Low-Angle Patent Foramen Ovale (PFO): High-Risk PFO Morphology Associated with Paradoxical Embolism

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INTRODUCTION

Patent foramen ovale (PFO) is one of the common causes of paradoxical embolism.[1-4] Low-angle PFO, defined as an angle of ≤10° between the inferior vena cava (IVC) and PFO flap, has been reported as a high-risk morphological feature that is associated with stroke.[5] A low angle between the IVC and PFO flap allows venous blood to flow directly from the IVC to the left atrium (LA) through the PFO. Therefore, thrombus in veins of the lower extremities is more likely to be carried to the left heart, causing an embolic stroke. However, there have been no reports showing a right-to-left shunt flowing directly from the IVC to the LA owing to low-angle PFO. Here we report a case of low-angle PFO in which IVC venous blood flowed directly into the LA in a patient with recurrent stroke.

CASE PRESENTATION

An 86-year-old woman with recurrent stroke and atrial fibrillation was referred to our hospital. The stroke was diagnosed as cardiogenic cerebral embolism by neurologists. Therefore, atrial fibrillation was initially considered to be the cause of the strokes.

Transesophageal echocardiography was performed to examine the source of embolization. Thrombi were not identified in the left atrial appendage. The Doppler flow velocity was not decreased. Spontaneous echo contrast was not observed. There was no shaggy aorta syndrome. However, PFO with a right-to-left shunt was detected by a saline contrast injection with the Valsalva maneuver (Video 1). The height of the PFO was 5 mm, and the length of the PFO tunnel was 3 mm (Figure 1). An atrial septum aneurysm with a total excursion distance of 20 mm between the right atrium and LA was observed (Video 2). The angle between the IVC and PFO flap, which was measured on an imaging plane that displayed the IVC and interatrial septum, was low (Figure 2). The structural position of the PFO flap was located on a straight line from the IVC (Figure 3). Transesophageal echocardiography with color Doppler showed a right-to-left shunt that flowed directly into the LA through the PFO, especially during inspiration (Video 3). Pulmonary arterial hypertension was not observed.

On the basis of the finding of direct blood flow from the IVC to the LA through the low-angle PFO, we concluded that the recurrent strokes were caused by the high-risk PFO. Transcatheter PFO closure was considered to be an effective treatment for preventing a recurrent

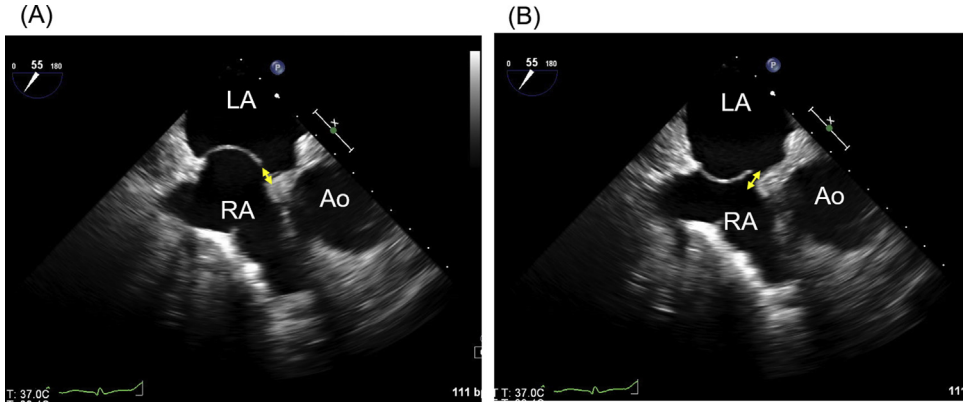

Figure 1 Patent foramen ovale morphology. **(A)** The height of PFO was 5 mm. **(B)** The length of the PFO tunnel was 3 mm. *Ao*, Aorta.

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Keywords: Patent foramen ovale, Low-angle PFO, High-risk PFO, Stroke

Conflicts of Interest: None.

2468-6441

https://doi.org/10.1016/j.case.2021.02.008

VIDEO HIGHLIGHTS

Video 1: A right-to-left shunt was demonstrated by a saline injection test with the Valsalva maneuver.
Video 2: Atrial septum aneurysm with a total excursion distance of 20 mm between the right atrium and LA was shown.
Video 3: Direct blood flow through the low-angle PFO. A right-to-left shunt flowing directly from the IVC to the LA through the low-angle PFO was observed.

