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Patient with patent foramen ovale and thrombophilia, after ischemic stroke, acute coronary syndrome and pulmonary embolism (RCD code: IV-2B.O)

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Abstract

Patent foramen ovale (PFO) is a residue of the foramen ovale, an integral part of the normal fetal circulation. It closes in most of newborns, however 25–30% of adults may have it patent. Conditions such as crytpogenic stroke, migraine and vascular headaches or decompression sickness are strongly related to the presence of PFO. Less frequently acute myocardial infarction, renal infarction or acute mesenteric ischemia may also occur. We present a case of a 67-year-old man after cerebral ischemic episode, acute myocardial infarction treated with primary coronary intervention and pulmonary embolism, who was eventually diagnosed with PFO and factor V Leiden mutation. Life-long anticoagulation was initiated in this patient as a standard-of-care. He additionally underwent successful percutaneous PFO closure. As a result no subsequent thromboembolic complication occurred in this patient at the follow-up period. JRCD 2015; 2 (2): 52–55

Key words: V Leiden mutation, anticoagulation, device closure

Background

Patent foramen ovale (PFO) is a residue of the foramen ovale, an integral part of the normal fetal circulation [1]. It is an oblique, slit-shaped tunnel formed by two septa, primum and secundum [2]. During the intrauterine period its role is to conduct oxygenated blood from the venal to the arterial part of the circulatory system [2]. In 70 to 75% of newborn the septa become fused by the age of two, however in up to 25 – 30% people of the adult population the connection remains patent [3]. Reasons for failing to close are unknown [4]. Although most often asymptomatic, several clinical conditions are known to be strongly related to the presence of a PFO. Crytpogenic stroke, migraine and vascular headaches or decompression sickness and air embolism are the most often observed complications [5,6,7]. Acute myocardial infarction as well other forms of paradoxical embolism such as renal infarction, acute mesenteric ischemia or fat embolism are observed less frequently [8,9].

Case Presentation

67- year old Caucasian man after cerebral ischemic episode, acute myocardial infarction and pulmonary embolism was referred to our Center for further cardiac evaluation.

In May 2011 he was hospitalized in a county hospital due to sudden loss of consciousness accompanied with right sided hemiparesis and aphasia. Accessory tests revealed ST segments elevation in leads V1 to V6 on an electrocardiographic (ECG) study. Brain computed tomography (CT) scan showed ischemic lesion located in left parietal lobe (Figure 1). Due to laboratory and electrocardiographic signs of cardiac ischemia coronary angiography was performed showing a thrombus in the left anterior descending (LAD)

Conflict of interest: none declared.

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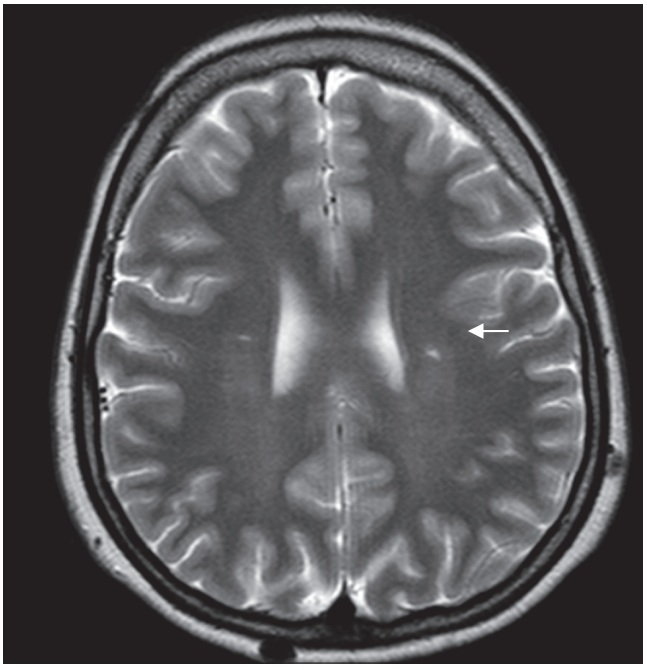

Figure 1. Brain computed tomography scan. Cerebral ischemia. Ischemic lesion in the left parietal lobe (arrow)

branch (Figure 2A). Subsequent revascularization was carried out with positive effect of thrombectomy (Figure 2B). Additional computed tomography angiography (angio-CT) of pulmonary arteries revealed pulmonary embolism (Figure 3). Successful anticoagulation therapy was initiated and the patient was discharged home with the diagnosis of transient ischemic attack (TIA), acute coronary syndrome (ACS) and pulmonary embolism (PE).

