

## Searching for patent foramen ovale in a 44-year-old female patient after ischemic stroke – diagnostic problems



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### Abstract

Patent foramen ovale (PFO) is associated with the occurrence of cryptogenic strokes in young patients. Transesophageal echocardiography with contrast is the established standard in PFO diagnostics. We present the case of a 44-year-old female patient after ischemic stroke, in whom PFO was not detected by echocardiography; the defect was ultimately diagnosed by right heart catheterization.

**Key words:** patent foramen ovale, cryptogenic stroke.

### Streszczenie

Drożny otwór owalny (*patent foramen ovale* – PFO) wiąże się z występowaniem udarów kryptogennych u młodych pacjentów. Przezprzetykowe badanie echokardiograficzne z kontrastem jest uznanym standardem w diagnostyce PFO. Przedstawiamy przypadek 44-letniej pacjentki po przebytym udarze niedokrwiennym mózgu, u której nie wykryto PFO w badaniu echokardiograficznym, natomiast wadę stwierdzono podczas cewnikowania prawego serca.

**Słowa kluczowe:** drożny otwór owalny, kryptogeny udar mózgu.

### Introduction

Patent foramen ovale (PFO) is observed in 25% of the general population; 46% of cryptogenic ischemic strokes are associated with its presence [1, 2]. Diagnostic examinations focusing on PFO are recommended in all patients following a neurological incident before the age of 55. The standard examination performed to detect or exclude PFO is transesophageal echocardiography (TEE) using contrast and the Valsalva maneuver [3, 4].

### Case report

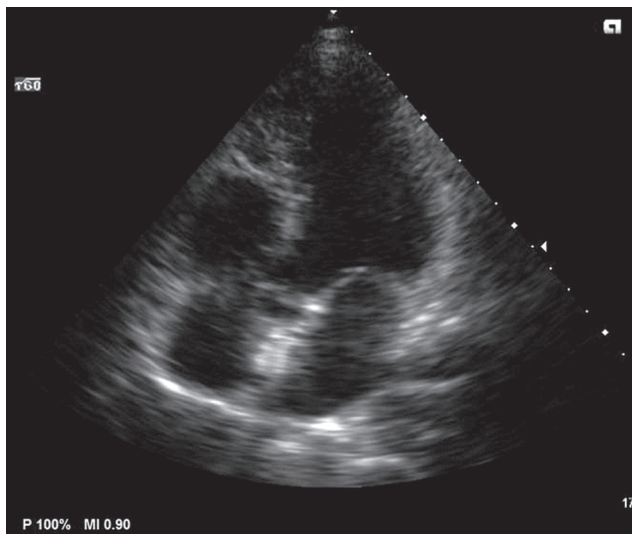
Following an ischemic stroke, the 44-year-old female patient was under out-patient observation for suspected PFO and was referred to the Department of Invasive Cardiology in order to undergo further diagnostics.

Eight months previously, the patient suffered from an ischemic stroke with right-sided hemiparesis and motor aphasia. At the time, computed tomography revealed a small hypodense focus (approx. 8 mm in diameter) in her white matter, on the left side, near the body of the lateral ventricle. No other abnormalities were found during ultrasonographic evaluation of the brain-supplying arteries and transthoracic echocardiographic (TTE) examination. During the hospitalization, the patient began motor reha-

bilitation and speech therapy, which were continued on an out-patient basis after her discharge from the hospital. After several months, her neurological symptoms abated completely. The search for the causes of the stroke was continued in out-patient conditions. After excluding hematological disturbances (antiphospholipid syndrome, thrombophilia, hormonal contraception), PFO was considered to be the most likely suspect. The TEE with contrast and the Valsalva maneuver was performed, but the suspicion was not confirmed. Furthermore, the patient had never smoked cigarettes, and, apart from small varicose veins of the lower legs, no other cardiovascular risk factors were found. After the patient's medical history was analyzed at the Department of Invasive Cardiology, PFO appeared to be the most probable cause of the stroke. The patient was qualified for an invasive examination.

On admission to the clinic, the patient was in good general condition, arterial pressure: 131/94 mm Hg, in ECG: normal sinus rhythm (69 bpm), normal axis. Apart from small varicose veins of the lower legs and slight obesity (body mass index (BMI) 31 kg/m<sup>2</sup>), physical examination revealed no neurological defects or other abnormalities. Similarly, no abnormalities were found by basic laboratory tests evaluating the patient's morphology (hemoglobin: 12.2 g/dl, erythrocytes: 4.41 million/ $\mu$ l, leukocytes:

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**Fig. 1.** Follow-up transthoracic echocardiography: the occluder at the level of the interatrial septum

7.63 thousand/ $\mu$ l, thrombocytes: 339 thousand/ $\mu$ l), coagulation system (fibrinogen: 371 mg/dl, INR: 1.00, APTT: 26.7 s), electrolytes (sodium: 138 mmol/l, potassium: 4.36 mmol/l), renal parameters (creatinine: 0.77 mg/dl), hepatic parameters (alanine aminotransferase: 9 IU/l), and lipid profile (total cholesterol: 171 mg/dl, LDL: 121 mg/dl, HDL: 49 mg/dl, triglycerides: 67 mg/dl).