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paradoxical embolism in this patient. However, because the patient was older, anticoagulation therapy was performed.

DISCUSSION

The present report shows that low-angle PFO is related to direct blood flow from the IVC to the LA. Our findings indicate the importance of the structural position between the IVC and PFO flap as a cause of paradoxical embolism.

The prevalence of PFO is approximately 25% in the general population.[6] However, few patients with PFO have a paradoxical embolism. Recent randomized trials have shown the benefits of transcatheter closure for reducing stroke compared with medical therapy, and patients with PFO at risk of stroke were selected as candidates.[7-9] Therefore, identification of high-risk PFO, which is more likely to be associated with a paradoxical embolism, is important for therapeutic management.

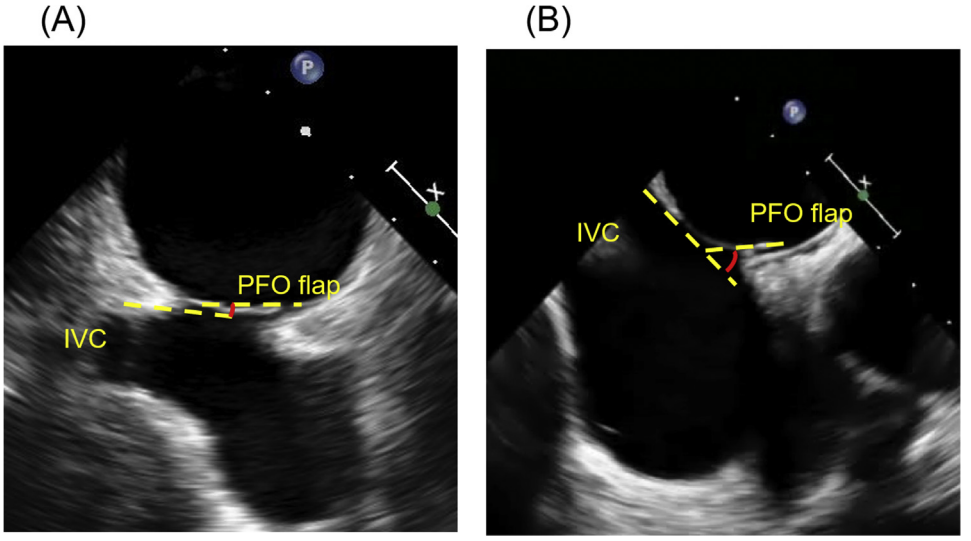

Figure 2 **(A)** The angle between the IVC and PFO flap was measured on an imaging plane that displayed the IVC and interatrial septum. In this patient, the angle between the IVC and PFO flap was low. **(B)** In contrast, the angle between the IVC and PFO flap was high in this other patient.

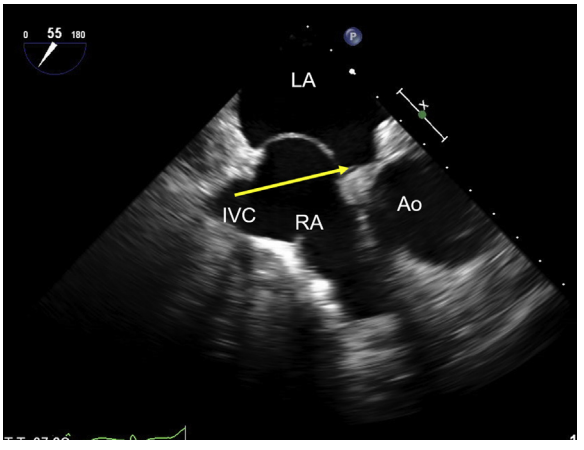

Figure 3 Low-angle PFO. The structural position of PFO flap was almost on a straight line from the IVC. *Ao*, Aorta.

A large-sized PFO with a height of ≥2 mm, a large right-to-left shunt, and the presence of trial septum aneurysm have been recognized as morphological features indicating high-risk PFO.[4,10-12] Patent foramen ovale with a long tunnel ≥10 mm and the presence of a prominent Eustachian valve or Chiari's network have been reported to be more common in patients with stroke.[11,13,14] In addition to these factors, we proposed that an angle of ≤10° between the IVC and PFO flap, which was defined as low-angle PFO, was associated with stroke.[5] As a possible mechanism, we consider the possibility that low-angle PFO, which aligns the PFO flap with the IVC, facilitates the passage of thrombus into the LA. We showed direct blood flow from the IVC to the LA through a low-angle PFO on transesophageal echocardiography with color Doppler. Direct blood flow frequently occurred during inspiration, owing to an increase in right atrial

pressure. This report is valuable in that it supports low-angle PFO as one of the high-risk morphologies of PFO. For these types of patients, transcatheter closure of PFO can be effective for preventing paradoxical embolization.