Due to suspicion of concomitant hypercoagulable condition further investigation was performed. It revealed factor V Leiden mutation and the patient was put on vitamin K antagonists (VKA) and aspirin.

On admission to our Center, he was hemodynamically stable with persistent right upper limb dysmetria and ataxia. Holter ECG monitoring, ambulatory blood pressure monitoring and tilt table test did not reveal any abnormalities. Eventual transesophageal cardiac echo (TEE) study was carried out showing PFO present. An agitated saline contrast injected to right basilic vein during Valsalva maneuver proved right-to-left shunting across the PFO (Figure 4). In order to confirm the hemodynamic significance of the PFO shunting a transcranial doppler study (TCD) was performed. Echo contrast signals were identified by the typical overloading spike artifacts and the examination was considered positive (Figure 5).

Therefore, taking into consideration his passed medical history and concomitant condition of thrombophilia related to the factor V Leiden mutation, we discussed, whether PFO device closure is indicated in this patient as secondary stroke prevention.

Discussion

There has been a growing clinical interest in PFO observed in recent years. Causal relationship of PFO and ischemic stroke has

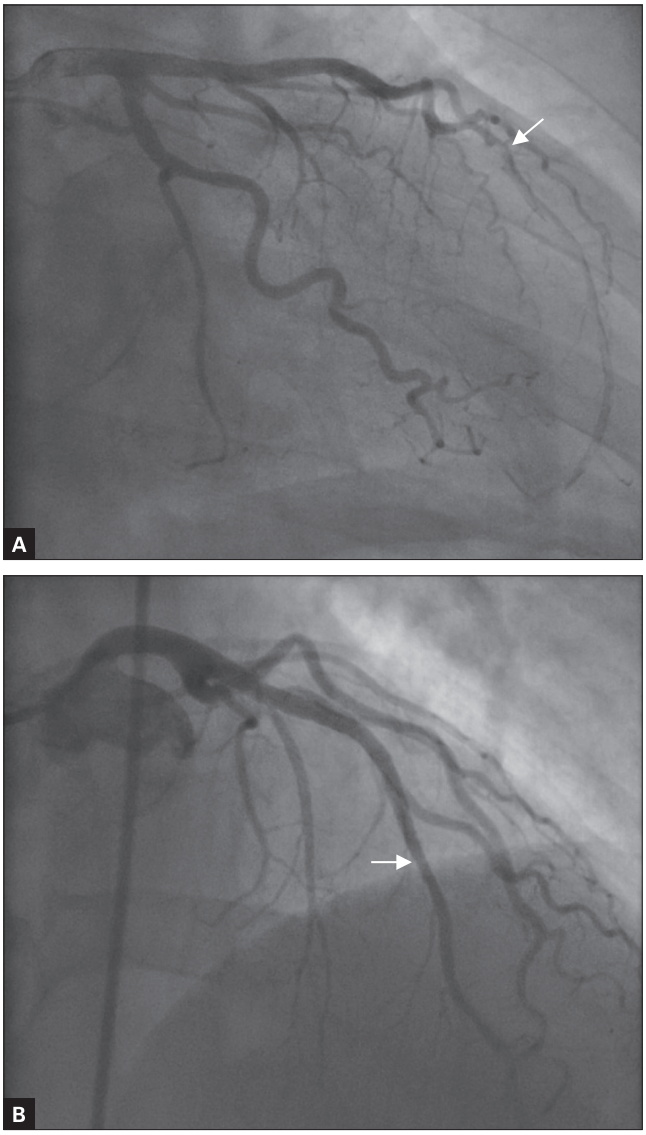

Figure 2. Coronary angiography. A. A thrombus in the left anterior descending branch (LAD) (arrow). B. Successful thrombectomy (arrow)

been evaluated in several studies. Around half of young patients with cryptogenic stroke have PFO, whereas coexistence of these two clinical conditions in general population is rather incidental [10,11].

Clinical evaluation towards the presence of PFO should be carried out in all patients with a paradoxical embolic event, as well as in patients with other forms of PFO manifestations.

