Clinical Findings and Outcome of Moyamoya Disease/ Syndrome

Moyamoya Hastalığı/Sendromu'nun Klinik Bulguları ve Sonuçları

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ABSTRACT

Objective: Moyamoya disease is a rare progressive cerebrovascular disorder. It is characterized by progressive stenosis in the terminal branches of the internal carotid arteries, leading to the formation of an abnormal vascular network. The aim of this study was to present the clinical findings and outcomes of pediatric patients diagnosed with Moyamoya disease by analyzing our cohort to identify the common clinical presentations, diagnostic challenges, and treatment outcomes associated with this rare cerebrovascular disorder.

Material and Methods: Nine pediatric cases of Moyamoya disease admitted over a 10-year period were retrospectively reviewed. Clinical presentations, associated diseases, radiological findings, treatments, and outcomes were analyzed.

Results: The median age at diagnosis was 48 months (3-87). Presenting symptoms included hemiparesis in five patients, seizures in six patients, headache in one patient, and choreathetosis with headache in one patient. Three patients experienced symptoms triggered by fever, and one patient by exposure to hot water. Seven patients presented with ischemic symptoms, while two presented with non-ischemic symptoms. Neurofibromatosis type-1 (NF-1) was associated with the disease in four patients. Recurrent attacks occurred in two patients. Interictal electroencephalograms (EEGs) showed hemispheric/focal slowing in five cases. Cranial magnetic resonance imaging (MRI) revealed infarctions in seven patients, and MR angiography showed bilateral findings in six patients. Two patients experienced no long-term sequelae.

Conclusion: Moyamoya disease manifests with both ischemic and non-ischemic symptoms. Recognition of non-ischemic presentations requires a high index of suspicion for accurate diagnosis.

Keywords: Children, Electroencephalogram, Moyamoya disease, Neuroimaging, Stroke

ÖZ

Amaç: Moyamoya hastalığı nadir görülen, ilerleyici bir serebrovasküler bozukluktur. İç karotid arterlerin terminal dallarında ilerleyici darlık ile karakterize olup, anormal bir vasküler ağın oluşumuna yol açar. Bu çalışmanın amacı, bu nadir serebrovasküler bozuklukla ilişkili yaygın klinik tabloları, tanısal zorlukları ve tedavi sonuçlarını belirlemek için Moyamoya hastalığı tanısı konan pediatrik hastaların klinik bulgularını ve sonuçlarını sunmaktır.

Gereç ve Yöntemler: On yıllık bir dönemde kabul edilen dokuz pediatrik Moyamoya vakası retrospektif olarak incelendi. Klinik tablolar, ilişkili hastalıklar, radyolojik bulgular, tedaviler ve sonuçlar analiz edildi.

Bulgular: Tanı anında median yaş 48 ay (3-87)'dı. Başvuru semptomları beş hastada hemiparezi, altı hastada nöbet, bir hastada baş ağrısı ve bir hastada koreoatetoz ile baş ağrısı içeriyordu. Üç hasta ateşle tetiklenen semptomlar yaşadı, bir hasta ise sıcak suya maruz kalma ile tetiklenen semptomlar yaşadı. Yedi hasta iskemik semptomlarla, iki hasta ise iskemik olmayan semptomlarla başvurdu. Dört hastada hastalık ile ilişkili olarak Nörofibromatozis tip 1 (NF-1) mevcuttu. İki hastada tekrarlayan ataklar gözlendi. İnteriktal elektroensefalogramlarda (EEG) beş vakada hemisferik/odaksal

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Ethics Committee Approval / *Etik Kurul Onayı*: This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Karadeniz Technical University, Faculty of Medicine, Clinical Research Ethics Committee 2023/173 - 10.03.2023.

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yavaşlama görüldü. Kraniyal manyetik rezonans görüntüleme (MRI) yedi hastada enfarktüsleri ortaya koydu ve MR anjiyografi altı hastada bilateral bulgular gösterdi. İki hasta uzun dönem sekelsiz kaldı.