In this patient, transcatheter PFO closure was not performed, owing to advanced age. This patient had other potential causes of stroke. Thus, the relationship between stroke and low-angle PFO with direct blood flow from the IVC to the LA is speculative. However, the risk of forming a left atrial appendage thrombus was low. Shaggy aorta was not observed. Therefore, we considered that this PFO was strongly associated with the cause of stroke.

The angle between the IVC and PFO flap may change with age. In this patient, the angle might have become low with increasing age, which allowed venous blood to flow directly from the IVC to the LA, leading to the occurrence of stroke. Further studies are needed to confirm the findings.

CONCLUSION

We showed direct blood flow from the IVC to the LA through PFO with a low angle between the IVC and PFO flap. Low-angle PFO should be recognized as a high-risk morphology of PFO associated with paradoxical embolism when assessing PFO.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2021.02.008.

REFERENCES

1. Lechat P, Mas JL, Lascault G, Loron P, Theard M, Klimczac M, et al. Prevalence of patent foramen ovale in patients with stroke. N Engl J Med 1988;318:1148-52.
2. Hart RG, Diener HC, Coutts SB, Easton JD, Granger CB, O'Donnell MJ, et al. Embolic strokes of undetermined source: the cause for a new clinical construct. Lancet Neurol 2014;13:429-38.
3. Overell JR, Bone I, Lees KR. Interatrial septal abnormalities and stroke: a meta-analysis of case-control studies. Neurology 2000;55:1172-9.
4. Mas JL, Arquizan C, Lamy C, Zuber M, Cabanes L, Derumeaux G, et al. Recurrent cerebrovascular events associated with patent foramen ovale, atrial septal aneurysm, or both. N Engl J Med 2001;345:1740-6.
5. Nakayama R, Takaya Y, Akagi T, Watanabe N, Ikeda M, Nakagawa K, et al. Identification of high-risk patent foramen ovale associated with cryptogenic stroke: development of a scoring system. J Am Soc Echocardiogr 2019;32:811-6.
6. De Castro S, Cartoni D, Fiorelli M, Rasura M, Anzini A, Pandian NG, et al. Morphological and functional characteristics of patent foramen ovale and their embolic implications. Stroke 2000;31:2407-13.
7. Saver JL, Carroll JD, Thaler DE, Smalling RW, MacDonald LA, Tirschwell DL, et al. Long-term outcomes of patent foramen ovale closure or medical therapy after stroke. N Engl J Med 2017;377:1022-32.
8. Sondergaard L, Kasner SE, Rhodes JF, Andersen G, Iversen HK, Thomassen L, et al. Patent foramen ovale closure or amtiplatelet therapy for cryptogenic stroke. N Engl J Med 2017;377:1033-42.
9. Mas JL, Derumeaux G, Guillon B, Massardier E, Hosseini H, Chatellier G, et al. Patent foramen ovale closure or anticoagulation vs. antiplatelets after stroke. N Engl J Med 2017;377:1011-21.
10. 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.
11. Schuchlenz HW, Weihs W, Horner S, Quehenberger F. The association between the diameter of a patent foramen ovale and the risk of embolic cerebrovascular events. Am J Med 2000;109:456-62.
12. Turc G, Lee JY, Brochet E, Kim JS, Song JK, Mas JL. Atrial septal aneurysm, shunt size, and recurrent stroke risk in patients with patent foramen ovale. J Am Coll Cardiol 2020;75:2312-20.
13. Schneider B, Hofmann T, Justen MH, Meinertz T. Chiari's network: normal anatomic variant or risk factor for arterial embolic events? J Am Coll Cardiol 1995;26:203-10.
14. Schuchlens HW, Saurer G, Weihs W, Rehak P. Persisting Eustachian valve in adults: relation with patent foramen ovale and cerebrovascular events. J Am Soc Echocardiography 2004;17:231-3.