3.2-4.6), Potassium 3.5 mmol/l (n.v 3.5-5.1), Sodium 135 mmol/l (n.v 136-146), Chlor 102 mmol/l (n.v 101-109), Glycemia 160 mg/dl (n.v 74-106), Bilirubin 1.13 mg/dl (n.v 0.5-1.2), TSH 0.76 mu/ml, HbA1C 6.5%, Ac.uric 6.3 mg/dl, Ferritin 42 ng/dl (22-234), CK 35 U/l (30-200), Ck-mb 1.0 ng/dl (<5.2), Troponin I <0.019 ng/dl (<0.034), NTproBNP 4779.8 pg/dl (<125), D-Dimer 2.9 ug/ml (<0.5)

Lipid profile: Cholesterol 112 mg/dl (n.v 140-220) and Trygliceride 145 mg/dl (n.v 50-150);

Urine analysis: Albumin 0.25 mg/dl; RBC 1-2/mm³ (0-5); WBC 1-2/mm³ (0-5);

Urine culture: Negative

Hemoculture: Positive *Enterococcus faecalis* (Vancomycin sensible, HLGR, HLSR)

Treatment

The anticoagulation therapy with Enoxaparin 0.6 ml SC was carried on and substituted Acenocoumarole (INR 4.63 when he was admitted in hospital). Secondly, he was treated with Furosemide 60 mg i.v./d, Spironolacton 25 mg/d, Nebivolol 5 mg/d p.os, Vancomycin 1g i.v. bid, Cerebrolysin 10 ml i.v. bid, Insulin Lantus 18 UI SC, Atorvastatin 20 mg/d p.os and Omeprazole 40 mg i.v./d. Anemia was detected as he was hospitalized with Hb 7.3 g/dl. That was followed by blood transfusion and after 2 packed red blood cells resulted Hb 9.1 g/dl, RBC 3530000/mm³ and HCT 28.5%.

Discussion and conclusions

This case is defined as early PVE (Based on ESC recommendations^{2,3}: An early prostatic valve endocarditis is considered every IE, that occurs within 1 year of surgery). There is also the term “late PVE”, which is defined as IE occurring beyond 1 year. The significance of this classification is the importance of microbiological profiles differences observed before and after this time point.

In this case, the patient was hospitalized initially in September 2021 (Implementation of Biological prosthetic Valve) and after 4 months, in January 2022, was rehospitalized initially with fever up to 38.8 °C, shivers, sweating and later with dyspnea and cough.

On the other side, the Duke criteria have been shown a lower sensitivity in the diagnosis of PVE. The early postoperative period and a persistent fever should be valued always carefully and the broad of examinations in this case can help us judge. The diagnosis of IE is based mainly on the results of echocardiography and blood cultures. Based on ESC recommendations⁴⁻⁹, the main causes of an early PVE are Staphylococci, Fungi and Gram-negative bacilli, especially Staphylococci and enterococci. The clinical conditions and positive blood cultures for *Enterococcus faecalis* made us think more as a suspect of IE. This followed immediately the treatment with antibiotics, in this case Vancomycin, based on Antibioqram.

The mortality rate in PVE is considered 20–40% because of its poor prognosis and late complications. There are several factors including older age, early PVE, heart failure, diabetes mellitus, stroke, healthcare-associated infections, staphylococcal or fungal infection etc.

There is also a high risk for complications, including embolic stroke, despite appropriate antimicrobial treatment. Based on studies, approximately 35% of patients with IE have symptomatic cerebrovascular complications and 80% of them have stroke evidence on imaging.

As a new Infective Endocarditis in a prosthetic valve should be followed by a new intervention. Based on studies, patients with IE are at risk for bleeding complications, particularly intracerebral hemorrhage. In these cases, intracerebral hemorrhage may result from hemorrhagic transformation of an embolic stroke, rupture of a mycotic aneurysm, or septic arteritis with hemorrhage from vessel wall erosions.

This followed a multidisciplinary consult, which based on clinical condition, laboratory findings, imaging, high risks of reintervention decided to postpone the surgery intervention until a new valuation after 4 weeks.

