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Recurrent Tia In A Nine-Year-Old Boy With Patent Foramen Ovale: A Grey Area In Medicine

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Abstract

Ischemic stroke in children is a relatively rare entity, relative to the adult population. The most common potential risk factors include cardiac embolism, prothrombotic states and vasculopathies. Paradoxical embolism via a PFO as a cause of TIA or stroke is a diagnosis of exclusion, which further complicates treatment decisions.

We present the case of a 9-year-old patient who presented with recurrent episodes of transient ischemic attacks, despite the initiation of anticoagulation therapy. The investigation revealed patent foramen ovale and because of the recurrent ischemic attacks, transcatheter closure of patent foramen ovale was performed. We have also presented a brief review of literature.

Key words: patent foramen ovale; cryptogenic stroke; paradoxical embolism; transcatheter pfo closure.

Introduction:

In adults, patent foramen ovale or other potential intracardiac shunts are established risk factors for stroke via paradoxical embolization. Stroke is less common in children and risk factors differ. Pediatric arterial ischemic stroke (AIS) ranks among the leading factors contributing to child mortality (1). Estimates of the incidence of childhood AIS are variable and highly dependent on the search strategy employed as well as the study population. The largest of such studies found an incidence of pediatric AIS of 1.2 per 100,000 person-years. (2)Cryptogenic (of unknown cause) ischemic strokes are now estimated to represent about 25% of all ischemic strokes. Between 20% to 30% of individuals diagnosed with ischemic stroke experience cryptogenic stroke (3). Cryptogenic stroke has been linked with patent foramen ovale (PFO). Around 40% to 50% of patients diagnosed with cryptogenic stroke also exhibit the presence of PFO.(4)

A patent foramen ovale (PFO) is a normal connection between the right and left atria, caused by the incompetence of the fossa ovalis valve during fetal life. The shunt is usually right to- left despite the gradient pressure between the atria. The connection closes in most people over a period after birth. However, if the septum primum fails to fuse with the septum secundum, the PFO remains patent, allowing interatrial blood flow in approximately 25% of the adult population.(5)

Paradoxical embolism from the venous system, or from thrombus formed in situ, has been presumed to be the causal mechanisms for this association.

The role of a PFO or other potential intracardiac shunts in stroke or stroke recurrence in childhood is unclear(1). PFO has been implicated in multiple disease states. Some have described it as a causative agent, whereas others describe it as an innocent bystander(6)

We present the case of a 9-year-old patient who presented with an ischemic brain insult which was repeated, despite the initiation of anticoagulation therapy. The investigation revealed patent foramen ovale and because of the recurrent ischemic events, transcatheter closure of PFO was done. A brief description of the literature is also presented.

Methods & Results

We describe the case of a 9-year-old male who was referred to us with history of recurrent episodes of transient ischemic attacks. He had three episodes of sudden onset left hemiparesis and deviation of the angle of mouth on the left side within six months period.

There was no history of tonic posturing, involuntary jerky movements, loss of consciousness, vomiting, headache or witnessed seizures. His MRI Brain revealed diffusion restriction in the right capsuloganglionic region. MR Angio shows normal vessel wall imaging. His last MRI revealed focal areas of gliosis involving the right corona radiate and right centrum semi ovale. No diffusion restriction or post contrast enhancement was present. MR angiogram and vessel wall imaging shows no features of CNS vasculitis or Moya Moya phenomenon. (Figure 1).

