

Case Report

Patent Foramen Ovale and Stroke in Adolescents - to Close or Not to Close?

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Abstract

Stroke is a rare condition in childhood and about half of the cases are due to an arterial ischemic event. Although the long list of known causes, many cases remain undetermined, so-called cryptogenic strokes. However, increasing evidence indicates that some of these cryptogenic cases can be a result of a paradoxical embolism via a Patent Foramen Ovale (PFO) with a right-to-left intracardiac shunt, but the exact contribution of PFO to stroke or stroke recurrence in childhood remains unclear. Considering this, as a second line of study, a transthoracic and transoesophageal echocardiogram should be done in all cases to rule out a possible right-to-left shunt, such as PFO. Optimal treatment for acute ischemic strokes in children is controversial, with lacking studies. Closure of PFO should be considered as a preventive measure depending on individual risk factors and anatomic features.

We present two cases of a 16-year-old boy and a 17-year-old girl who had an event of cerebral ischemia documented on MRI, and in whom was found a PFO with a shunt, with the remaining exhaustive etiologic investigation all negative. Both of them underwent percutaneous closure of the PFO.

Keywords: Patent foramen ovale; Pediatric arterial ischemic stroke; Right-to-left shunt; Stroke

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Citation: Silva S, Silva CT, Fonseca J, Melo C, Sampaio M, et al. (2019) Patent Foramen Ovale and Stroke in Adolescents - to Close or Not to Close? J Neonatol Clin Pediatr 6: 041.

Received: December 06, 2019; **Accepted:** December 20, 2019; **Published:** December 27, 2019

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Case Report

A healthy 16 year-old boy, presented with neck, chest and right upper limb involuntary movements, followed by headache, vertigo, left tinnitus, nausea, vomiting, blurred vision, tongue tickling and paresthesia of right limbs, with multidirectional nystagmus, ataxia and right dysmetria on examination. There was a family history of stroke in his grandparents. Cerebral Computerized Tomography (CT) revealed a well delimited area of hypodensity located in the superior region of the right cerebellar hemisphere, suggesting a recent ischemic stroke. Cerebral Magnetic Resonance Imaging (MRI) showed bilateral acute ischemic lesions on the cerebellum, with normal vessels and arteries in the angio-MRI. At admission, electrocardiograph monitoring and Transthoracic Echocardiogram (TTE) normal. Basal Transcranial Doppler (TCD) with bubble test showed right-to-left shunt with and without Valsalva manoeuvre. Afterwards, an elective Transesophageal Echocardiogram (TEE) revealed a Patent Foramen Ovale (PFO) with shunt, and he was submitted to a percutaneous catheterization for closure of PFO five months after discharge.

A second case is a 17 year-old girl, with a previous history of migraine and under oral contraceptive, who presented with left brachiofacial hemiparesis, left visual neglect and dysarthria. Previously of that, she had 7 days of headache, with the same characteristics of her normal migraine. Her mother and sister had history of migraine too. CT scan showed an area of acute ischemia in the right frontal cortico-subcortical region, with an image suggestive of thrombus in the right Middle Cerebral Artery (MCA) and an important penumbra zone into its territory. She underwent intravenous recombinant tissue Plasminogen Activator (rtPA) and mechanical embolectomy after 3 hours of the initial presentation. The control CT scan had no hemorrhagic complications. MRI confirmed an acute ischemic event in the territory of MCA. TTE and TEE revealed a PFO with shunt and an ostium secundum interatrial communication. Basal TCD with bubble test confirmed the right-to-left shunt with Valsalva manoeuvre. A percutaneous catheterization with successful closure of PFO and the interatrial communication was performed during the admission.

Both patients underwent complete haematological and biochemical investigations, including coagulation abnormalities and genetic study for thrombophilia, autoimmune, inflammatory and infectious diseases, and doppler ultrasonography of lower limbs, all with normal results. Both patients were started on aspirin, and had complete resolution of symptoms at 18 months of follow-up.