Sonuç: Moyamoya hastalığı hem iskemik hem de iskemik olmayan semptomlarla kendini gösterir. İskemik olmayan tabloların tanınması, doğru tanı için yüksek düzeyde şüphe gerektirir.

Anahtar Sözcükler: Çocuklar, Elektroensefalogram, Moyamoya hastalığı, Nörogörüntüleme, İnme

INTRODUCTION

Moyamoya disease (MMD) is a rare chronic cerebrovascular condition of unknown etiology. The disease is particularly prevalent in East Asian populations, with a higher incidence in Japan, Korea, and China compared to Western countries. In Japan, the annual incidence is estimated to be between 0.35 and 0.94 per 100.000 individuals. The peak onset typically occurs in children between 5 and 10 years of age. The disease is characterized by progressive occlusion or narrowing of the supraclinoid internal carotid artery and its major branches in the circle of Willis, usually bilaterally and idiopathically. Patients may present with recurrent ischemic or hemorrhagic strokes, as well as non-ischemic manifestations (1).

Moyamoya disease is referred to as moyamoya syndrome (MMS) when it co-occurs with another clinical condition such as neurofibromatosis type-1, genetic disorders (e.g., trisomy 21, Williams syndrome, PHACE syndrome), sickle cell disease, among others (2). The presence of familial cases and regional disparities in epidemiological data suggests a genetic component in its pathogenesis.

There are extensive series on moyamoya disease in the literature, with many studies originating from regions like Japan where the prevalence is high. Some of these studies include both adult and pediatric patients. However, in our country, it is rarely seen. We aimed to contribute to the literature by presenting our cohort, which, despite the small number of patients, includes a young age group and a high proportion of patients with Neurofibromatosis type 1 (NF1), as well as diverse clinical presentations.

MATERIALS and METHODS

Patients diagnosed with moyamoya disease/syndrome in the pediatric neurology outpatient clinic between 2013 and 2023 were included in the study. All patients with a diagnosis confirmed by clinical and imaging findings were enrolled. Patients with insufficient data or follow-up duration were excluded from the study.

Demographic data such as age, gender, and age at diagnosis were recorded from hospital charts. The presenting complaints, neurological examination findings, clinical symptoms, concomitant diseases of the patients were documented in detail. Brain MRI, magnetic resonance angiography (MRA), and other relevant imaging results were reviewed and recorded. Surgical interventions (e.g., revascularization surgeries), medical treatments were detailed. The clinical course, prognosis, complications, and outcomes during the follow-up period were recorded.

Diagnostic delay was defined as cases diagnosed at least one year after the initial presentation.

The study was approved by Karadeniz Technical University, Faculty of Medicine, Clinical Research Ethics Committee 2023/173 - 10.03.2023.

Statistics:

Data analysis was performed using the Statistical Package for the Social Sciences version 23 (SPSS Inc., Armonk, NY, IBM Corp., USA) software. Numerical data were expressed as median (min-max) and categorical variable as number and percentage

RESULTS

Nine patients were diagnosed with Moyamoya disease/syndrome (MMD/MMS). None of the patients had a family history of Moyamoya, and there was no consanguinity between the parents. The median age at diagnosis was 48 months (3-87). Diagnostic delay was observed in three patients. The male-to-female ratio was 2:1. Seizures were observed in five patients, hemiparesis in five patients, headache in one patient, and headache with choreoathetosis in one patient. One of the cases presented with status epilepticus. Symptoms were triggered by fever in three patients and exposure to hot water in one patient. MMS was associated with neurofibromatosis type 1 in four patients. Recurrence occurred in two patients. MMD/MMS was bilateral in five patients and unilateral in three patients initially. Disease progression to bilateral involvement was observed during follow-up in one patient initially diagnosed with unilateral disease. Interictal EEGs showed hemispheric slowing in six cases. Baseline thrombophilia tests (anticardiolipin antibodies, factor V Leiden mutation, prothrombin II mutation, homocysteine, Protein C, protein S) were negative in all patients. All patients received aspirin therapy, with one patient additionally receiving fraxiparine. Direct revascularization procedures were performed in two patients. No sequelae were observed in two patients. Genetic testing revealed a positive result for a mutation in the RNF213 gene in one patient, while genetic analysis was not conducted for the other patients. The results are presented in Table I.