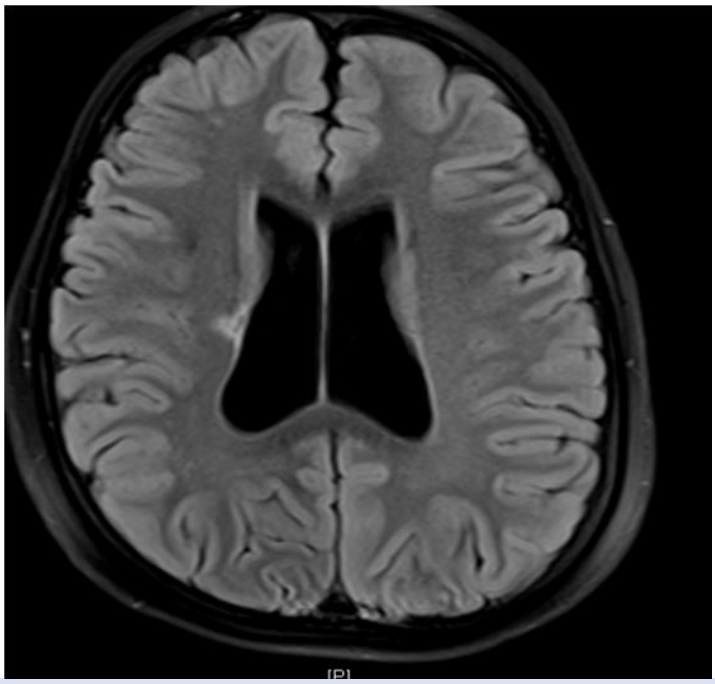

Figure 1: *MRI brain showing focal areas of gliosis involving the right corona radiate and right centrum semi ovale.*

The diagnostic work up for the recognition of the underlying cause of the AIS included the investigation of possible prothrombotic conditions and thrombophilia, vasculitis, but it did not reveal any underlying pathologic condition. The patient underwent a detailed cardiologic work up, which included a transoesophageal echocardiographic examination. It revealed the presence of a patent foramen ovale (Figure 2).

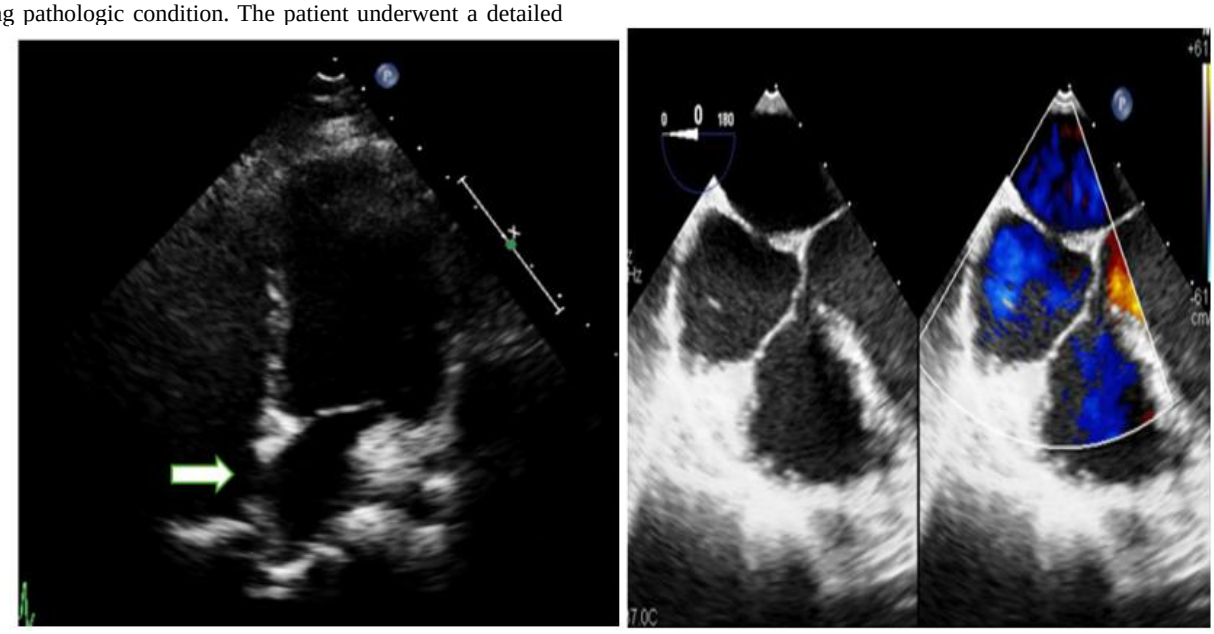

Figure 2: *TTE and TEE showing a patent foramen ovale*

(Defect size: 1.4mm, Shortest distance from defect to Aorta: 7mm, Shortest distance from defect to SVC: 9mm and Length of the tunnel : 12mm)

