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WHEN CHRONIC HEADACHES POINT TO MOYAMOYA DISEASE: A RARE CASE REPORT AND LITERATURE REVIEW.

General Medicine

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ABSTRACT

Background: Moyamoya disease (MMD) is a rare cerebrovascular disorder characterized by progressive stenosis of the internal carotid arteries and its branches. MMD is also associated with the formation of collateral blood vessels, creating distinctive network like "puff of smoke", meaning moyamoya in Japanese. The symptoms of MMD arise from reduced blood flow due to carotid arteries narrowing leading to brain ischemia causing stroke, transient ischemic attacks (TIAs), and seizures, and compensatory mechanisms leading to hemorrhage due to weak collateral blood vessels. Headaches are caused by the dilatation of meningeal and leptomeningeal collateral vessels, which activate dural pain receptors. **Case:** A 27-year-old women presented with a chief complaint of headache, which was intermittent, occurring and resolving over a duration of 2 months, and with increasing frequency. On physical examination, there was slurring of speech. All laboratory tests and special investigations results were normal and unremarkable. A magnetic resonance imaging (MRI) of brain with intravenous contrast showed hyperintensity in cortex of right frontal lobe suggestive of subacute infarct. Subsequently, magnetic resonance angiography (MRA) of brain revealed narrowing of numerous intracerebral arteries, and presence of prominent collateral vessels creating a "puff of smoke" appearance, which is consistent with MMD. **Conclusion:** This report underscores the importance of considering Moyamoya disease as a potential diagnosis in patients with persistent, unexplained headaches, even in the absence of classic ischemic or hemorrhagic symptoms. Advanced imaging modalities, particularly MRI and MRA, are invaluable in establishing the diagnosis. Hence increased clinical awareness, early recognition and timely intervention are essential to reduce morbidity and mortality associated with this rare but significant cerebrovascular disease and preventing severe outcomes such as permanent neurological deficits or life-threating complications.

KEYWORDS

moyamoya disease, headache, collaterals, magnetic resonance angiography

INTRODUCTION

Moyamoya disease (MMD) is a rare cerebrovascular disorder that is characterized by progressive stenosis of the internal carotid arteries and its branches (Suzuki & Takaku, 1969). MMD is also associated with the formation of small collateral blood vessels that emerge to compensate for the diminished blood flow in the arteries supplying the brain's anterior circulation, creating distinctive network famously compared to something hazy like "puff of smoke", which inspired the term moyamoya in Japanese (Scott et al., 2009).

MMD was initially thought to primarily affect Asians, is now seen globally across various ethnic groups (Caldarelli et al., 2001; Suzuki & Kodama, 1983). The US incidence is 0.086 cases per 100,000, with higher rates in Asian Americans and Black individuals compared to whites and hispanics (Uchino et al., 2005). In Europe, the incidence is about one-tenth of Japan's (Yonekawa et al., 1997). MMD disease shows bimodal distribution in age of onset, with the highest cases observed in adults aged 45 to 49 years and the second in children aged 5 to 9 years (Baba et al., 2008). It is twice as prevalent in females as males (Baba et al., 2008; Wakai et al., 1997).

The symptoms of moyamoya disease arise from reduced blood flow due to carotid arteries narrowing which leads to brain ischemia causing stroke, transient ischemic attacks (TIAs), and seizures, and compensatory mechanisms leading to hemorrhage due to weak collateral blood vessels and headaches due to dilated transdural collateral vessels (Scott et al., 2009). The diverse clinical presentation of MMD can be attributed to individual differences in the extent of arterial narrowing, vessel stenosis, affected areas of the brain, and how the body adapts to reduced blood flow (Scott et al., 2009). Overall MDD most commonly presents with ischemic symptoms in both adults and children, 53.5% and 78% respectively (Baba et al., 2008). The likelihood of experiencing hemorrhage is nearly seven times greater in adults than in children (20% vs 2.8%) (Hallemeier et al., 2006; Scott et al., 2004). Headaches are rarely a presenting symptom and are a very non-specific symptom among MMD patients (Scott et al., 2009). Headaches are caused by the dilatation of meningeal and leptomeningeal collateral vessels, which activate dural pain receptors (Seol et al., 2005).