Presence of PFO in patient with an embolic event should include careful assessment of the likelihood that the PFO is causally related to the event including identification of other potential causes of thromboembolism and stroke.

Diagnosis of a PFO is made based on an ultrasound technique. Several modalities have been adopted for this purpose including transthoracic echocardiography (TTE), TEE, TCD or transmitral Doppler (TMD). TEE has evolved to be the "gold standard" method and as such is most commonly used [12,13]. It has the advantage of visualizing the site of the right-to-left shunt together with its mor-

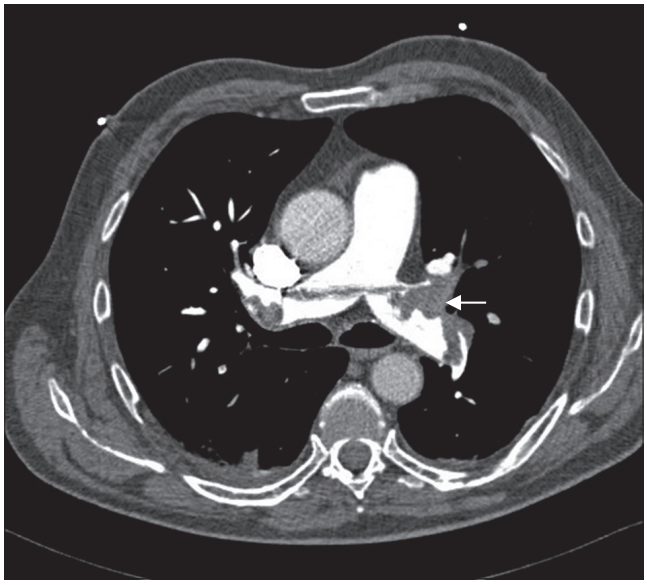

Figure 3. Cardiovascular computed thomography. Angiography of the pulmonary arteries. Massive pulmonary embolism (arrow)

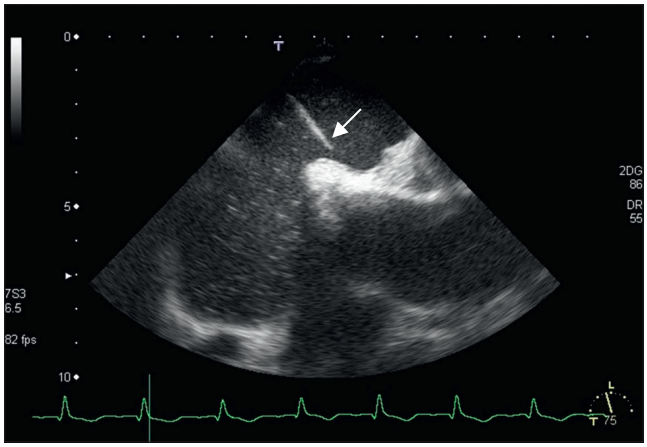

Figure 4. Transesophagela echocardiography. Patent foramne ovale wiht right-to-left shunting (arrow)

phology and hemodynamic significance. TTE has been found to be less sensitive in diagnosing PFO than TEE, although supported by detection of right to left bubble passage after intravenous administration of agitated saline contrast on TMD, its utilization becomes considerable [14,15] TCD, as a noninvasive tool, is a potential alternative to TEE, however it evidences the presence of right-to-left shunt solely without indicating its site [16].

There are several controversies regarding the therapeutic possibilities for secondary stroke prevention. Medical therapy with antiplatelet agents or anticoagulation *versus* surgical or percutaneous closure are the most widely discussed treatment options [17].

Rationale for the use of aspirin comes from a few non randomized trials, suggesting its potential benefit and is recommended by the 2012 American College of Chest Physicians and the 2011 American Heart Association/American Stroke Association guidelines [18,19,20]. These guidelines, however, do not recommend the use