On the 2<sup>nd</sup> day of hospitalization, a multipurpose catheter was introduced into the patient's right atrium through the femoral vein under intravenous analgosedation (midazolam) and TEE control. Subsequently, the catheter was directed through the interatrial septum into the left atrium, demonstrating the presence of a PFO. Concurrently, the defect in the atrial septum was successfully closed through the percutaneous implantation of an Amplatzer system (Amplatzer PFO Occluder, St. Jude Medical) with the diameter of both discs equal to 18 mm. The position of the occluder and the lack of leakage at its level were verified using echocardiography, and the system was released. Perioperatively, the patient received 2 g of intravenous ampicillin, 600 mg of clopidogrel, and 300 mg of acetylsalicylic acid (ASA).

The perioperative period and further hospitalization were uneventful; in terms of pharmacotherapy, the double antiplatelet therapy was continued (clopidogrel 75 mg/day and ASA 75 mg/day).

On the 2<sup>nd</sup> postoperative day, follow-up TTE was performed, confirming proper occluder position and no signs of leakage within the interatrial septum (Fig. 1). The patient was discharged home in good general condition; she was advised to take her medication regularly (clopidogrel 75 mg/day for 3 months, ASA 75 mg/day for 6 months, and pantoprazole 20 mg/day during clopidogrel use) and to continue infective endocarditis prophylaxis for 6 months after the procedure.

Three months after the procedure, the patient reported to the clinic for a follow-up echocardiographic examination. The patient feels well and does not raise any complaints.

The TTE demonstrated that the occluder remains in the proper position at the level of the interatrial septum without signs of leakage.

## Discussion

A PFO results from the lack of anatomical closure which should normally take place soon after birth; the closure, however, may be only functional. In this case, it may become patent under particular circumstances, e.g., during a Valsalva maneuver or due to significant atrial dilatation. The PFO occurs in 25% of the general population and has a tendency to grow with each decade of life. When the pressure in the right atrium is higher than in the left, a right-to-left shunt may develop through the PFO. Shunting through a PFO promotes the development of paradoxical embolisms (with embolic material from systemic veins moving into the arterial system), which may cause cryptogenic strokes, constituting 40% of strokes in individuals below the age of 55 [1-3, 5, 6].

Recommendations of American cardiological and neurological associations consider contrast TEE with Valsalva to be the first and only method of PFO diagnostics. The standards recommend the performance of transesophageal echocardiography in all stroke patients below the age of 55 in order to exclude PFO [7, 8]. Although TEE is characterized by very high sensitivity in PFO diagnostics, false negative results are obtained in a small percentage of patients [9]. Van *et al.* assessed the sensitivity of TEE with Valsalva in 38 patients after neurological incidents with confirmed PFOs, who were qualified for percutaneous defect closure. Transcranial Doppler (TCD) was used to verify the findings. In 7.9% of the patients, the results were false negative, which was explained by significant discomfort associated with the transesophageal probe during the Valsalva maneuver and by insufficient pressure gradients between the right and left atrium [10].

Our clinic cooperates closely with neurological departments, which refer patients with PFO and patients after (probably cryptogenic) strokes to our clinic in order to extend the diagnostics and qualify the patients for percutaneous PFO closure. As our center lacks experience with transcranial ultrasonography, each patient undergoes TEE with contrast and Valsalva.

In the described patient, a cryptogenic stroke was diagnosed after all other causes of the cerebral incident were excluded. Transesophageal echocardiography did not reveal the presence of a PFO. However, taking into account the patient's young age, responsible occupation (school principal), and engagement in rehabilitation and the diagnostic process, as well as the possibility of a false negative TEE result, a decision was made to verify the examination using right heart catheterization, which confirmed the presence of PFO. Considering the patient's preference concerning treatment, concurrent percutaneous closure of the PFO was performed.

The heretofore published recommendations concerning secondary prevention of stroke in PFO patients are signifi-

cantly limited by the lack of unambiguous data from randomized studies [11-16]. American cardiological and neurological associations recommend the use of antiplatelet agents in PFO patients after stroke or transient ischemic attack (TIA) to prevent repeated cerebral incidents (class IIa, level B). The use of oral anticoagulants (class IIb, level B) and percutaneous PFO closure (class IIB, level C) can also be considered to prevent repeated neurological incidents [17]. Although advantages of percutaneous PFO closure over pharmacological treatment in the prevention of repeated strokes have not yet been demonstrated, surgical treatment is undoubtedly an attractive and often preferred alternative for young patients who wish to avoid the burdensome anticoagulative treatment. Many centers using this procedure, including our clinic, perform percutaneous PFO closures in patients as soon as after the first cerebral incident [18, 19].

After the successful detection of PFO during right heart catheterization in the described patient, we will consider invasive diagnostics in each patient with high probability of prior cryptogenic stroke in whom TEE fails to confirm the presence of PFO.

## Disclosure

Authors report no conflict of interest.

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