In our series, there was only one patient who presented with a movement disorder. This case initially experienced migraine-like headaches for six months, which resolved spontaneously. However, one year later, an 8-year-old boy presented with a two-week history of involuntary movements in his upper extremities. General physical examination revealed no abnormalities, and neurological examination showed bilateral involuntary, brief, irregular, and wavering movements, predominantly in his upper extremities. There was no history of drug therapy or family history of similar conditions. Laboratory studies, including routine blood count, blood amino acids, urine acids, electrocardiogram, chest radiography, tests for collagen vascular disease, renal

Table I: Clinical findings

Case Number	Gender Age (m)	DA (m)	FP (m)	Trigger	Sympton on presentation 1./2./3.	Treatment	AC	R	GMFCS	Outcome	Genetic RNF213	EEG	MRI 1./2./3. a	Angiography
1	M/4	4	24		Left hemiparesis	Aspirin, AE, IR	-	-	3	Hemiparesis NCF	-	N	Brush sign, Infarct	Bilateral ICA occlusion
2	M/8	8	46	f*	Left focal seizure, febril status	Aspirin, AE	NF-1	-	N	No sequelae	-	Right hemisferic slowing	Infarct	Right MCA occlusion
3	F/3		36	f	Seizure, status Hemiparesis	Aspirin, AE	-	-	2	Hemiparesis NCF	-	Right CTO slowing	Infarct	Bilateral ICA stenoz
4	F/24	54	68	hw	Headache, seizure	Aspirin, AE	NF-1	-	1	Mild ID	-	Right hemisferic slowing	-	Right ICA; MCA ACA stenosis
5	F/30	48	48	f	Febril seizure/ seizure and aphasia	Aspirin	NF-1	2	3	Hemiparesis Mild ID	-	N	Brusch sign, Infarct/Infarct	Right ICA, MCA ,PCA occlusion, Right ACA stenoz Then Bilaretal ICA MCA stenosis
6	F/48	48	42	-	Seizure, Right Hemiparesis	Aspirin, AE, IR	NF-1	-	2	Hemiparesis Mild ID	-	N	IVY sign, Infarct	Bilateral ICA stenosis
7	M/84	87	80	-	Headache Choreatethosis	Aspirin	-	-	N	No sequelae	+	N	IVY sign	Bilateral ICA stenosis
8	F/48	48	26	-	Right hemiparesis	Aspirin, Fraxiparine	-	-	3	Hemiparesis NCF	-	Left FC slowing	Infarct	Left ICA stenoz
9	F/48	48	38	-	Seizure, right hemiparesis / seizure/seizure	Aspirin	-	3	5	Tetraparesis Severe MR Exitus	-	Left TPO slowing	İnfarct/ Infarct/ Infarct	Bilateral ICA, MCA stenosis

AC: *Associated condition,* ***AE:*** *Antiepileptic,* ***CTO:*** *Centro-temporo-occipital,* ***DA:*** *Diagnose age,* ***F:*** *Female,* ***FC:*** *Fronto-central,* ***FP:*** *Follow up period,* ***f:*** *Fever,* ***P:*** *Patient,****H:*** *Hemisferic,* ***hw:*** *Hot Water,* ***ICA:*** *Internal carotid artery,* ***IR:*** *Indireck revascularation,* ***ID:*** *Intellectual Disability,* ***M:*** *Male,* ***MCA:*** *Middle cerabral artery,* ***m:*** *months,* ***N:*** *Normal,* ***NCF:*** *Normal Cognitive Functioning,* ***NF-1:*** *Neurofibromatosis type-1,* ***PCA:*** *Posterior cerebral artery,* ***R:*** *Recurrence,* ***S:*** *Sex,* ***TPO:*** *Temporo-parieto-occipital*