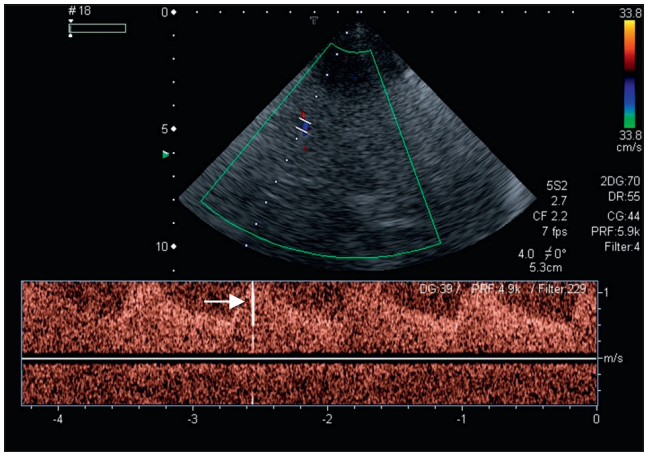

Figure 5. Transcranial Doppler. Microbubble artifact (spike) detected in the middle cerebral artery (arrow)

of anticoagulants in this group of patients, unless an additional indication such as hypercoagulable state is present.

The benefits of surgical closure of a PFO in patients with a history of stroke are inconclusive [21,22,23]. No randomized trials comparing medical therapy have been performed so far. Introduction of noninvasive, percutaneous PFO device closure procedures has enhanced the research in this filed, although their effectiveness in secondary cryptogenic stroke prevention has not yet been established [24]. Competing data regarding the reduction of stroke recurrence rate and potential drawbacks including periprocedural vascular complication, new-onset arrhythmias or device failure are still the matter of ongoing debate. Several randomized clinical trials and meta-analyses have not shown clear benefit of this procedure [25–30].

Management strategy

Considering the fact that the patient already receives anticoagulant therapy with VKA we referred to the panel of experts for their recommendations before PFO closure. Experts consensus stated, that no PFO closure is advisable at present. Thorough haematologic evaluation is necessary, in order to constitute the risk of thromboembolic episodes. VKA application should be the treatment of choice.

Several months later the patient was admitted to the Clinic for the follow-up visit. At admission he had no new neurological symptoms or sequent thromboembolic complications. His clinical state was good. However, he expressed concerns regarding the decision of no PFO device closure. He admitted that he would feel much safer if the procedure was performed. Taking into consideration this fact together with his passed medical history and concomitant conditions, that is thrombophilia related to the factor V Leiden mutation, we reconsidered indications for the PFO closure. He eventually was qualified for the PFO closure. The procedure was performed safely. He remains under regular follow-up without any complications.

Conclusion

The hypercoagulable state of this patient and the history of thrombosis in situ puts him at the high risk of thromboembolic consequences per se, including ischemic stroke. Coexistence of PFO increases the likelihood of recurrent strokes. Closure of the PFO, being potential source for further formations of thromboembolic materials remains uncertain. Therefore, life- long anticoagulation therapy is the recommended treatment of choice for this patient.