In this report, we discuss a rare case of Moyamoya disease which presents with headaches rather than usual and common presenting symptoms. This report underscores the diagnostic challenges associated with Moyamoya disease particularly when the typical presenting symptoms like stroke, transient ischemic attacks, or hemorrhage are absent. By sharing this case, we aim to emphasize the importance of maintaining a high level of suspicion and timely intervention to prevent severe complications, including significant morbidity and mortality (Zach et al., 2009).

Case Report

A 27-year-old women with past medical history of Polycystic Ovarian Disease (PCOD) 5 years ago which is completely treated now and no other significant past history and comorbidities. She was born from a non-consanguineous marriage. The patient presented with a chief complaint of headache, which was intermittent, occurring and resolving over a duration of 2 months, and with increasing frequency. Patient reported similar headache episodes in the past, but she denied history of trauma, epilepsy, smoking, or a family history of cerebrovascular diseases. On examination, there was slurring of speech and no motor deficit with normal tone and reflexes. Sensations were intact, with no cerebellar signs, normal gait and no other apparent neurological deficits. Her vital signs were all within normal limits.

Table 1 On Admission, All Laboratory Tests Results Were Normal And Unremarkable.

Investigation	Patient range	Normal range
Hemoglobin	12.1 gm/dL	13 – 17 gm/dL
Total leucocyte count	9,800/µL	4,000 – 10,000/µL
Platelets	1,90,000/µL	1,50,000 – 4,10,000/µL
Blood urea level	29 mg/dL	19 – 44 mg/dL
Creatinine	1.0 mg/dL	0.7 - 1.3 mg/dL
Total bilirubin	1.0 mg/dL	0.0 - 1.2 mg/dL
Direct bilirubin	0.3 mg/dL	0.0 - 0.3 mg/dL
Indirect bilirubin	0.7 mg/dL	0.20 - 0.8 mg/dL
Serum sodium	142 mmol/L	136 – 145 mmol/L
Serum potassium	4.2 mmol/L	3.5 - 5.1 mmol/L
Serum calcium	9.4 mg/dL	8.6 - 10.0 mg/dL

Table 2 Special Investigations Were Also Normal And Unremarkable.

Investigation	Patient range	Normal range
ESR	9 mm/hr	0 – 15 mm/hr
Total T3	1.19 ng/dL	0.80 - 2.00 ng/dL
Total T4	7.73 µg/dL	5.10 - 14.10 µg/dL
TSH	2.230 µIU/mL	0.27 - 4.20 µIU/mL
Serum homocysteine	14 µmol/L	< 15 µmol/L
Protein C	80 %	70 – 140 %
Protein S	56.9 %	54.7 - 123.7 %
aPTT	24 seconds	22-40 seconds
PT	14 seconds	10-16 seconds
INR	1.56	
HIV	Negative	
HBsAg	Negative	
HCV	Negative	
ANA screening	Negative	
ANCA profile	Negative	
Sickle screen	Negative	
Peripheral smear	Normal (no abnormal cells noted)	

A magnetic resonance imaging (MRI) of brain with intravenous contrast was performed which showed hyperintensity in cortex of right frontal lobe on T2WI/FLAIR (T2-weighted Imaging with Fluid-Attenuated Inversion Recovery) and hypointense on T1WI (T1-weighted Imaging). It shows mild restriction on DWI (Diffusion-Weighted Imaging) and no blooming on GRE (Gradient Echo), and mild enhancement is noted on post-contrast study. These findings were suggestive of subacute infarct. No intracranial hemorrhage was noted.

Subsequently, magnetic resonance angiography (MRA) of brain with intravenous contrast on 3T with Time-of-Flight (TOF) sequence was performed which revealed narrowing of right supraclinoid ICA (Internal Carotid Artery) with severe narrowing of origins of bilateral MCA (Middle Cerebral Artery) and ACA (Anterior Cerebral Artery), bilateral MCA M1 segment and ACA A1 segments. Also, the left MCA is poorly visualized. MRA also revealed presence of fine, irregular vessels and prominent collateral vessels at the base of the brain creating a "puff of smoke" appearance, which is consistent with Moyamoya disease. But the bilateral ICA, basilar artery, circle of willis, PCA (Posterior Cerebral Artery), ACOM (Anterior Communicating Artery), PCOM (Posterior Communicating Artery), and the rest of the right MCA and rest of bilateral ACA were visualized normal.

