CASE REPORT

Exploring the Intersection of Autism and Moyamoya Angiopathy: A Case Report

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Received on: 24 April 2024; *Accepted on:* 02 June 2024; *Published on:* 26 July 2024

Abstract

Aim and background: This case report explores the potential overlap between autism spectrum disorder (ASD) and moyamoya angiopathy (MMA). While the association between ASD and ischemic stroke is established, the link to MMA remains unclear. This case highlights the importance of recognizing ischemic stroke, particularly MMA, as a possible comorbidity of ASD.

Case description: A 6-year-old girl presented at the Psychiatry Outpatient Department (OPD) with complaints of behavioral and communication disturbances with a prior history of MMA and revascularization surgery. Following school enrolment, her symptoms worsened, including increased irritability, temper tantrums, and self-injurious behaviors. A comprehensive evaluation confirmed ASD and led to adjustments in her medication regimen. Consent was obtained from the parents for the publication of the case.

Conclusion: This case suggests a potential link between ASD and MMA. Early detection and intervention for both conditions are crucial for improved outcomes.

Clinical significance: This case emphasizes the need for healthcare professionals to consider ischemic stroke, especially MMA, in the evaluation of ASD.

Keywords: Autism spectrum disorder, Case report, Childhood stroke, Comorbidity, Genetic, Moyamoya.

Indian Journal of Private Psychiatry (2024): 10.5005/jp-journals-10067-0181

Introduction

Autism spectrum disorder (ASD), previously known as the pervasive developmental disorders, is a phenotypically heterogeneous group of neuro-developmental syndromes, with polygenic heritability, characterized by a wide range of impairments in social communication and restricted and repetitive behaviors.[1]

The current global prevalence of autism is supposed to be 1 in 100 childrens as reported by the World Health Organization (WHO).[2] According to a report published by the Rehabilitation Council of India, the prevalence rate is suspected to be approximately 1 in 500 or 0.20% or more than 2,160,000 people in India.[3] ASD and features of ASD are comorbid with several known genetic disorders. Multiple neurological disorders have been known to be associated with ASD. However, the association of moyamoya disease (MMD) or moyamoya syndrome (MMS) with ASD is not very well established.

The Japanese term "MOYAMOYA" denotes a state of haziness, resembling the dispersion of cigarette smoke in the air. Moyamoya angiopathy (MMA) represents a distinctive cerebrovascular pathology characterized by the progressive stenosis or occlusion of the distal segments of the internal carotid arteries (ICAs) and their terminal branches, concomitant with the emergence of a delicate network of collateral vessels at the cranial base. Diagnosis primarily hinges on radiological angiographic modalities. While MMD commonly manifests without an identifiable etiology, referred to as idiopathic, it can also be correlated with acquired or hereditary factors, designated as MMS.[4,5]

A single-centered cross-sectional study done over 5 years (2016–2021) in Eastern India revealed that 1.56% of all stroke and transient ischemic attack (TIA) were found to have MMA. 46.9% of those cases were childhood onset MMA.[6]

Even with the staggering number of cases in India, there are few data suggestive of an overlap of MMA and ASD. Hence, we report a case of ASD diagnosed in a child who had undergone revascularization surgery for MMA.

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How to cite this article: Mondal A, Bhuyan D, Gohain R, *et al*. Exploring the Intersection of Autism and Moyamoya Angiopathy: A Case Report. Ind J Priv Psychiatry 2024;18(2):91–93.

Source of support: Nil

Conflict of interest: None

Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

Case Description

A 6-year-old girl, coming from a middle-income, urban background nuclear family, suddenly became drowsy and was unable to recognize family members and this was followed by a sudden onset left sided upper and lower limb weakness, there was difficulty in following parents' commands and also problems in vision as manifested by inability to track objects. Magnetic resonance imaging (MRI) brain with magnetic resonance angiography (MRA) showed features consistent with MMD involving the supra clinoid part of both internal carotid arteries and posterior cerebral arteries with bilateral large acute infarct in temporal-parietal occipital lobes. A diagnosis of bilateral MMA was confirmed. She underwent right followed by left mini temporal craniotomy and superficial

temporal artery (STA)—middle cerebral artery (MCA) direct anastomosis and encephalo-dural synangiosis. Her recovery was satisfactory with reversal of symptoms and she was discharged with tablet levetiracetam and tablet Aspirin 75 mg and physiotherapy. However, 2 days after discharge she was admitted again with complaints of excessive irritability, restlessness, and inability to fall asleep. She was managed conservatively with tablet risperidone and tablet melatonin and was discharged.

Six months later she presented to the Neurosurgery Outpatient Department (OPD) for follow-up. She has been manageable so far and coming for regular follow-ups but since she was admitted to first standard in a new school last month, her symptoms have worsened and have raised significant concern among the parents. The parents complained that she has become increasingly irritable in the last 1 month and her temper tantrums have increased than before. During the outbursts, she keeps rolling on the floor, violently moves her extremities, also bites herself and bangs her head on the floor. There has also been one episode of abnormal jerky movement in the past month which, on eliciting proper history, was suggestive of a generalized tonic-clonic seizure. A non-contrast CT scan brain was done to rule out any recent traumatic brain injury. Right parietal gliosis was seen.