In view of recurrent transient ischemic attacks, we decided to occlude the foramen ovale with the use of the amplatzer PFO occluder device.

Procedure details

The PFO was crossed with Multipurpose catheter and 0.018" Fielder guidewire under TEE guidance. A 4Fr JR was taken over the 0.018" Fielder and the position was confirmed by LA pressure and taking across the mitral into LV and measuring LV pressures. The 4 Fr JR was exchanged for a 6 Fr MPA over a terumo wire. Attempts to enter the PV was difficult hence the MPA coiled int LA. An Preshaped ASS wire was taken through the MPA and kept coiled in the LA. The 8.5 Fr long sheath was taken across the PFO into the LA. The preloaded 18-25 Talisman amplatzer PFO occluder device was positioned under TEE guidance. Minnesotta wiggle was performed for stability. Device deployed under fluoroscopic and TEE guidance. (Fig 3) Post deployment echocardiogram confirmed no residual shunt. (Fig 4)

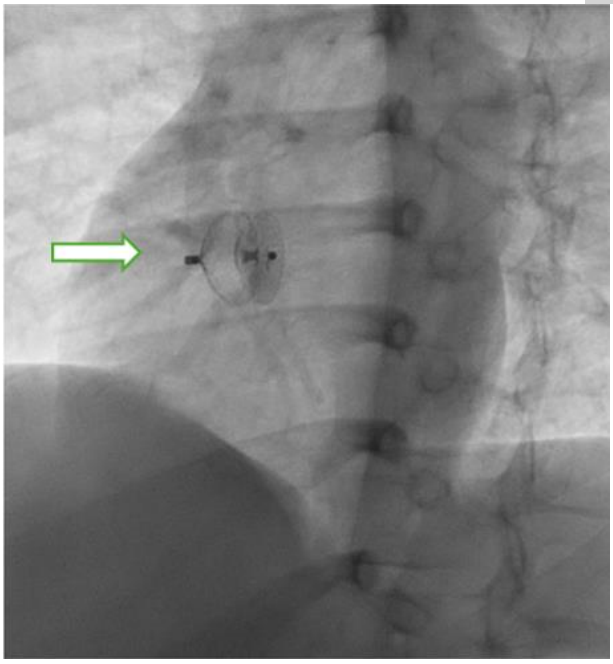

Figure 3: *Device deployed under fluoroscopic and TEE guidance*

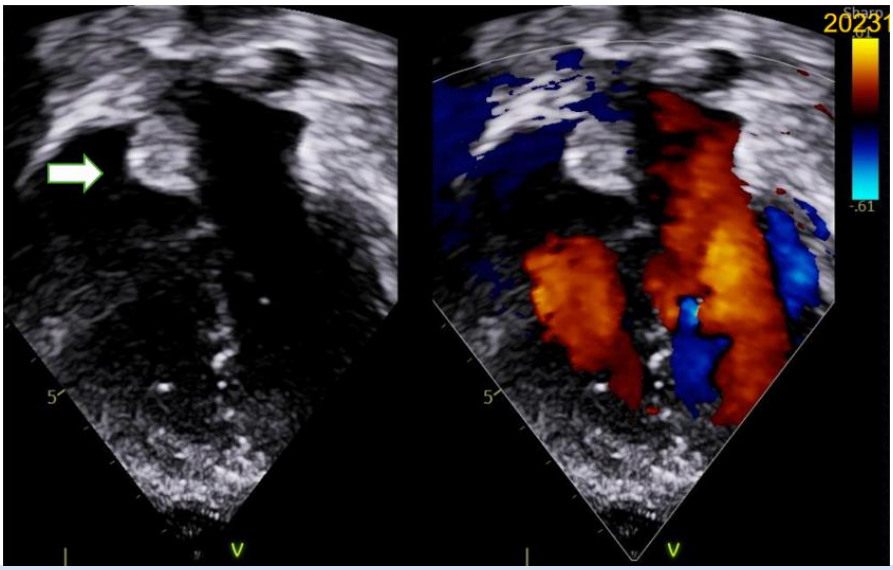

Figure 4: *Post deployment echocardiogram showing device in situ and no residual shunt*

The follow-up period extends to approximately two and a half years, during which neither adverse effects from the therapy were noted, nor any new ischemic strokes.

Discussion

Cryptogenic stroke is a clinical condition characterized by localized or widespread neurological impairment which lacks a discernible underlying cause even after comprehensive diagnostic assessments.(7) With a high prevalence in the general population of approximately 25%, and a prevalence in the cryptogenic stroke population approaching 40%, the propensity of a PFO to precipitate or enable stroke, especially in young, otherwise healthy individuals, has been debatable.(8) High quality research in the paediatric population is lacking and most of the data is extrapolated from adults.

There are several ways to investigate a suspected PFO. These include Transesophageal echocardiogram (TEE) with color Doppler, TEE with agitated saline injection, Transthoracic Echocardiogram (TTE) with color Doppler, TTE with agitated saline injection (bubble contrast study), and Transcranial Doppler (TCD).