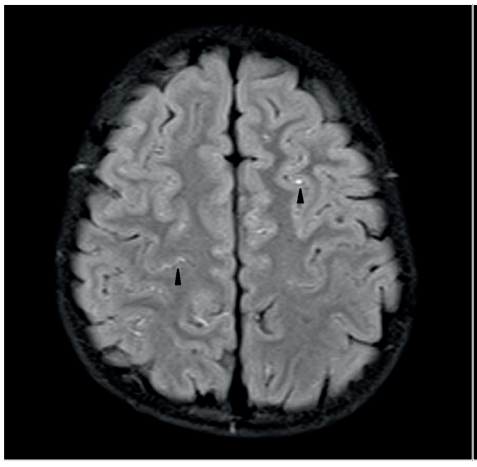

Figure 1 : Axial FLAIR image shows high signal intensity at sulci called 'ivy sign' (black arrowheads) (Case 7).

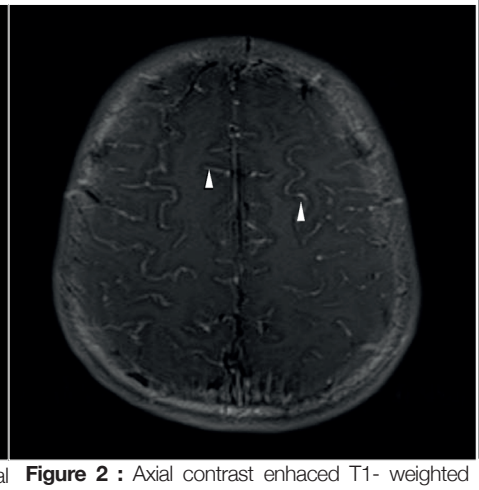

Figure 2 : Axial contrast enhaced T1- weighted image at same level shows diffuse leptomeningeal-sulcal enhacement (white arrowheads) (Case 7).

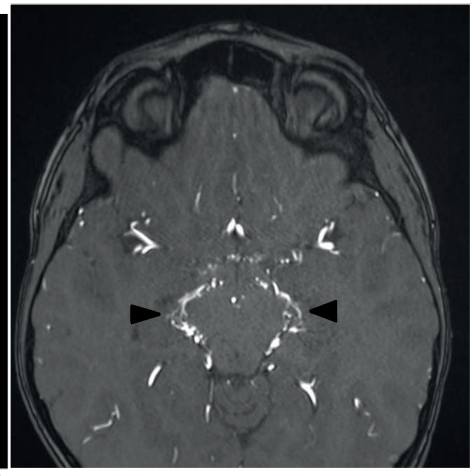

Figure 3 : TOF (time of flight) MRA shows the multiple tortuous dilated collateral vessels called 'moya moya vessels' (arrowheads) (Case7).

function, liver function, and coagulation tests, were all normal. Echocardiography showed normal findings. Baseline thrombophilia tests were negative. A heterozygous mutation of the MTHFR gene was identified. On imaging, axial Fluid-Attenuated Inversion Recovery (FLAIR) images revealed high signal intensity at the sulci, known as the 'ivy sign,' and axial contrast-enhanced T1-weighted images showed diffuse leptomeningeal-sulcal enhancement (Figure 1-2). Time-of-flight (TOF) MRA demonstrated multiple tortuous dilated collateral vessels, characteristic of 'moyamoya vessels (Figure 3). Contrast-enhanced MRA maximum intensity projection (MIP) images of bilateral cervical and petrous segments of the internal carotid arteries revealed diffuse narrowing, more pronounced on the right side. Bilateral occlusion of the cavernous and clinoid segments of the internal carotid artery was observed (Figure 4). Following this finding, genetic testing was requested, which identified a heterozygous variant, RNF213 c.12037G>A