She was referred to Psychiatry OPD, Assam Medical College due to these behavioral abnormalities. On eliciting history, it was found that her mother was 36 years old when she was born and she had low birth weight. Her motor and speech developmental milestones were appropriate for her age; however, she would often use a single word repetitively without context as if she was stuck at the same. And also, she would have problems in using the pronouns properly. Often, she would use "you" and "your" while referring to herself. She has never been interested in people including her parents and also liked to stay aloof from children of her own age. She was taken to a pediatrician as parents suspected something odd about her but they were advised not to worry as it might get better with age. In preschool, she has been found to be exceptionally good at memorizing rhymes or tables. However, she has not made any friends in preschool. Her teachers do not have any complaints regarding her but she becomes excessively upset if she does not get to sit at her regular desk at school and creates a fuss. At home also she has some unusual fixations. She always eats with a particular spoon, and when not given, she starts screaming inappropriately.

In the OPD she remained very restless and was flapping both her hands near her face and never established eye contact. The mother reported that these hand movements are relatively new and started after recovery from the surgical procedure; she does that whenever she is annoyed by a particular situation.

With this history of difficulty in communication and restricted pattern of interest, which started in the early developmental period a diagnosis of ASD was established as per Diagnostic and Statistical Manual 5 (DSM-5), and current tantrums and anger outbursts were supposedly episodes of meltdown. Indian Scale for Assessment of Autism (ISAA) was used to ascertain the degree of autism. The score came out to be 110, which is suggestive of moderate autism. Risperidone was stopped and aripiprazole 2 mg was started to control her meltdown episodes. She was advised a complete hemogram, thyroid function test, and electro encephalogram (EEG), and a follow-up was scheduled after 1 month.

A Neurology referral was also given owing to the history of seizures and current CT scan findings. Tablet levetiracetam was stopped and tablet brivaracetam was started along with a short course of tablet clobazam 10 mg/day for 7 days.

On a follow-up visit after a month, her restlessness and irritability had decreased with the new medication, there had been no further seizure episodes and all the investigation came out to be normal. Appropriate behavioral intervention and social skill training were recommended. The consent was obtained from the parents for publication of the case.

Discussion

Historically, one of the major difficulties faced by parents of children with autism in India has been obtaining an accurate diagnosis. Lack of awareness plays a major role in the delay in diagnosis. By the time families of autistic children become aware that there is help available specifically to deal with their needs, valuable time has often been lost.[3]

The link between pediatric ischemic stroke and autism has been well established. In a study conducted by Sundelin et al., it was found that individuals who experienced pediatric ischemic stroke faced a threefold higher likelihood of developing ASD later in life (increasing to 3.3-fold for childhood stroke). Additionally, first-degree relatives of children who had suffered an ischemic stroke exhibited an elevated risk of autism compared to controls, primarily driven by the heightened risk observed among siblings. This increased risk persisted even among siblings of those who did not have autism themselves. While autism is generally understood to be predominantly genetic and not acquired later in life, stroke may serve as an additional contributing factor, potentially acting as a catalyst due to the multifaceted and intricate nature of autism's etiology.[7] Now the question is how common an etiology MMA is for pediatric ischemic stroke. A descriptive cross-sectional study undertaken by Das et al. from a single tertiary care center in eastern India, over 5 years, screening consecutive stroke and TIA patients with intracranial angiography to look for moyamoya angiopathic changes, found that 15.3% of the etiological fraction of childhood stroke and TIA was shared by MMA, with a female preponderance.[6] This percentage was high enough for the researchers to conclude that MMA contributes significantly to the etiological consideration of childhood stroke and must be considered during its evaluation in India.

So, is there a link between MMA and ASD? Multiple heritable diseases have been found to be associated with both ASD and MMS. Two such important inherited disorders are neurofibromatosis and tuberous sclerosis.[5,8,9] Hence there is some evidence, even though weak, to believe that some biological association might exist for these two disorders.

The genetic underpinnings of MMA have not been broadly elucidated. However, investigations of a recent genome-wide association study (GWAS) attempting to identify genetic modifiers, predicting with adult MMD in Koreans, reported multiple single nucleotide polymorphisms (SNPs) at 17q25.3 region to be significantly associated with MMD. 17q25.3 region among other loci associated with MMD were detected with high statistical power (more than 80%) in the study.[10] Another recent case series by Sahajpal et al. pointed at an overlap between MMA and ASD due to copy number variations (CNVs) involving 17q25.3 region, especially CNVs impacting RNF213. Additionally, CNVs involving other genes in 17q25.3 region such as SEPTIN9 & B3GNTL1 have been linked to neuro-developmental disorders like ASD. It is important to note that the clinical manifestations of MMD may include developmental delays, cognitive impairments, and seizures. These symptoms overlap with some of the features seen in individuals with ASD.[11]

Conclusion

The case underscores the intriguing, even though unclear link between ASD and MMD, suggesting shared genetic and pathophysiological mechanisms. While this association warrants further exploration, recognizing ischemic stroke especially MMD as a potential comorbidity of ASD is crucial. Early detection of neuro-developmental disorders, especially in pediatric ischemic stroke cases like MMD, is vital for improved outcomes. Healthcare professionals should remain vigilant for signs of ASD in such patients and integrate standardized screening protocols into routine assessments. Further prospective studies are needed to elucidate the complex relationship between MMA and ASD, facilitating more targeted interventions for neuro-developmental disorders in India.

Clinical Significance

This case emphasizes the need for healthcare professionals to consider MMD as a cause of childhood ischemic stroke in the evaluation of ASD. Conversely, If MMD is diagnosed, the possibility of coexisting ASD should be ruled out as the former could be part of the etiology, have a shared etiology, or may influence the course of the latter. Early diagnosis and intervention for both ASD and MMD can significantly improve a child's quality of life.

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