The probability that a PFO incidentally identified during patient's evaluation and it is etiologically related to the arterial ischemic stroke or not, depends on the patient's age, presence of traditional risk factors, and location of cerebral infarct.(9) Therefore, there have been efforts to isolate the specific patient characteristics that could be important in patient selection in therapeutic decision-making. The approach incorporates an evaluation for other possible causes of ischemic stroke, PFO features, and methods (ie, the Risk of Paradoxical Embolism [RoPE] score and PFO-associated stroke causal likelihood [PASCAL] classification) that estimate the likelihood of paradoxical embolism through a PFO as the mechanism of the stroke. There are certain clues from history including specific the circumstances immediately preceding the event that might increase right-to-left shunt flow through a PFO, such as straining, coughing vigorously, or lifting or pushing a heavy object. Presence of risk factor for deep venous thrombosis (DVT), such as prolonged immobility can raise concern for paradoxical embolism. However, absence of these features does not exclude paradoxical embolism.

By definition, PFO-associated stroke is embolic. An embolic

mechanism is especially likely when neuroimaging reveals infarcts in multiple vascular territories or a single wedge-shaped infarct involving cortex and the underlying subcortical white matter. With embolic stroke, the neurologic deficit is typically maximal from the onset, with a possibility of rapid improvement if there is spontaneous recanalization.

Another important issue is the possible association of stroke recurrence in patients with PFO-related stroke, as seen in our patient and no similar episodes were noted after PFO closure. The Risk of Paradoxical Embolism (RoPE) score, as shown in the table (Table 1), estimates the probability that a PFO is incidental or pathogenic in a patient with a seemingly cryptogenic stroke(10). High RoPE scores, as found in younger patients who lack vascular risk factors and have a cortical infarct on neuroimaging, suggest pathogenic, higher risk PFOs. By contrast, low RoPE scores, as found in older patients with vascular risk factors, suggest incidental, lower-risk PFOs.