Discussion

Stroke is a rare condition in childhood [1]. Acute Ischemic Strokes (AIS) accounts for about half of all strokes in children [1-2]. Although hospitalizations for AIS in children have been rising in the past decade, with the improvement of medical knowledge, it is likely to be underdiagnosed or misdiagnosed, because of the low level of suspicion and frequent presentation of subtle symptoms that mimic other diseases [1,2]. The most well described risk factors in pediatrics for AIS are congenital heart disease, sickle cell disease, fection and

hypercoagulable states [1]. Cerebral or cervical arteriopathy can be identified in 50% to 80% of cases, corresponding to an independent risk factor [3-5]. Multiple risk factors are present in as many as 25% of children with stroke, which means further investigations are warranted even when one risk factor has been identified [2].

In spite of the long list of known causes and risk factors, the term “cryptogenic stroke” is used to define stroke in 20-30% of children where the etiology remains undefined despite extensive investigations [3,6]. A possible explanation for some AIS in children considered cryptogenic might be a paradoxical embolism in the presence of a right-to-left shunt in the heart such as PFO, with the microemboli going through right atrium into the systemic cerebral circulation [6,7]. Different studies found that the prevalence of PFO among cryptogenic stroke patients is higher than in the general population (40-50% versus 20-25%) [4,5,7]. However, the exact rule of PFO to stroke or stroke recurrence in childhood remains unclear and this should be considered as a diagnosis of exclusion [3,7]. Venous thromboembolism, genetic coagulation disorders or atrial septal aneurysm seems to confer an additional risk to stroke in presence of a PFO [1,3,4,6]. An association between migraine and PFO has been suggested too [3].

There are several ways to investigate a suspected PFO, including TTE, TEE and TCD. TTE with colour doppler remains the initial mandatory investigation for the cardiac assessment of pediatric patients with stroke. TEE with color doppler is semi-invasive procedure, requiring sedation and esophageal intubation, but provides providing high-resolution pictures of the posteriorly left atrium and interatrial septum and is considered the gold standard to investigate the embolic source in stroke. TCD with bubble test detects particulate embolic material or gaseous microbubbles in the cerebral circulation in real time, but does not portray cardiac anatomy [3].

In the absence of age-appropriate safety data or dosing guidelines, children who present with AIS are sometimes treated outside of the recommended guidelines with rtPA or mechanical embolectomy, often extrapolated from data in adult stroke trials [1]. Anticoagulation and/or antiplatelet therapy can be used as prophylaxis. The risk and benefit likely by age and underlying stroke etiology, but again, in children there is a lack of definitive data [1,4,6,7]. In the absence of a deep vein thrombosis or known hypercoagulable state antiplatelet therapy is typically recommended. Modifiable risk factors should be aggressively addressed [4]. The percutaneous closure of PFO with intracardiac shunting to prevent recurrent stroke in children is controversial and should be individualized, based on significant shunting and risk factors. It is considered as a simple procedure with low risk. Patients with large shunts and those with a hypermobile interatrial septum receive particular benefit from PFO closure [6-8].

The mortality rate of AIS in children approaches 4%; over 50% of survivors have persistent neurologic, cognitive or psychiatric deficits and nearly a third of patients develop epilepsy within the first decade after stroke [1-2]. The annual risk of stroke recurrence in patients with cryptogenic stroke is relatively low, about 1% to 2% per year, but that misrepresents what may be a significant accumulated lifetime risk [7].

With the presentation of those two cases we pretend to highlight the importance of a high level of suspicion of stroke in children with neurological symptoms. The earlier diagnosis in the second case of stroke (with more suspicious symptoms on presentation) and PFO allowed respectively the treatment with pharmacologic thrombolysis and mechanical embolectomy and the closure of PFO during the first days of admission. An exhaustive study to exclude all the possible causes of AIS should be done, and paradoxical embolism via PFO with right-to-left shunt should be considered, as well as the execution of TEE. Research about the treatment and prophylaxis of recurrence of AIS in the pediatric population is lacking and should be a priority. Closure of PFO should be considered as a preventive measure depending on individual risk factors and anatomic features.

Conflict of Interest

No conflict of interest is declared by all authors.

Patient Consent

Parental/guardian consent obtained.

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