After diagnosis the patient with MMD, she was started on Aspirin (81 mg) and clopidogrel (75 mg) to address her headaches and decrease the risk of adverse cerebrovascular events. Acetaminophen (650 mg) was also added for break through headaches and to be taken as needed every six hours to help her with headaches. Neurology suggested adding atorvastatin (20 mg) to her medicine regime. The patient had no headaches during the 3-month follow-up to date and didn't undergo any surgical treatment.

DISCUSSION

Moyamoya disease is a rare, progressive cerebrovascular condition that often presents with diagnostic challenges due to its diverse clinical manifestations and progression across completely different age groups, particularly when typical presenting symptoms such as stroke, TIAs, or intracranial hemorrhage are absent. This case highlights an atypical and less common presentation of MMD, where persistent headaches were the primary symptoms, highlighting the need for high levels of clinical suspicion and diagnostic strategies for such non-specific manifestations. The lack of typical presenting symptoms like focal neurological deficits or classic ischemic symptoms in our patient initially obscured the diagnosis, highlighting the complexity in diagnosing of MMD.

Headache as a presenting symptom in MMD is underreported due to its vague nature. The mechanism of headache in MMD may be due to dilatation of transdural and leptomeningeal collateral vessels, which irritate dural pain reception was hypothesized by Seol et al. (2005). The same study by Seol et al. (2005) also found that 44 out of the total 204 patients diagnosed with MMD had headaches with milder ischemic or non-ischemic forms of the disease. This aligns with our patient who presented with chronic headaches in the absence of overt ischemic events.

In a large-scale descriptive analysis done by Muljadi et al. (2024) using 5-year MRI data from picture archiving and communication system (PACS), majority of cases presented with ischemic symptoms, and in contrast non-specific symptoms like headache were documented in fewer than 30% of cases. The commonness of such atypical presentations is usually ignored and neglected, as highlighted in our case, underscores the importance of including MMD in the differential diagnosis for patients with unexplained persistent headaches.

Imaging modalities, such as MRI and MRA remain the cornerstone for diagnosing MMD. In this case, MRI revealed a subacute infarct in the right frontal lobe. MRA further identified stenosis of ICA, MCA, and ACA, alongside the characteristic "puff of smoke" appearance of collateral vessels, confirming the diagnosis of Moyamoya disease. The report done by Kuroda et al. (2022) mentioned the importance of MRI and MRA in confirming the diagnosis of MMD and also in differentiating MMD from other differential diagnosis like atherosclerotic diseases, etc. Excluding atherosclerosis may be challenging in elderly patients with unilateral disease, but MRA may help in differentiating. As the stenosis caused by atherosclerosis reveals narrowing of the vessel lumen only and not the vessel's outer diameter as seen in MMD (Kaku et al., 2012).

Patients with moyamoya disease are found to have increased platelet aggravation activity, which plays a role in symptoms like headache and aspirin can help reduce headaches by preventing the activation of platelets (Aihara et al., 2021). Also adding another antiplatelet drug may help to potentiate inhibiting platelet aggregation, which was successfully used by Singh et al. (2023). Managing headaches in MMD requires a careful and balanced approach, focusing on enhancing quality of life and symptom relief without exacerbating the risk of cerebrovascular complications and other adverse events.

This case report adds to the growing body of literature documenting atypical presentations of MMD and emphasizing the need to consider MMD as differential in patients with unexplained persistent headaches, even in absence of classical neurological symptoms. Also, the severity and presentation of patients with MMD varies significantly due to individual differences in vascular involvement and collateral formation. Hence early recognition and timely intervention are critical in preventing sever outcomes such as permanent neurological deficits or life-threating complications.

CONCLUSION

In summary, this report underscores the importance of considering Moyamoya disease as a potential diagnosis in patients with persistent, unexplained headaches, even in the absence of classic ischemic or hemorrhagic symptoms. Advanced imaging modalities, particularly MRI and MRA, are invaluable in establishing the diagnosis and guiding management. Early imaging and prompt diagnosis can help mitigate the risks of catastrophic outcomes associated with MMD. Hence increased clinical awareness and timely intervention are essential to reduce morbidity and mortality associated with this rare but significant cerebrovascular disease. By highlighting this atypical presentation, we hope to contribute to a broader understanding of MMD and encourage further research into its diverse manifestations.

Author Contributions

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