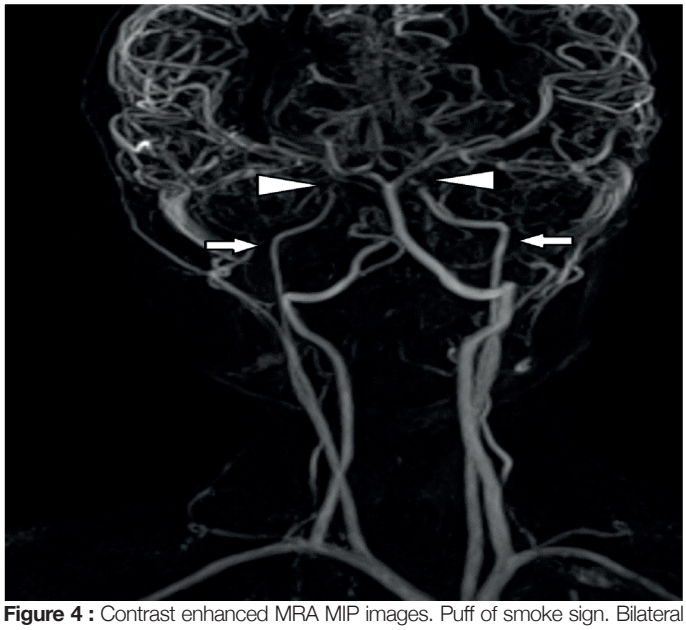

Figure 4 : Contrast enhanced MRA MIP images. Puff of smoke sign. Bilateral cervical and petrous segments of internal carotid arteries show diffuse narrowing more obvious at right (white arrows). Bilateral cavernous and clinoid segments of ICA are occluded (white arrowheads) (Case 7).

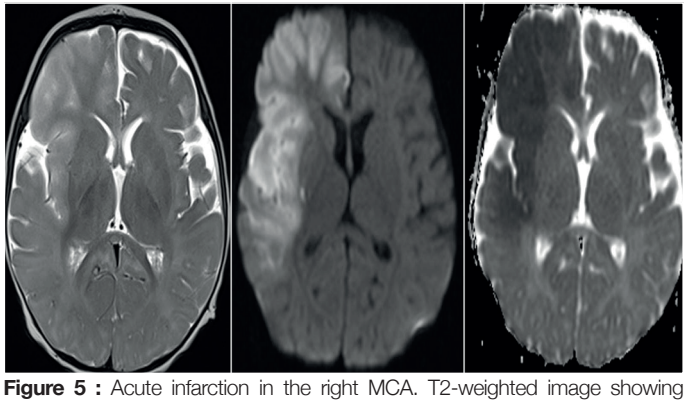

Figure 5 : Acute infarction in the right MCA. T2-weighted image showing hyperintensity. DWI showing restricted diffusion and ADC map showing low signal, confirming restricted diffusion (Case 6).

(p.D4013N) (p.Asp4013Asn). This variant has been previously documented and is listed in the HGMD database as associated with Moyamoya disease. Furthermore, it is classified in the ClinVar database as highly likely pathogenic. Treatment with acetylsalicylic acid rapidly resolved the choreic movements, and no recurrence was observed thereafter. Cranial MRI findings revealed evidence of infarction in seven patients, consistent with the ischemic events associated with Moyamoya disease/syndrome (Figure 5).

DISCUSSION

MMD is a rare chronic cerebrovascular occlusive disorder with a multifactorial inheritance pattern, although its exact etiology remains unknown. The primary manifestation of the disease is cerebral ischemia. Transient ischemic attacks (TIAs) can be triggered by events such as hyperventilation, dehydration, fever, and crying in infants, leading to reduced cerebral blood flow (3). In our cohort, presenting symptoms were triggered by fever in three patients and by exposure to hot water in one patient. Fever is the most commonly reported trigger in the literature (4). Therefore, MMD should be considered in cases of TIAs triggered by hyperventilation, dehydration, fever, and crying, highlighting the importance of recognizing and managing these potential triggers in clinical practice.

