

Unusual Presentation of Moyamoya Disease with Seizure and Syncope Successfully Managed with Magnesium Sulfate: A Case Report

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Abstract

Idiopathic pulmonary hypertension is a rare lung vasculopathy with an unknown etiology. Moyamoya disease (MD) is characterized by diffuse distal intracranial stenosis. MD associated with pulmonary hypertension is a rare presentation. Here we report a child who presented with recurrent and intractable syncope and seizure that was diagnosed with MD with pulmonary hypertension. The episodes of syncope and seizure successfully reduced with administration of Magnesium sulfate and Sildenafil.

Keywords: moyamoya, syncope, pulmonary hypertension, pediatrics

Introduction

The present report described a case of Moyamoya disease in a child with idiopathic pulmonary hypertension which responded to magnesium sulfate therapy.

The spontaneous occlusion of the circle of Willis or Moyamoya syndrome is a chronic vascular disease with unknown etiology which commonly seen in East Asian countries. The prevalence of the disease has been reported to be 16.1 in 100000 (1). The disease is manifested by transient ischemic attacks, headache, confusion and epilepsy. However, some clinical symptoms including mental decline, involuntary movements and seizure are more common in pediatric population (2). It has been recently suggested that single nucleotide variants in *RNF213* gene is associated with increased risk of developing the disease and genetic testing is now considered for excluding differential diagnoses for Moyamoya syndrome (3). Although cerebrovascular vessels are the main affected organs in pediatric population, it has been rarely reported that other vascular complications may be accompanied alongside of the brain involvement (4). The treatment of this vascular disorder is controversial and the management strategies mainly depend of controlling the clinical symptoms and prevention of thrombotic events (5). The present describes a case of moyamoya disease in a child with idiopathic pulmonary hypertension responded to magnesium sulfate.

Case Report

A 4.5 year old baby from a consanguineous couple, referred with history of recurrent Seizure and Syncope during physical activity and bruising in contact activities which did not response to Phenobarbital treatment. The patient referred for neurologic consultation and anti-epileptic agents consist of Phenobarbital and Sodium Valproate were administrated. While the patient's symptoms did not respond to anti-epileptic medications, electroencephalography (EEG) and brain imaging study include brain CT scan and MRI were performed. The EEG was unremarkable while the Brain scan suggested suspicious of Moyamoya disease (MD). Therefore the patient underwent genetic study for Moyamoya disease. The Genetic study detected a pathogenic mutation in *RNF213* gene which has been reported to increase the susceptibility to development of MD.

The cardiac evaluation by 12 lead electrocardiogram (ECG) showed right axis deviation (RAD) and prominent R wave in V1 (Figure: 1), and the chest x ray showed enlargement of the right atrium (Figure: 2).

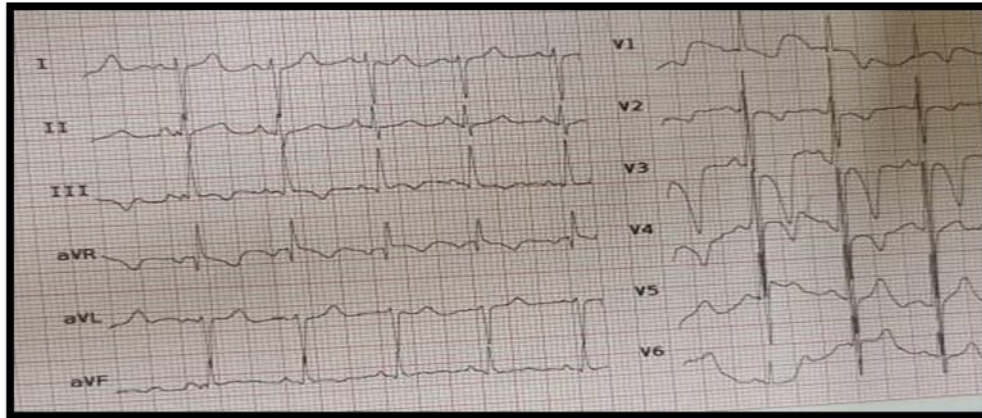


Figure 1: The figure shows 12 lead electrocardiograms with Right axis deviation, right ventricular hypertrophy.



Figure 2: The posteroanterior chest X ray shows enlargement of right atrium and prominent pulmonary artery.

Results & Discussions

The echocardiography study showed dilation in right ventricle and Atrium, Main pulmonary dilation, Mitral Valve billowing, Mild mitral valve regurgitation, Mild tricuspid valve regurgitation, Patent foramen oval (size= 0.3 cm) with right to Left shunt (Table 1).

