Case Report

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Paediatric Moyamoya disease: acute presentation with fever and confusion in an 8-year-old: a case report

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Introduction and importance: Moyamoya is a chronic vaso-occlusive cerebrovascular disorder which involves internal carotid artery and its proximal branches, forming compensatory Moyamoya vessels. It may manifest with diverse symptoms, but early detection is crucial for a favourable prognosis.

Case presentation: The authors present a case of an 8-year-old child who presented to the emergency with acute onset fever and confusion in speech. Although the symptoms were vague, she was advised for a thorough investigation. MRI of the brain revealed an infarct on the brain that raised suspicion of a vaso-occlussive disorder. Subsequent magnetic resonance angiography and digital subtraction angiography revealed underlying Moyamoya disease.

Clinical discussion: Although the initial diagnosis of Moyamoya disease can be challenging, prompt diagnosis and simple medical measures like single antiplatelet regimens are useful for secondary ischaemic prevention.

Conclusion: This case highlights the essence of considering Moyamoya disease as one of the differentials while dealing with children presenting with subtle cerebrovascular symptoms.

Keywords: Case report, cerebral angiography, child, Moyamoya disease, stroke

Introduction

Moyamoya disease is a chronic occlusive cerebrovascular disease characterized by progressive stenosis or occlusion of intracranial part of internal carotid artery (ICA) and its proximal branches[1]. The resulted hypo-perfusion is compensated by Moyamoya vessels which are abnormal, fragile and fibrous root-like collateral vasculature that develop around the stenotic vessels[2]. The name arises from Japanese word "Moyamoya" that translates to 'something hazy, like a puff of cigarette smoke floating in the air' seen on cerebral angiography[3]. It usually involves the anterior circulation more than posterior and bilateral vessels more than unilateral[1]. Previously, Unilateral disease were classified as Moyamoya syndrome, but the recent diagnostic criteria (2021) states both unilateral and bilateral cases can be diagnosed as Moyamoya disease[4]. Moreover, contralateral development is seen with almost 40% cases with initial unilateral presentation[5].

HIGHLIGHTS

- This case represents first paediatric onset Moyamoya disease reported from Nepal.
- Moyamoya disease should be considered as a differential even when patients present with subtle symptoms that may be easily overlooked.
- Moyamoya is a disease of complex pathogenesis but it can be managed with simple medical measures upon early diagnosis.

The exact aetiology of the disease is obscure, but is thought to be due to genetic, environmental or idiopathic causes, or a combination of three. Genetic studies have linked RNF213 gene, particularly its Arg4810Lys variant as the probable gene involved[6,7]. A clear racial variation exists with higher incidence among Asians compared to Whites because the Whites carry a less common 'non-Arg4810Lys' variant of the gene[6]. The highest incidence is found in Japanese population affecting 3 individuals per 100 000 population, whereas it is only 0.086 per 100 000 among Americans[2]. Moyamoya shows bimodal age distribution with the first peak at 6–15 years and second peak at 31–40 years of age [8]. The differentials for children presenting with fever and confusion include meningitits, encephalitis, seizure disorder, electrolyte imbalance etc[9].

In this case report, we present a case of an 8-year-old female child with Moyamoya Disease, Suzuki Angiography grade of Stage 2. To the best of our knowledge, this is the first reported case of paediatric onset Moyamoya Disease from Nepal. This case report is in line with CARE guidelines[10].

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Case presentation

An 8-year-old female, presented to the Emergency Department of our tertiary care centre with complaint of abnormal behaviour in terms of confusion in speech, a day before the presentation. Otherwise a healthy individual with no past medical/surgical history, the patient initially developed fever that lasted for four days accompanied by decrease in appetite. Following this, there was an episode of abnormal behaviour, as confusion in speech that lasted for about an hour. However, there was no history of headache, dizziness, loss of consciousness, abnormal body movements, apraxia following the event. There is negative history of cerebrovascular incidents in the family. There exists no comparable historical precedent. The birth history of the patient is uneventful; the baby was born via a normal vaginal delivery and all the developments milestones were achieved within normal age. Given this unusual presentation of the child, she was suggested for a thorough evaluation. The major events in the case are presented in the timeline below (Fig. 1).

Diagnostic assessments

Physical assessment at the time of presentation showed 15/15 Glasgow Coma Scale (GCS), all her vitals were within the normal range. The patient was well oriented to time, place and person. No motor deficits were noted with 5/5 power in all limbs. Sensation was found intact and equal bilaterally. Deep tendon reflex was 2 + bilaterally. Cerebellar function was found intact with no gait abnormality. No anomalies were found on Echocardiogram with normal ejection fraction. Carotid Doppler showed normal flow and calibre of bilateral common carotid and internal carotid arteries with no plaques.

