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Case report

Paradoxical brain embolism in a young man: Is it only a patent foramen ovale?

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A B S T R A C T

Paradoxical embolism is considered the major cause of cerebral ischemic events in young patients. The most common cause of paradoxical embolism, which has been widely described, is right-to-left shunting (RLS) at cardiac level through a patent foramen ovale (PFO). Rarely paradoxical embolism can also be caused by RLS at pulmonary level due to pulmonary arteriovenous fistula (PAVF). Herein, we present a case of a young man, who experienced transient ischemic attack (TIA) due to paradoxical embolism, in whom both abovementioned abnormalities coexisted. This coincidence is very rare (noted in only 1% of patients with cryptogenic stroke or TIA), but it highlights the importance of searching for extracardiac RLS in patients with cryptogenic stroke, even if a PFO has been detected.

1. Introduction

The incidence of ischemic stroke is strongly correlated with increasing age. Consequently stroke in children and young adults is a relatively rare condition and the etiology and risk factors are different from those of older patients. Paradoxical embolism associated with intracardiac shunting through a patent foramen ovale (PFO) is considered the major cause of cerebral ischemic events in young patients. An often unrecognized cause of paradoxical embolism is intrapulmonary right-to-left shunting through a pulmonary arteriovenous fistula (PAVF).

Herein, we present a case of a young man, who experienced transient ischemic attack (TIA) due to paradoxical embolism, in whom both abovementioned abnormalities coexisted. This coincidence is very rare (noted in only 1% of patients with cryptogenic stroke or TIA), but it highlights the importance of searching for extracardiac RLS in patients with cryptogenic stroke, even if a PFO has been detected.

2. Case report

A 15-year-old man, with no previous medical history, experienced two episodes of transient ischemic attacks (TIA) within a year, which manifested in sudden dysarthria and paresis of the right upper and lower limb. He was admitted to the Department of Neurology where his general and neurological examination was normal. Brain magnetic resonance imaging (MRI) revealed

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multifocal cerebral infarctions. There was no history of atherosclerosis risk factors such as smoking, diabetes or hyperlipidemia and family history was unremarkable. His complete coagulation work-up (including Protein S and C levels, anticardiolipin antibodies, antithrombin, Factor V Leiden, Prothrombin gene mutation) and carotid ultrasound did not reveal any abnormalities. Therefore, paradoxical embolism was suspected. Doppler ultrasound did not reveal any potential source of embolism in deep veins of the lower limbs as well as in the iliac veins. However, transcranial Doppler (TCD) showed right-to-left shunting after saline contrast infusion. The patient was referred to the Department of Cardiology. On admission, he had normal physical examination, the oxygen saturation measured by pulse oximeter was 97%. Holter ecg monitoring did not reveal any arrhythmia. Transesophageal echocardiogram (TEE) showed a small shunt from the left to the right atrium across the PFO and right-to-left shunting (RLS) with microbubbles after saline contrast infusion and Valsalva maneuver. The patient was qualified for a transcatheter closure of the patent foramen ovale (PFO). A chest radiography performed prior to the procedure demonstrated a round shadow measuring 21 mm × 25 mm, located in the upper part of the left lung (Fig. 1). Contrast enhanced chest computed tomography (CT) showed a polycyclic mass of uniform density, measuring 20 mm × 14 mm and surrounded by feeding vessels located in the central part of the upper lobe of the left lung. The image suggested vascular malformation. There was no thrombus within the PAVF and no evidence of pulmonary embolism. Under general anesthesia we performed a selective left pulmonary arterial angiography, which revealed an arteriovenous fistula in the upper lobe of left lung (Fig. 2). The diameter of the vessel supplying the malformation was 7 mm. Occlusion of the malformation was performed successfully by embolization using Amplatzer Vascular Plug 10 mm device (Fig. 3). At the same time PFO closure was performed with Occlutech Figulla

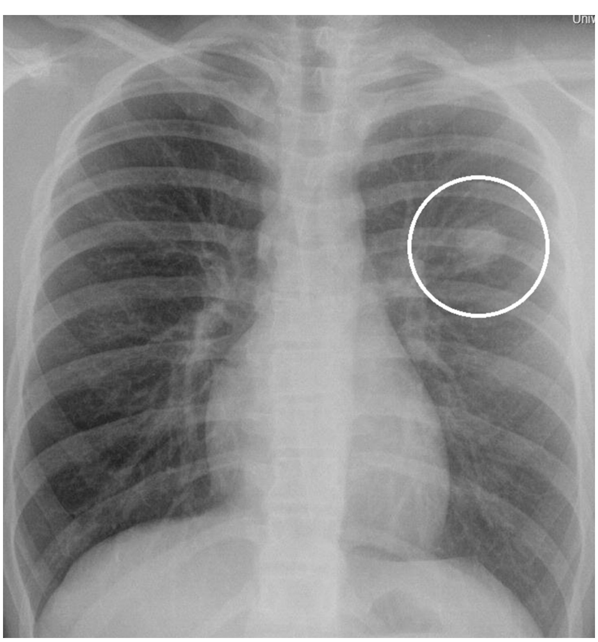

Fig. 1 – Posteroanterior chest radiograph showing a single PAVF in the upper part of the left lung (white circle).