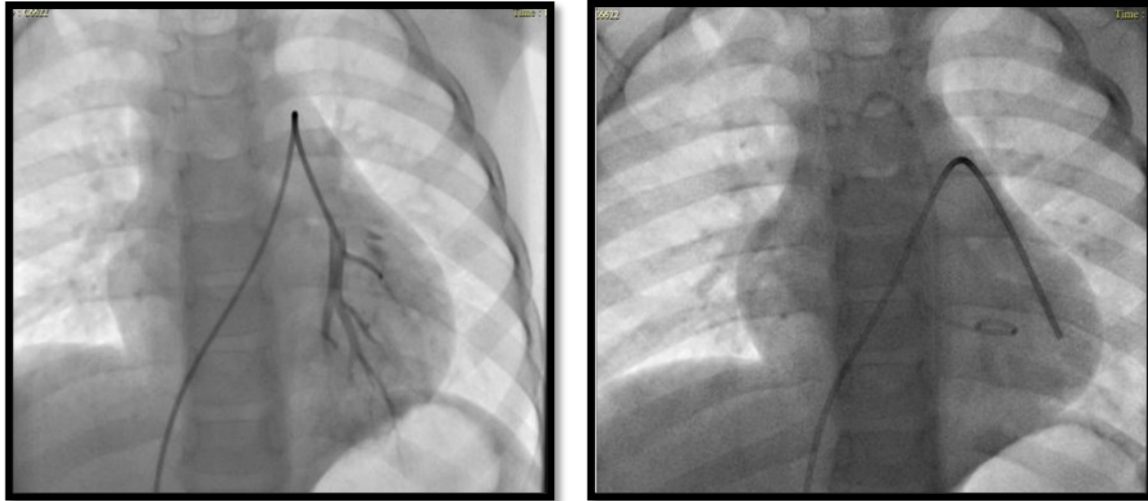
Catheterization study was done for evaluation of pulmonary pressure (Table2) (Figure 3). The PAP (Pulmonary Arterial Pressure) was sub systemic and with elevated Pulmonary Capillary Wedge Pressure (PCWP). The patient had normal thyroid function and the serologic tests for connective tissue disorders and coagulation studies were unremarkable. The patient received Sildenafil (1mg/kg/day) and Magnesium sulfate (200 mg daily) and the episodes of seizure like symptoms and bruising diminished. The dose of magnesium sulfate was reduced to every other day but the symptoms did not return.

Table 1: Comparison of echocardiography findings before and after treatment.

Echocardiography finding	TR PG (mm HG)	PI PG (mm HG)	RV TAPSE (mm)
Before treatment	70	50	18
After treatment	27	15	20

Table 2: Comparison of Catheterization data before and after treatment.

Cath finding	RAP	RVP	PAP	PCWP	LVP	AOP	O2 sat%
Before treatment	10/5 (8)	72/0-10	73/27(40)	27	83/0-10	80/40 (55)	100
After treatment	18/8 (12)	83/0-10	85/23(60)	27	136/0-10	134/83 (106)	100

**Figure 3:** Simultaneous pulmonary and systemic pressure in Cath study.

The present report described a case of Moyamoya disease in a child with idiopathic pulmonary hypertension which responded to magnesium sulfate therapy. It has been reported that Moyamoya disease is common in East Asia and is rarely reported in other parts of the world. Although management of the disease is controversial, some suggested the use of magnesium sulfate in these patients. The magnesium sulfate has theoretical vasodilatory effects and was successfully controlled the clinical manifestations of the disease in our patient. Such treatment has been usually used in pregnant patients who develop the disease during their pregnancy rather than pediatric population (6). Most of the Moyamoya cases in pediatric population present with syncope and seizure like episodes. Recent studies suggested that involvement of brain and lung during Moyamoya disease could be predicted by genetic testing. While heterozygote mutations in *RNF213* has been reported to be associated with classic cerebral vascular disease, a study by Fukushima et al. reporting two unrelated cases of Moyamoya disease in pediatric population suggested that homozygous mutation of p.Arg4810Lys in *RNF213* gene could be responsible for development of extracranial vasculopathies including pulmonary vasculopathy (7). On the other hand, it has been reported that some pulmonary manifestations including peripheral pulmonary arterial stenosis can be associated with homozygous mutations of *RNF213* regardless of developing the symptoms of Moyamoya disease (8). However, most of the reported cases in the literature have reported co-occurrence of Moyamoya disease with pulmonary manifestations carrying different *RNF213* mutations. Kramert et al. reported a case of Moyamoya disease in 10 years old girl which was initially diagnosed because of recurrent syncope episodes (4). Similar to our report, their patient had late onset pulmonary arterial hypertension which was diagnosed by hypertrophy of right ventricle which was confirmed by cardiac catheterization. They treated their patient with combination of Amlodipine and Sildenafil with a platelet inhibitor. After 2 years, they escalated their treatment to Bosentan because of progression of the disease (4). Further genetic study of their patient revealed heterozygous *c.12341C>T* mutation in the *RNF213* gene (4). Kizilkaya et al. reported a 15 years old boy with recurrent syncope episodes who was diagnosed to have right ventricular hypertrophy on echocardiography. Their patient was treated with Carbamazepine for focal seizures in his early childhood. In contrast to our patient, they retrospectively diagnosed their patient by reviewing his previous cranial magnetic resonance imaging indicating small collateral vessels striking in brain hemispheres. They confirmed the diagnosis of Moyamoya syndrome by cranium magnetic resonance angiography without performing any further genetic study. Their patient tolerated Bosentan and Aspirin as a treatment for the disease (9). While the clinical symptoms of Moyamoya disease can be controlled by medications in many cases, there are some reports regarding the lethal outcomes of the disease in adulthood. Takahashi et al. reported a case of lethal Moyamoya disease presented in a 24 years old who was diagnosed to have Moyamoya disease when he was 16 and idiopathic pulmonary hypertension since 10 years of age (10). Their patient was managed by Beraprost and Warfarin until 24 when the patient died because of sudden cardiopulmonary arrest (10).

Conclusion

The present report demonstrated a case of Moyamoya disease a children who developed idiopathic pulmonary hypertension carrying *RNF213* mutation. Although the co-occurrence of these clinical features are rare; the affected patients can be successfully managed by magnesium sulfate.

Conflict of Interest

The authors declare no conflict of interest.

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