An IV line was set up, intravenous fluids and paracetamol were administered to control fever. Necessary laboratory tests including complete and differential blood counts, serum electrolyte levels, renal function tests were sent, all of which were within normal range. With consideration of appropriate differential diagnosis, MRI of the brain was sent showed multifocal acute infarct in the left fronto-parietal region involving the internal and external watershed territory (Fig. 2). One day after MRI, on magnetic resonance angiography (MRA), diffusely narrow calibre of left distal ICA, left A1 ACA, left Middle cerebral Artery and its branches were noted. A digital subtraction angiography (DSA) was planned for the next day for the confirmation of findings that were consistent with Moyamoya Disease, which showed stenosis of supraclinoid segment of left ICA along with stenosis of Proximal A1, Proximal M1, distal M1 and M3 segments reformed by perforator collaterals from posterior circulation (Fig. 3).

With the consideration of radiological findings, a diagnosis of Moyamoya disease, Suzuki Grade 2 was made.

Treatment

She was prescribed 75 mg aspirin once daily as a secondary prophylactic therapy for stroke. Her fever was managed with antipyretics and adequate rest. At the time of discharge, she was hemodynamically stable with GCS 15/15.

Follow-up

Initially, she was called for follow-up every month for 2 months. There were no similar episodes on subsequent visits with negative history of any cerebrovascular symptoms. At present, the patient is under follow-up every two months.

Discussion

Moyamoya disease is a rare cerebrovascular disease with the highest incidence in Asia, especially Japan followed by Europe, North and South America, and Africa[11,12]. Despite being an Asian country, only three cases have been reported from Nepal, that too in adults. This is the first reported case of Childhood-onset Moyamoya Disease from Nepal.

The aetiology of Moyamoya is still largely unknown, but studies have suggested genetic, immunologic and environmental linkages. RNF213 gene is the major susceptibility gene and has synergistic relationship with environmental factors[6]. Recently, evidence of infiltration of T cells and Macrophages in the intima of thickened stenotic vessels suggests an immunological role for the disease[13]. The risk for MMD was found to be 132-fold higher in individuals with affected first degree relatives than in those with no familial history[14]. However, our patient has no history of similar cerebrovascular events in the family, suggesting sporadic onset in our case.

The clinical symptoms of Moyamoya disease in children were divided by Maki *et al.*[15] into four categories: Infarction type, Transient ischaemic attack (TIA), Bleeding type and Epileptic type, where Infarction and TIA types account for 70–80% of cases. Our patient falls under the infarction type according to this classification. The common presenting symptoms in children include headache, fever, seizures, blindness, and aphasia[15,16]. A retrospective review by Sana Shoukat *et al.*[16] described fever as the most common symptom in children, which is consistent with our findings. As per our knowledge, there is not adequate literature showing a direct relationship between fever in Moyamoya disease. However, Shoukat *et al.*[16] have hypothesized that hyperthermia induces vasoconstriction which leads to

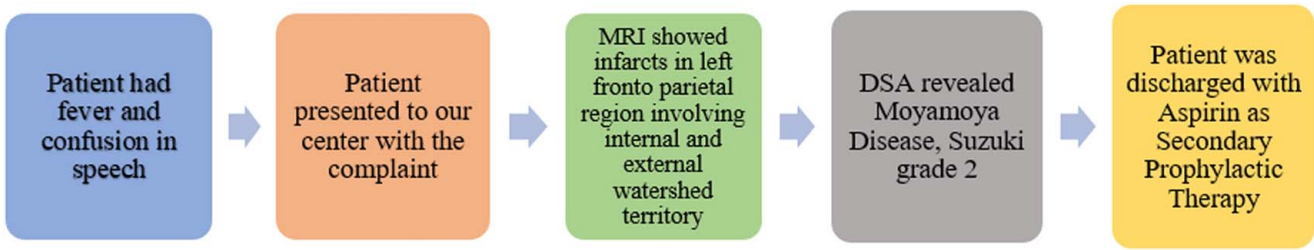

Figure 1. Timeline showing major events. DSA, digital subtraction angiography.