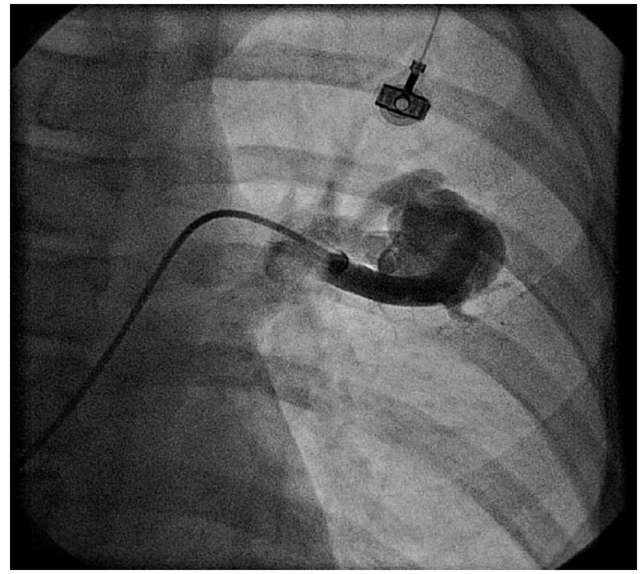

Fig. 2 – Angiogram showing a single PAVF in the upper lobe of the right lung.

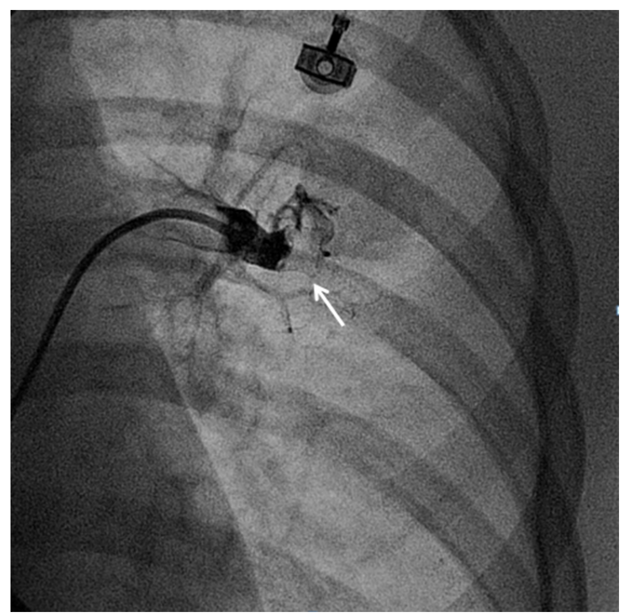

Fig. 3 – Angiogram showing complete occlusion of PAVF with 10 mm Amplatzer Vascular Plug device (arrow).

Flex II 23/25 mm device (Fig. 4). The patient was discharged two days later. There was no recurrence of TIA noted at the 6 months follow-up and there are no signs of right-to-left shunting in contrast TCD.

3. Discussion

The most common cause of paradoxical embolism is widely described right-to-left shunting (RLS) at cardiac level through a patent foramen ovale (PFO). Our case emphasizes the fact that other RLS could exist simultaneously and be responsible for

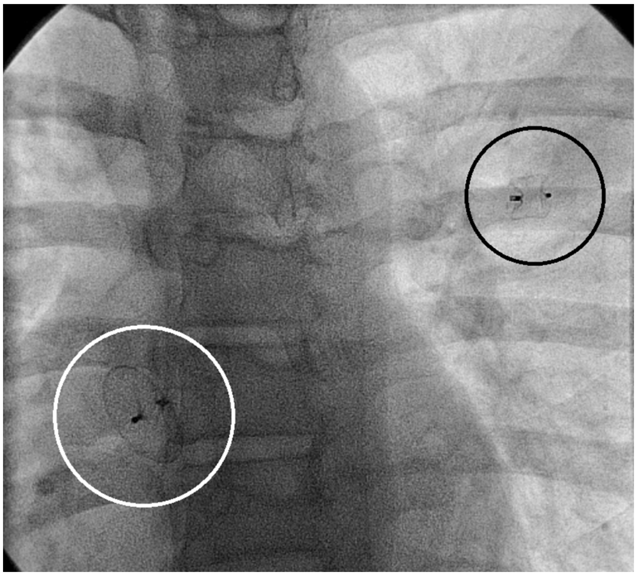

Fig. 4 – Chest radiograph showing two implanted devices: 10 mm Amplatzer Vascular Plug occluding PAVF (black circle) and Occlutech Figulla Flex II 23/25 mm occluding PFO (white circle).