The mean age at diagnosis of MMD has been reported between 5.4 and 10.1 years in previous studies (5-7). In our series, the age at diagnosis was lower, with a mean of 38.6 months (3-87). This difference is a significant aspect of our study, possibly attributed to the inclusion of patients with very early symptom onset and a high rate of presentation with hemiparesis, facilitating prompt diagnosis. Three patients were diagnosed before the age of one; two presented with status epilepticus, and one with hemiparesis. Seizure control was achieved with levetiracetam in these patients. One of these patients presents with hemiparesis, while both exhibit no significant impairments in cognitive function. Consistent with findings in the literature, female predominance was observed (8,9).

In the current study, diagnostic delay was observed in three patients (22.2%) with NF-1. This delay can be attributed to nonischemic symptom presentations in two patients and the initial manifestation of a febrile seizure in one patient. Delayed or incorrect diagnoses have been documented in various series investigating MMD. For instance, Graf et al. (10) reported a diagnostic delay exceeding one year in 55.2% of their 192-case series. The relatively low rate of diagnostic delay in our study may be attributed to the small sample size and the predominant presentation of infarction in most cases.

While MMD predominantly presents with hemorrhagic strokes in adults, it more commonly manifests as TIAs or ischemic strokes in children (11-13). Jung et al. (14) reported that acute ischemic infarcts were more frequent in children under 5 years of age, typically showing a gyral pattern, whereas hemorrhagic infarcts were more prevalent in adolescents. In our series, the most frequent clinical presentation was hemiparesis associated with ischemic infarction, with one patient presenting with TIA (Figure 5). In a study by Yoko Sato et al. (15) in Japan, TIAs were the most common clinical presentation (52.11%), followed by infarctions (26.6%). Similar rates were reported in a Chinese series, with TIAs at 48.8% and infarctions at 20.5% (6). In an Italian series, the rates were 26% for TIAs and 29% for infarctions. These regional differences in clinical presentation suggest variability in disease manifestation. Our study was limited by the small number of cases, which may have influenced the observed clinical patterns.

Patients with MMD may also present with non-ischemic manifestations such as headache and choreoathetosis (1). Some patients are incidentally diagnosed (16,17). In our study, two patients presented with headache, one of whom developed choreoathetosis one year after the initial headache. Tomohito et al. (8) reported that approximately 20% of MMD patients experience symptomatic headaches, which are more prevalent in pediatric and young populations. Migraine-like headache is a common symptom in MMD, potentially attributed to chronic hypoxemia in pediatric patients (8,18-21). Furthermore, cortical ischemia often leads to

the frequent occurrence of epilepsy among pediatric patients, with five of our patients receiving antiseizure medication.

Presentation with movement disorders is rare in MMD and typically results from basal ganglia damage (18,22-25). The frequency of movement disorders in MMD is estimated to be between 3% and 6% (5,22). Cerebral ischemia is a recognized cause of movement disorders in MMD, with chorea being the most prominent symptom, along with choreo-athetosis, dystonia, limb-shaking, epilepsia-partialis continua, paroxysmal dyskinesia, hemidystonia, and hemichoreoathetosis also observed (8,11). These conditions are thought to arise from ischemic events affecting specific brain areas, particularly the basal ganglia and thalamocortical regions. In our case of chorea presentation, MRI did not reveal any ischemic changes. This clinical condition likely results from vascular bed inadequacy and cerebral hypoperfusion. Hara et al. (26) demonstrated microstructural damage in normal-appearing brain parenchyma using neurite orientation dispersion and density imaging, suggesting that symptoms in our patient may stem from such microstructural changes in the basal ganglia. Chorea is uncommonly seen as an initial presentation of MMD. Despite our study's small sample size, the coexistence of rare presentations represents another notable aspect of our series.