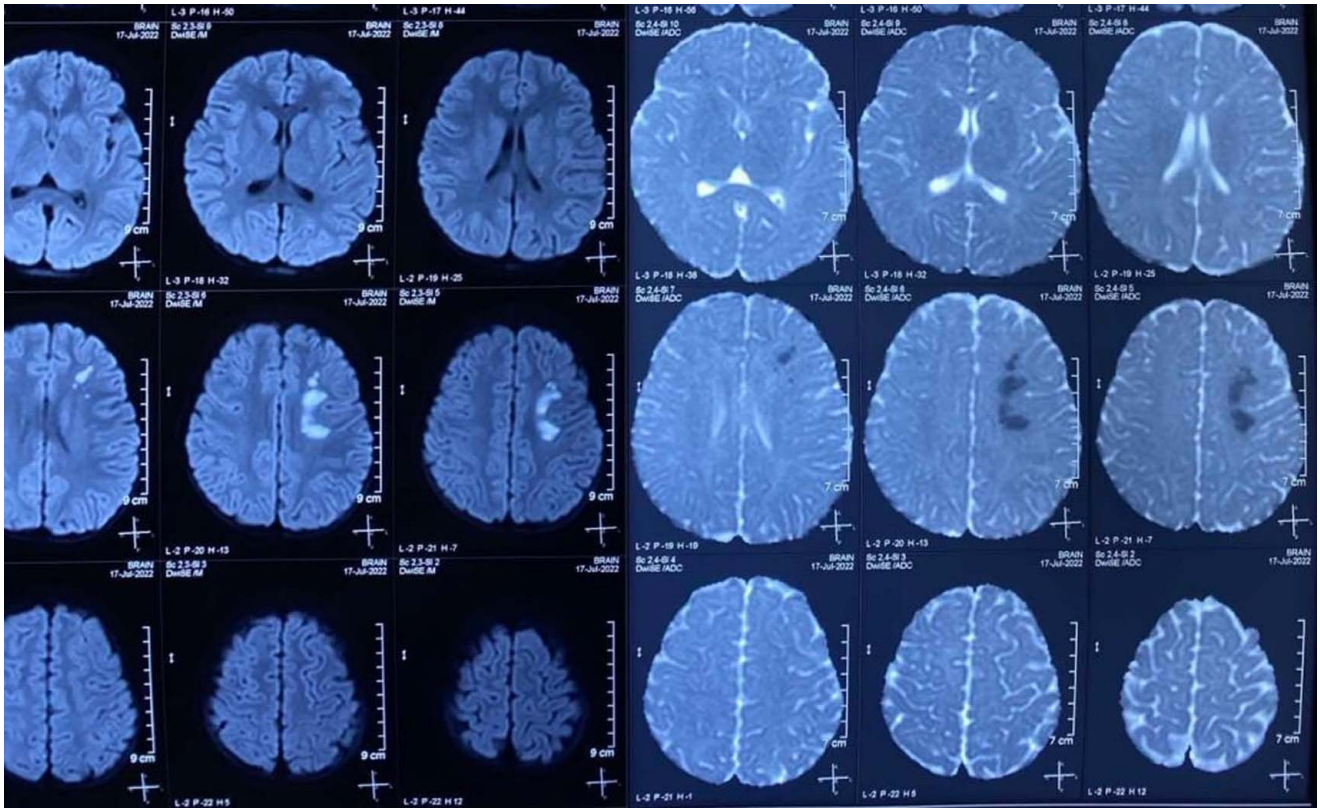

Figure 2. Magnetic Resonance Imaging of the brain (DWI/ADC and T2WI axial images) showing multifocal ACA/MCA watershed infarct in left fronto-parietal region.

hypo-perfusion in the patient, which in turn would trigger the symptoms in the patient. This is solely a hypothesis and would require further controlled experiments for confirmation. In our case, fever and speech confusion were both noticed by the parents, and other symptoms could have been missed due to the child's inability to explain them.

The clinical diagnosis is made by cerebral angiography, where stenosis or occlusion of arteries centred on the internal carotid