cryptogenic stroke. Rarely paradoxical embolism can be caused by RLS at pulmonary level due to pulmonary arteriovenous fistula (PAVF). Paradoxical embolism typically originates in the veins of the lower extremities and occasionally in the pelvic veins. The emboli can be also derived directly from a local thrombosis within the PAVF [1]. However, due to the small size of embolic material its certain origin often remains undetermined.

Pulmonary arteriovenous fistulas are rare pulmonary vascular malformations with direct communications between the branches of the pulmonary artery and pulmonary veins. The incidence of PAVFs is 2–3 per 100 000 population [2]. More than 80% of PAVFs are congenital, and of these 47–80% are associated with Osler–Weber–Rendu disease or hereditary hemorrhagic teleangiectasia (HHT) [3,4]. In contrast to systemic arteriovenous malformation, PAVFs do not affect cardiac hemodynamics and most patients are asymptomatic [5]. Rarely, if the right-to-left shunt is large, PAVFs can cause desaturation and exertional dyspnea, cyanosis, clubbing and polycythemia [4,6]. Their associated central nervous system complications include: migraine, transient ischemic attack, stroke, abscess, and seizures [7]. In one study the reported incidence of neurological events in patients with PAVFs was 37% for TIA and 18% for stroke [8]. In a different study the prevalence of cerebral infarction in a single PAVF was 32% and it increased up to 60% in cases of multiple PAVFs [9]. In a large scale registry of 642 patients, intrapulmonary shunting was shown to be an independent predictor of ischemic stroke or TIA, especially in the group of cryptogenic events.

In young patients with cryptogenic strokes PFOs is detected by contrast transesophageal echocardiography (c-TEE) and contrast transcranial Doppler (c-TCD). Contrast-enhanced TEE with Valsalva maneuver is considered the, gold standard'' for revealing PFOs. It is characterized by very high sensitivity and specificity. In the case of an extracardiac shunt, the echocardiogram will show bubbles entering the left atrium three to eight cardiac cycles after they were seen in the right atrium [10]. In contrast, in cardiac RLS, the ''three-beat rule'' is used, which means that bubbles should appear between first and third cardiac cycle. In patients with positive contrast echocardiogram study, but with delayed contrast appearance and no evidence of interatrial communication, PAVF should be immediately considered. In well performed TEE examination the flow of bubbles from the pulmonary vein may also be visualized.

RLS can also be identified by the use of contrast-enhanced TCD. The technique is based on the detection of an intravenously injected contrast within intracranial arteries. In case of an RLS, the contrast enters the arterial circulation and produces microembolic signals (MES) [11]. Recent studies demonstrate that TCD is as sensitive as TEE for revealing RLS, but it does not determine the level of RLS. To distinguish a PFO from a PAVF the timing of MES appearance in the cerebral circulation during TCD has been proposed. MES passing pulmonary shunts appear later in the cerebral circulation than those passing cardiac shunts. The appropriate diagnostic time window may increase the specificity of the test [12]. The time window characteristic for PAVF is about 15 s (11 s for intracardiac shunts), but it depends on the heart rate (duration of about 6 heart beats) [11,13]. Classical diagnostic tools to confirm PAVF are contrast enhanced chest CT or MRI, however pulmonary angiography is considered the ''gold standard''. Chest radiography shows abnormalities in about 45–98% of patients with PAVF, it does not provide any details, but it may help as a screening tool [14,15]. Most patients with PAVF should be treated. There is evidence that PAVFs progressively enlarge over time, which is associated with higher incidence of neurological events [16,17]. It was shown that recurrences of TIA and strokes occurred more often in patients with PAVF than with PFO [18]. Apart from preventing neurological complications occlusion of PAVF protects from progressive hypoxia and its consequences. Therapeutic options include percutaneous embolotherapy using coils or vascular plugs and surgical resection.

In conclusion, our case highlights the importance of searching for extracardiac RLS in patients with cryptogenic stroke. The existence of PAVF should be always considered even if PFO has already been detected. For complete prevention of recurrent strokes or TIA caused by paradoxical embolism, it is necessary to not only close a PFO, but all existing shunts.

Conflict of interest

None declared.

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Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical

Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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