References

1. Hara H, Virmani R, Ladich E, et al. Patent foramen ovale: current pathology, pathophysiology, and clinical status. J Am Coll Cardiol. 2005; 46: 1768–1776.
2. Podolec P, Suchoń E, Kabłak-Ziembicka A. Przetrwały otwór owalny – diagnostyka i wskazania do przezskórnego zamykania PFO. Echokardiografia Praktyczna, Vol. III, Chapter 14, Medycyna Praktyczna 2005: 183–191.
3. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin Proc.1984; 59: 17–20.
4. Clark EB. Pathogenetic mechanisms of congenital cardiovascular malformations revisited. Semin Perinatol 1996; 20: 465–472.
5. Kerut EK, Norfleet WT, Plotnick GD, et al. Patent foramen ovale: a review of associated conditions and the impact of physiological size. J Am Coll Cardiol. 2001; 38: 613–623.
6. Larrue V, Berhoune N, Massabuau P et al. Etiologic investigation of ischemic stroke in young adults. Neurology 2011; 76: 1983–1988.
7. Anzola GP, Magoni M, Guindani M, et al. Potential source of cerebral embolism in migraine with aura: a transcranial Doppler study. Neurology 1999; 52: 1622–1625.
8. Agostoni P, Gasparini G, Destro G. Acute myocardial infarction probably caused by paradoxical embolus in a pregnant woman. Heart. 2004; 90: e12.
9. Carey HB, Boltax R, Dickey KW, et al. Bilateral renal infarction secondary to paradoxical embolism. Am J Kidney Dis. 1999; 34: 752–755.
10. Mas JL, Arquizan C, Lamy C, et al. Recurrent cerebrovascular events associated with patent foramen ovale, atrial septal aneurysm, or both. N Engl J Med. 2001; 345: 1740–1746.
11. Alsheikh-Ali AA, Thaler DE, Kent DM. Patent foramen ovale in cryptogenic stroke: incidental or pathogenic? Stroke. 2009; 40: 2349–2355.
12. Pinto FJ. When and how to diagnose patent foramen ovale. Heart. 2005; 91: 438–440.
13. Lee RJ, Bartzokis T, Yeoh TK, et al. Enhanced detection of intracardiac sources of cerebral emboli by transesophageal echocardiography. Stroke1991; 22: 734–739.
14. Pearson AC, Labovitz AJ, Tatineni S, et al. Superiority of transesophageal echocardiography in detecting cardiac source of embolism in patients with cerebral ischemia of uncertain etiology. J Am Coll Cardiol 1991; 17: 66–72.
15. Kerr AJ, Buck T, Chia K, et al. Transmitral Doppler: a new transthoracic contrast method for patent foramen ovale detection and quantification. J Am Coll Cardiol. 2000; 36: 1959–1966.
16. Blersch WK, Draganski BM, Holmer SR, et al. Transcranial duplex sonography in the detection of patent foramen ovale. Radiology 2002; 225: 693–699.
17. Ringleb PA, Bousser MG, Ford G, et al. Guidelines for Management of Ischaemic Stroke and Transient Ischaemic Attack 2008. Cerebrovasc Dis. 2008; 25: 457–507.
18. Homma S, Sacco RL, Di Tullio MR, et al. Effect of medical treatment in stroke patients with patent foramen ovale: patent foramen ovale in Cryptogenic Stroke Study. Circulation 2002; 105: 2625–2631.
19. Lansberg MG, O'Donnell MJ, Khatri P, et al. Antithrombotic and thrombolytic therapy for ischemic stroke: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141(2 Suppl): e601S.
20. Furie KL, Kasner SE, Adams RJ, et al. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the american heart association/american stroke association. Stroke 2011; 42: 227–276.
21. Homma S, Di Tullio MR, Sacco RL, et al. Surgical closure of patent foramen ovale in cryptogenic stroke patients. Stroke 1997; 28: 2376–2381.
22. Dearani JA, Ugurlu BS, Danielson GK, et al. Surgical patent foramen ovale closure for prevention of paradoxical embolism-related cerebrovascular ischemic events. Circulation 1999; 100 (19 Suppl): II171-175.
23. Devuyst G, Bogousslavsky J, Ruchat P, et al. Prognosis after stroke followed by surgical closure of patent foramen ovale: a prospective follow-up study with brain MRI and simultaneous transesophageal and transcranial Doppler ultrasound. Neurology 1996; 47: 1162–1166.
24. O'Gara PT, Messe SR, Tuzcu EM, et al. Percutaneous device closure of patent foramen ovale for secondary stroke prevention: a call for completion of randomized clinical trials. A science advisory from the American Heart Association/American Stroke Association and the American College of Cardiology Foundation. J Am Coll Cardiol. 2009; 53: 2014–2018.
25. Bruch L, Parsi A, Grad MO, et al. Transcatheter closure of interatrial communications for secondary prevention of paradoxical embolism: single-center experience. Circulation 2002; 105: 2845–2848.
26. Windecker S, Wahl A, Nedeltchev K, et al. Comparison of medical treatment with percutaneous closure of patent foramen ovale in patients with cryptogenic stroke. J Am Coll Cardiol. 2004; 44: 750–758.
27. Agarwal S, Bajaj NS, Kumbhani DJ, et al. Meta-analysis of transcatheter closure versus medical therapy for patent foramen ovale in prevention of recurrent neurological events after presumed paradoxical embolism. JACC Cardiovasc Interv. 2012; 5: 777–789.
28. Furlan AJ, Reisman M, Massaro J, et al. Closure or medical therapy for cryptogenic stroke with patent foramen ovale. N Engl J Med. 2012; 366: 991–999.
29. Meier B, Kalesan B, Mattle HP, et al. Percutaneous closure of patent foramen ovale in cryptogenic embolism. N Engl J Med. 2013; 368: 1083–1091.
30. Carroll JD, Saver JL, Thaler DE, et al. Closure of patent foramen ovale versus medical therapy after cryptogenic stroke. N Engl J Med. 2013; 368: 1092–100.