Optimal treatment of a PFO with intracardiac shunting to prevent recurrent stroke in children is controversial. Paradoxical embolism as a cause of a cerebrovascular event is a diagnosis of exclusion, which further complicates treatment decisions. There are two strategies for cryptogenic stroke patients with PFO: transcatheter PFO closure after antiplatelet therapy or antithrombotic therapy only (antiplatelet or anticoagulant drug). However, the optimal treatment for the patients is unclear. The 2014 Guidelines for the Prevention of Stroke in Patients with Stroke and Transient Ischemic Attack recommend antiplatelet therapy in patients with an ischemic stroke or TIA and a PFO who are not undergoing anticoagulation therapy (Class I; Level of Evidence B); for patients with an ischemic stroke or TIA and both a PFO and a venous source of embolism, anticoagulation is indicated, depending on stroke characteristics (Class I; Level of Evidence A)(6)

A non-randomized comparison of 308 cryptogenic stroke patients and PFO who underwent percutaneous closure with those that received medical treatment alone suggested that PFO closure may be especially beneficial in patients who have had more than one event in the past.(11) The American College of Chest Physicians evidence-based clinical practice guidelines recommend surgical closure of a PFO RTLS if an AIS occurs secondary to cardio-embolic causes but the recommendation stems from low or very low-quality evidence.(12) A multidisciplinary Italian task force on the management of patients with a PFO and cryptogenic stroke recommends that those with an initial or recurrent ischemic event while on medical therapy (antiplatelet or anticoagulants) should be offered transcatheter closure of the PFO(13) Closure of the PFO may also be considered in patients with an initial stroke who have one or more anatomical (atrial septal aneurysm, large PFO >4 mm, Eustachian valve >10 mm, long PFO tunnel) or clinical (recurrent stroke, multiple ischemic lesions radiologically, thrombophilia, deep venous thrombosis) risk factors with the understanding that the procedure may not prevent recurrence within two years(13) To date, three large, multicentre randomized controlled trials have been published examining PFO closure in the secondary prevention of stroke:

- Closure or Medical Therapy for Cryptogenic Stroke with Patent Foramen Ovale (CLOSURE),(14)
- Percutaneous Closure of Patent Foramen Ovale in Cryptogenic Embolism (PC trial), (15) and
- Closure of Patent Foramen Ovale versus Medical Therapy after Cryptogenic Stroke (RESPECT)(16)

The initial clinical investigations, namely the CLOSURE I and the PC trial, indicated that PFO closure showed no notable decrease in the potential for another stroke or embolic incidents, nor did it substantially impact mortality when contrasted with medical therapy. (14)The RESPECT trial found that in the intention-to-treat cohort, there was no significant disparity in stroke recurrence between the group that underwent closure and the one receiving medical therapy. Pooled Analysis of Completed Randomized Trials comparing PFO closure versus medical therapy in patients with cryptogenic stroke concluded that closure reduced recurrent stroke and had a statistically significant effect on the composite of stroke, transient ischemic attack, and death in adjusted but not unadjusted analyses.(17) Overall, high-quality evidence and robust recommendations for the management of a PFO in conjunction with a stroke in childhood are still awaited.

The rationale we present the current case is that we treated a patient with three documented ischemic events, which were attributed after extensive laboratory and clinical investigation to a PFO. Our treatment modality seems to be in concordance with the most recently adopted treatment policy of such situations, that is closure of the patent foramen ovale.

Conclusion

Paradoxical embolism via a PFO as a cause of TIA or stroke is a diagnosis of exclusion. A young person with a cerebrovascular event merits complete investigations to rule out other etiologies. A PFO can potentially contribute to cryptogenic stroke in pediatric patients. The recent clinical trials showed that PFO closure, followed by antiplatelet therapy for a few months, outperforms sole medical therapy in adult patients. However, high-quality evidence and robust recommendations for the management of a PFO in conjunction with a stroke in childhood are still awaited.

Ethics approval

The patient's father provided written informed consent to be published as a case report. **Acknowledgments**

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Competing interests

No conflict of interest is to be declared by the authors.

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