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Case Report

Cryptogenic stroke in a 5-year-old girl with patent foramen ovale: A rare case

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Abstract

Stroke ranks among the prevalent factors contributing to child mortality. Cryptogenic stroke has been linked with patent foramen ovale (PFO), which has been suggested as a possible route for thrombus, gas bubble, or another particulate that comes through systemic venous circulation to the brain artery. Yet, the most effective approach for managing cryptogenic stroke involving a PFO remains uncertain. This case aims to report a PFO patient with complications of stroke. A 5-year-old girl was admitted to the emergency department at Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia, after experiencing numbness and weakness on her right side and a sudden onset of slurred speech three days before admission. Laboratory findings only showed leukocytosis, while coagulation tests were normal. Non-contrast brain CT revealed an occurrence of cerebral infarction in the left hemisphere. Transcranial Doppler showed no atherosclerosis in cerebral arteries, and carotid Doppler ultrasound results were reported normal. Transthoracic echocardiography showed a PFO with the right-to-left shunt. The patient was treated with an intravenous infusion of citicoline 250 mg twice daily, oral aspirin 80 mg daily, and oral mecobalamin 250 mg daily and was planned to undergo a PFO closure procedure. However, the patient's parents rejected the plan to perform a PFO closure procedure. PFO has the potential to be a contributing factor to cryptogenic stroke among children. PFO closure followed by antiplatelet therapy for a couple of months has been shown to outperform medical therapy alone. However, additional evaluation should be done to cautiously consider the PFO closure procedure in children.

Keywords: Stroke, cryptogenic stroke, patent foramen ovale, children, Indonesia

Introduction

Stroke ranks among the leading factors contributing to child mortality [1]. Between 20% to 30% of individuals diagnosed with ischemic stroke experience cryptogenic stroke [2]. Cryptogenic stroke has been linked with patent foramen ovale (PFO). Notably, between 40% to 50% of patients diagnosed with cryptogenic stroke also exhibit the presence of PFO [3,4].

PFO is a possible route of thrombus, gas bubble, or another particulate that comes through systemic venous circulation to the brain artery. On the other hand, it is a potential place to form an embolic thrombus in situ, which can cause ischemic stroke [5]. Nevertheless, the mechanism of the PFO causing stroke or stroke recurrence is still unclear in pediatric patients [1].

For individuals diagnosed with Cryptogenic Stroke and a concomitant PFO, the preferred treatment involves PFO closure followed by a two-month regimen of dual antiplatelet therapy instead of solely relying on antiplatelet or anticoagulant therapy. However, the optimal treatment is unclear [6,7]. This case aims to report a PFO patient with complications of stroke.

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Case

A 5-year-old girl was admitted to the emergency department of Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia, presenting with numbness and weakness on her right side and a sudden onset of slurred speech three days before hospital admission. The patient felt the complaint after playing with her friends. There were no complaints of chest pain or difficulty in breathing. The patient was born full-term without complications, had no chronic disease and had neither diabetes mellitus nor hypertension.

On arrival, her blood pressure was 100/60 mmHg, heart and respiratory rates were 64 beats per minute and 24 cycles per minute. The temperature was 36.9°C and oxygen saturation was 96% with room air. Physical examination showed the seventh cranial nerve paresis with peripheral type of lesion. Muscle strength examination of the right arm and leg showed right-side weakness of the body. Blood examination revealed leukocytosis with 14,900/mm^3, hemoglobin of 11.9 g/dl, and platelet count of 369,000/mm^3, while the electrolytes were normal. Kidney function tests were normal, and coagulation tests were normal as well.

The chest X-ray came out normal. A non-contrast brain CT showed a left hemispheric cerebral infarction (**Figure 1**). Then, transcranial Doppler was performed on the patient, in which no atherosclerosis in cerebral arteries was found. Carotid Doppler ultrasound results were also reported to be normal.