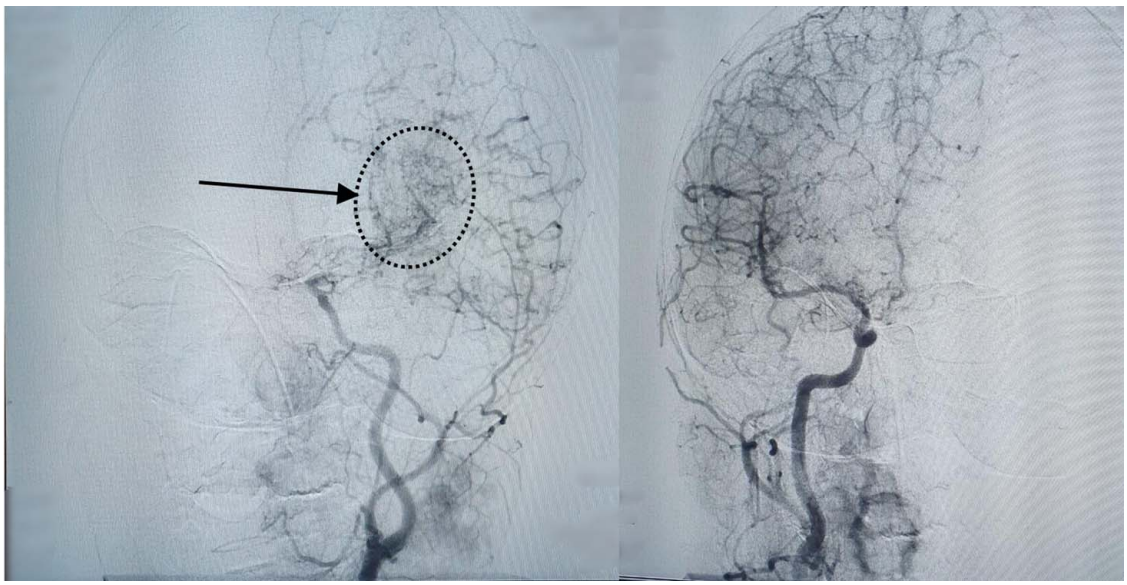

Figure 3. Digital Subtraction Angiography showing stenosis in left terminal ICA after giving PCOM branch. Compensatory basal artery collaterals seen as puff of smoke. ICA, Internal Carotid artery; PCOM, Posterior Communicating Artery.

artery with appearance of Moyamoya vessels or presence of similar findings under MRI/MRA with decrease in the outer diameter of the terminal portion of the ICA and the horizontal portion of the middle cerebral artery under heavy T2-weighted MRI[4]. Our case was initially evaluated with MRI which showed multifocal acute ischaemic infarct in the fronto-parietal region involving internal and external watershed territory. Following this, an MRA was done, the findings of which were confirmed using DSA, which showed stenosis in the Supraclinoid Segment of left ICA along with stenosis of Proximal A1, Proximal M1, distal M1 and M3 segments reformed by Moyamoya vessels from posterior circulation. Conte and colleagues describe an interesting case of Moyamoya disease in an 18 month old presenting with features of acute febrile gastroenteritis, the diagnosis of which was made months later only after the patient presented again with left sided hemiparesis. Picking up the condition early can prevent such adverse sequela to the disease[17].

The patients with Moyamoya disease can be managed both surgically and medically. The surgical treatment includes Direct, Indirect and Combined Revascularization techniques[18]. It is well known that MMD worsens over time; those who are treated conservatively have a disease progression rate of about 20% after 6 years. Although better outcomes have been observed with surgical revascularization procedures, with partial or complete resolution of ischaemic symptoms in 87% of the patients, they are indicated when recurrent symptoms of cerebral ischaemia are observed[19]. As our case presented with a single episode of ischaemic symptoms, it was managed medically. Studies have found single antiplatelet regimen with Aspirin, Clopidogrel, or Cilostazol to be useful for secondary ischaemic prevention in Moyamoya patients with cerebral infarct or TIA[20]. Our patient was similarly managed with a single antiplatelet therapy consisting of Aspirin. Our patient was discharged after improvement with conservative treatment and recovered well with no neurological deficits in the subsequent follow-up visits.

On contrast to other reported cases in the literature, we present this case of Moyamoya disease in a child who presented with features resembling an underlying infectious pathology; possibly encephalitis or meningitis. However, upon thorough investigation, underlying Moyamoya disease could be successfully diagnosed. Our case underscores the critical importance of considering Moyamoya disease as one of differentials while attending patients with subtle cerebrovascular symptoms, or else such cases may be easily missed.

Conclusion

Moyamoya disease is a rare cerebrovascular condition, with limited reported cases in Nepal. The case described is the first reported childhood-onset case in Nepal. Early recognition and diagnosis are crucial for appropriate management. Surgical revascularization procedures have shown favourable outcomes, while medical management with antiplatelet therapy are suitable for selected cases. Regular monitoring and individualized treatment approaches are essential for optimal outcomes in children with Moyamoya disease.

Ethical approval

Not applicable.

Consent

Written informed consent was obtained from the patient's informant for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor- in- Chief of this journal on request.

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Author contribution

D.K.: conceptualization, methodology, visualization, supervision, writing—original draft. P.P.: conceptualization, investigation, validation, writing—original draft, writing—review and editing. S.P.: conceptualization, writing original draft, writing—review and editing, visualization, project administration. S.K.S.: conceptualization, writing—original draft, writing—review and editing, resources, supervision. S.R.: conceptualization, project adminstrationresources, writing—original draft, writing—review and editing. S.B.: resources, supervision, writing—review and editing.

Conflicts of interest disclosure

There is no conflict of interest.

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Our paper was not invited.

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