The diagnostic criteria for Moyamoya disease were updated in 2021, resulting in the abolition of the bilaterality rule and the terms "definite case" and "probable case" from the MRI and MRA criteria (18). In the revised criteria, the entity known as Moyamoya syndrome is recognized in the presence of associated conditions such as Down syndrome, brain tumors, and meningitis. In our study, Moyamoya syndrome was diagnosed in four patients due to their association with NF-1.

Gatti et al. (27) reported stroke occurrence in 11% of 11 patients with NF-1 in their study focusing on stroke rates according to different etiologies. In our study, stroke developed in three out of four patients with NF-1, as well as in three out of four patients without any associated conditions. Larger series are necessary to comprehensively assess the clinical presentation and prognosis based on different etiologies in Moyamoya disease.

In patients with MMD, specific MRI and EEG findings such as the 'ivy sign', 'brush sign', and the 'rebuilt up phenomenon' can provide important diagnostic clues. The 'ivy sign' is characterized by diffuse leptomeningeal-sulcal enhancement visible on FLAIR and post-contrast T1-weighted images (Figure 1). The 'brush sign' refers to increased visibility of deep medullary vessels, best observed on susceptibility-weighted MRI. Another characteristic feature is the presence of tiny abnormal intracranial collateral vessels, often referred to as the 'puff of smoke', which is the most iconic sign seen on MRA images (Figure 4). The 'rebuilt up phenomenon' in EEGs describes the emergence of high-voltage slow waves following the termination of hyperventilation in children with MMD. This finding has been linked to impaired cerebral perfusion, reinforcing the consideration of MMD in patients exhibiting these EEG characteristics (28). In our series, interictal EEGs revealed hemispheric or focal slowing in five cases. While not specific to the diagnosis, this finding can serve as a warning sign, particularly in cases where hyperventilation testing cannot be performed.

The primary goal of treating MMD is to reduce the risk of ischemic attacks and hemorrhage. As per the literature, aspirin has been widely used in our series, being the preferred medical therapy for pediatric patients with asymptomatic or symptomatic ischemic type MMD or MMS (29). However, recent discussions suggest that the ischemic state in MMD is primarily due to hemodynamic rather than embolic factors, which may limit the efficacy of aspirin in preventing recurrent infarctions (6,30). Yamada et al. (31) found no significant difference in cerebral infarction rates between groups receiving and not receiving antiplatelet therapy in ischemic Moyamoya patients, with lower recurrence of infarcts observed in the surgical treatment group. Additionally, the surgical group experienced longer periods free of ischemia, and no significant variation was noted among different surgical techniques in terms of ischemia or bleeding-free intervals. Consequently, surgical interventions have gained acceptance as a more effective treatment approach. Patients who experience recurrent progressive ischemic attacks with reduced perfusion reserve are considered candidates for surgical intervention.

MMD is recognized as a progressive condition with a generally poor prognosis, particularly evident in patients under the age of four, who often experience a high incidence of cerebral infarction (32). In our study, eight patients were aged four years or younger, and six of these patients developed sequelae. This poor outcome can be attributed to the younger age distribution among these patients. Additionally, involvement of the posterior cerebral artery and recurrent episodes of bleeding are identified as additional factors contributing to a poorer prognosis in MMD.

In conclusion, MMD can manifest with both ischemic and nonischemic symptoms, necessitating a high index of suspicion for diagnosis. MRI and EEG are valuable diagnostic tools offering important clues in clinical practice.