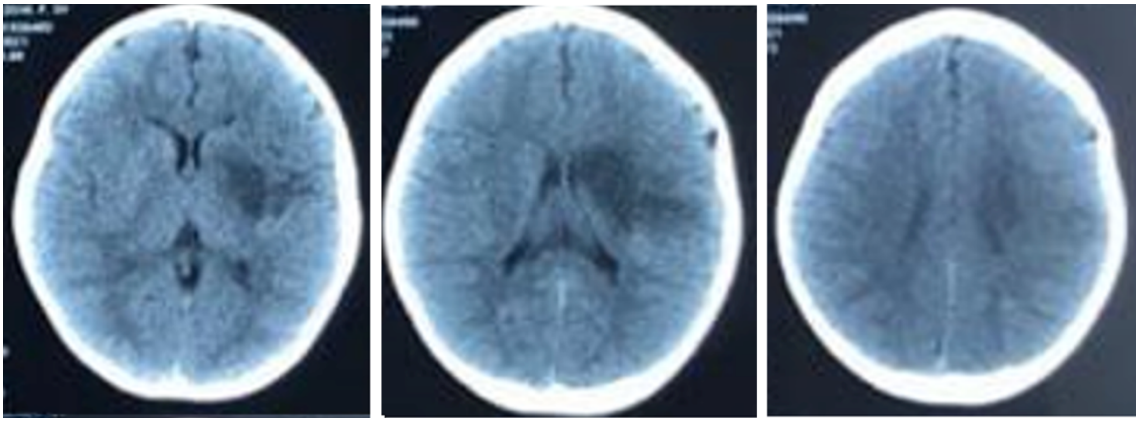

Figure 1. Non-contrast brain CT showed a left hemispheric cerebral infarction.

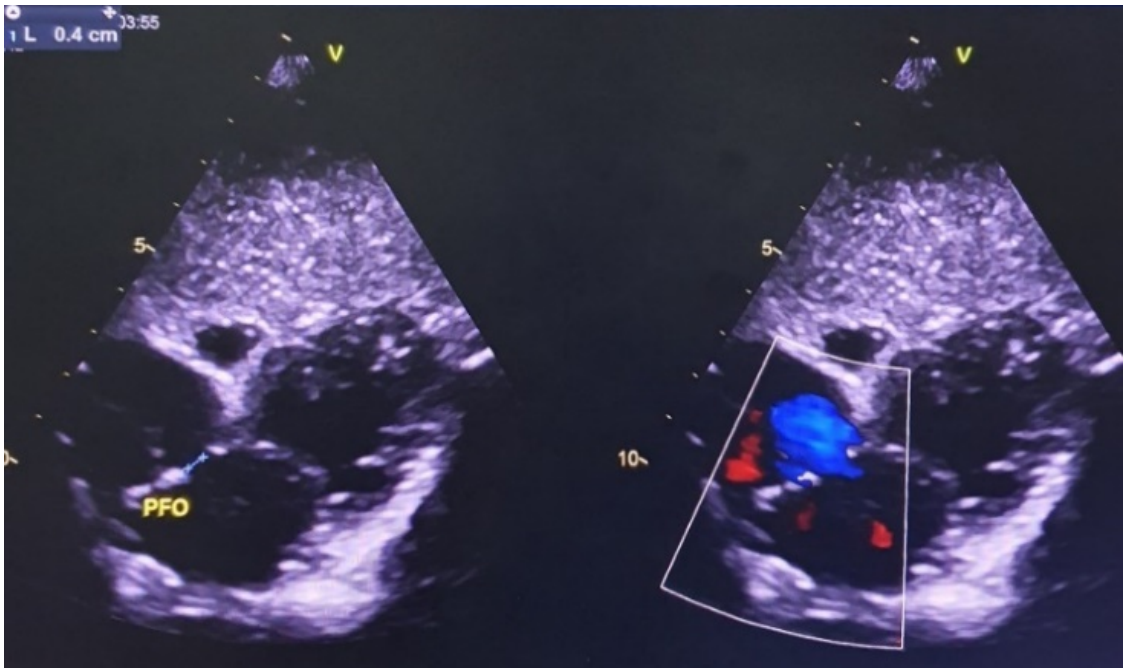

Figure 2. The transthoracic echocardiography showed a PFO (4 mm) with the right-to-left shunt.

Transthoracic echocardiography (TTE) was carried out based on a consideration of a paradoxical embolism that has caused the ischemic stroke in this patient. The examination showed a 4 mm in diameter PFO with the right-to-left shunt (**Figure 2**). The patient was then diagnosed with cryptogenic stroke and a PFO and was treated with an intravenous infusion of citicoline 250 mg twice daily, oral aspirin 80 mg daily, and oral mecobalamin 250 mg daily. The medical plan for the patient involved conducting a PFO closure procedure. However, the patient parents rejected the plan to perform a PFO closure procedure due to financial.