Infective endocarditis can present with a wide variety of symptoms and early diagnosis can be challenging. Establishing the diagnosis early in the course of the disease would enable a prompt implementation of empiric antibiotic therapy, potentially preventing serious complications. Keeping a high index of suspicion when evaluating patients at high risk for IE might lead to more favorable outcomes of major complications associated with it.

References

1. Vongpatanasin W, Hillis LD, Lange RA. Prosthetic heart valves. *N Engl J Med* 1996; 335:407–416
2. Horstkotte D, Follath F, Gutschik E, Lengyel M, Oto A, Pavie A, Soler-Soler J, Thiene G, von Graevenitz A, Priori SG, Garcia MA, Blanc JJ, Budaj A, Cowie M, Dean V, Deckers J, Fernandez BE, Lekakis J, Lindahl B, Mazzotta G, Morais J, Oto A, Smiseth OA, Lekakis J,

- Vahanian A, Delahaye F, Parkhomenko A, Filipatos G, Aldershvile J, Vardas P. Guidelines on prevention, diagnosis and treatment of infective endocarditis executive summary: the Task Force on Infective Endocarditis of the European Society of Cardiology. *Eur Heart J* 2004;25: 267–276.
3. Lopez J, Revilla A, Vilacosta I, Villacorta E, Gonzalez-Juanatey C, Gomez I, Rollan MJ, San Roman JA. Definition, clinical profile, microbiological spectrum, and prognostic factors of early-onset prosthetic valve endocarditis. *Eur Heart J* 2007;28:760–765.
 4. Wang A, Athan E, Pappas PA, Fowler VG Jr, Olaison L, Pare C, Almirante B, Munoz P, Rizzi M, Naber C, Logar M, Tattevin P, Iarussi DL, Selton-Suty C, Jones SB, Casabe J, Morris A, Corey GR, Cabell CH. Contemporary clinical profile and outcome of prosthetic valve endocarditis. *JAMA* 2007;297:1354–1361.
 5. Amat-Santos IJ, Messika-Zeitoun D, Eltchaninoff H, Kapadia S, Lerakis S, Cheema A, Gutierrez-Ibanes E, Munoz-Garcia A, Pan M, Webb JG, Herrmann H, Kodali S, Nombela-Franco L, Tamburino C, Jilaihawi H, Masson JB, Sandoli dB, Ferreira MC, Correa LV, Mangione JA, Jung B, Durand E, Vahanian A, Tuzcu M, Hayek SS, Angulo-Llanos R, Gomez-Doblas JJ, Castillo JC, Dvir D, Leon MB, Garcia E, Cobiella J, Vilacosta I, Barbanti M, Makkar R, Barbosa RH, Urena M, Dumont E, Pibarot P, Lopez J, San Roman A, Rodes-Cabau J. Infective endocarditis following transcatheter aortic valve implantation: results from a large multicenter registry. *Circulation* 2015;131:1566–1574.
 6. Pericas JM, Llopis J, Cervera C, Sacanella E, Falces C, Andrea R, Garcia de la Maria C, Ninot S, Vidal B, Almela M, Pare JC, Sabate M, Moreno A, Marco F, Mestres CA, Miro JM. Infective endocarditis in patients with an implanted transcatheter aortic valve: Clinical characteristics and outcome of a new entity. *J Infect* 2015;70:565–576
 7. Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service. *Am J Med* 1994;96:200–209.
 8. Lamas CC, Eykyn SJ. Suggested modifications to the Duke criteria for the clinical diagnosis of native valve and prosthetic valve endocarditis: analysis of 118 pathologically proven cases. *Clin Infect Dis* 1997;25:713–719.
 9. Perez-Vazquez A, Farinas MC, Garcia-Palomo JD, Bernal JM, Revuelta JM, Gonzalez-Macias J. Evaluation of the Duke criteria in 93 episodes of prosthetic valve endocarditis: could sensitivity be improved? *Arch Intern Med* 2000;160:1185–1191.