On day 5 of hospitalization, the patient exhibited clinical improvement. The patient was discharged with antiplatelet therapy (oral aspirin 80 mg once daily) and oral citicoline 250 mg twice daily. In addition to physical rehabilitation and language therapy. The patient's motoric strength improved after a week of rehabilitation and therapy.

Discussion

Cryptogenic stroke is a clinical condition characterized by localized or widespread neurological impairment, determined by the location of the lesion and confirmed through initial examination using brain CT or magnetic resonance imaging (MRI). This condition lacks a discernible underlying cause even after comprehensive diagnostic assessments [2,8,9]. In this case, the brain CT showed a left cerebral infarction. On the other hand, some diagnostic procedures were normal, including a laboratory test, transcranial Doppler, and carotid Doppler ultrasound. The examination of murmurs or other medical issues during childhood, which requires transthoracic echocardiography (TTE), frequently detects PFO.

The excellent quality of the subcostal acoustic window of TTE, whether with or without contrast saline, is sufficient for diagnosing a PFO due to its superior acoustic characteristics [10,11]. The transseptal flow by color Doppler is needed to confirm the PFO. Furthermore, the TTE with contrast saline with an adequate Valsalva maneuver improves the visualization of the PFO shunt [10,11]. TEE utilizing agitated saline contrast remains the established reference for diagnosing PFO [1]. We performed TTE with subcostal acoustic window and transseptal flow by color Doppler to detect the PFO.

The likelihood of experiencing another stroke in individuals diagnosed with ischemic stroke increased three-fold in patients with PFO [12]. For younger patients with fewer atherosclerotic risk predictors, a PFO is a potential stroke source. This relationship suggests that cryptogenic stroke might be attributable to paradoxical emboli originating in the systemic venous circulation, traversing to the systemic arterial circulation via a PFO in the atrial system through a right-to-left shunt [2,13-15]. This is by this patient, where transthoracic echocardiography showed the PFO and a right-to-left shunt.

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 [6,7,16]. A recent meta-analysis of randomized controlled trials comparing PFO closure to medical treatment revealed that individuals experiencing cryptogenic stroke or TIA in conjunction with a patent PFO and treated with PFO closure were inclined to a lower likelihood of recurrent ischemic stroke when compared to patients who exclusively received medical intervention [17]. Another meta-analysis showed that the likelihood of experiencing another stroke in individuals with cryptogenic stroke/TIA increased 6.3-fold in patients who got medical therapy compared to individuals who received PFO closure [18]. In this case, the patient was treated with an intravenous infusion of citicoline 250 mg twice daily, oral aspirin 80 mg daily, and oral mecobalamin 250 mg daily.

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 [19,20]. In another clinical trial, 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 [21]. Nonetheless, the long-term follow-up data indicated that PFO closure notably lowered the occurrence of recurrent stroke compared to medical therapy [22].

The recent trials, the CLOSE trial, and the Gore-REDUCE trial exhibited a lower incidence of recurrent ischemic stroke in the closure group than in the medical therapy group [23,24]. In children, complete evaluation of neuroimaging findings suspicious of embolism, prothrombotic disorders, high-grade right-to-left shunt, and abrupt onset of ischemic stroke should be evaluated before considering percutaneous PFO closure [25]. Nevertheless, due to the absence of clinical trials involving the pediatric cohort that elucidate the advantages of PFO closure compared to medical therapy, a meticulous assessment of the balance between benefits and potential drawbacks associated with the therapeutic intervention is essential. For specific youngsters who have encountered cryptogenic stroke and exhibit a noteworthy right-to-left shunt with no concurrent risk factors, recommendations from experts on pediatric ischemic stroke propose an astute contemplation of PFO closure in the pediatric population [26]. In this case, the patient was given medical treatment and was planned to undergo PFO closure. However, the patient's parents rejected the plan to perform a PFO closure procedure because of their financial problem.

Furthermore, further clinical trials are requisite to elucidate the importance of a right-to-left shunt in pediatric patients with ischemic stroke. Additionally, these trials are necessary to delineate the precise role and establish the criteria for implementing percutaneous PFO closure in children suffering from cryptogenic stroke [25].

Conclusion

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, additional evaluation should be made to cautiously consider the PFO closure procedure in children.

Ethics approval

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

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Competing interests

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

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Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

How to cite

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