REFERENCES

1. Gatti JR, Sun LR. Nonischemic Presentations of Pediatric Moyamoya Arteriopathy: A Natural History Study. Stroke 2022;53:219-20.
2. Kuroda S, Fujimura M, Takahashi J, Kataoka H, Ogasawara K, Iwama T, et al. Research Committee on Moyamoya Disease (Spontaneous Occlusion of Circle of Willis) of the Ministry of Health, Labor, and Welfare, Japan. Diagnostic Criteria for Moyamoya Disease - 2021 Revised Version. Neurologia Medico-Chirurgica (Tokyo) 2022;62:307-12.
3. Takanashi J. Moyamoya disease in children. Brain Development 2011;33:229-34.
4. Das S, Ray BK, Pandit A, Ghosh R, Diehl R, Dubey S, et al. Profile of precipitating factorwws and its implication in 160 Indian patients with Moyamoya angiopathy Journal of Neurology. 2023;270:1654-61.
5. Po' C, Nosadini M, Zedde M, Pascarella R, Mirone G, Cicala D, et al. Pediatric Moyamoya Disease and Syndrome in Italy: A Multicenter Cohort. Frontiers in Pediatrics 2022;6:892445.
6. Zheng J, Yu LB, Dai KF, Zhang Y, Wang R, Zhang D, et al. Clinical Features, Surgical Treatment, and Long-Term Outcome of a Multicenter Cohort of Pediatric Moyamoya. Front Neurol 2019;22:14.
7. Zhao M, Zhang D, Wang S, Zhang Y, Deng X, Zhao C, et al. The Collateral Circulation in Moyamoya Disease: A Single-Center Experience in 140 Pediatric Patients. Pediatr Neurol 2017;77:78-83.

8. Hishikawa T, Sugiu K, Date I. Moyamoya Disease: A Review of Clinical Research. Acta Medica Okayama 2016;70:229-36.
9. Zhang X, Xiao W, Zhang Q, Xia D, Gao PSu J, et al. Progression in Moyamoya Disease: Clinical Features, Neuroimaging Evaluation, and Treatment. Curr Neuropharmacol 2022;20:292-308.
10. Graf J, Schwitalla JC, Albrecht P, Veltkamp R, Berlit P, Hartung HP et al. Misdiagnoses and delay of diagnoses in Moyamoya angiopathy-a large Caucasian case series. J Neurol 2019;266:1153-9.
11. Fukui M, Kono S, Sueishi K, Ikezaki K. Moyamoya disease. Neuropathology 2000;20 Suppl:S61-4.
12. Hong YH, Ahn TB, Oh CW, Jeon BS. Hemichorea as an initial manifestation of moyamoya disease: reversible striatal hypoperfusion demonstrated on single photon emission computed tomography. Mov Disord 2002;17:1380-3.
13. Gonzalez-Alegre P, Ammache Z, Davis PH, Rodnitzky RL. Moyamoya-induced paroxysmal dyskinesia. Mov Disord 2003;18:1051-6.
14. Jung MY, Kim YO, Yoon W, Joo SP, Woo YJ. Characteristics of brain magnetic resonance images at symptom onset in children with moyamoya disease. Brain Dev 2015;37:299-306.
15. Sato Y, Kazumata K, Nakatani E, Houkin K, Kanatani Y. Characteristics of Moyamoya Disease Based on National Registry Data in Japan. Stroke 2019;50:1973-80.
16. Zanoni P, Steindl K, Sticht H, Oneda B, Joset P, Ivanovski I, et al. The genetic landscape and clinical implication of pediatric Moyamoya angiopathy in an international cohort. Eur J Hum Genet 2023;31:784-92.
17. Malone M, Ritchie D. The Mystery of a Unilateral Headache Ultimately Diagnosed as Moyamoya Disease. Cureus 2022;14:e26816.
18. Smith ER, Scott RM. Spontaneous occlusion of the circle of Willis in children: pediatric moyamoya summary with proposed evidence-based practice guidelines. A review. J Neurosurg Pediatr 2012;9:353–60.
19. Gao B, Kang K, Zhang J, Zhang D, Zhao X. Clinical Characteristics and Long-Term Outcome of Headaches Associated With Moyamoya Disease in the Chinese Population-A Cohort Study. Front Neurol 2020;11:605636.
20. Hao Z, Lai X. Sturge-Weber Syndrome Coexisting With Moyamoya Disease in the Fifth Decade: A Case Report and Literature Review. Neurologist 2019;24:13-6.
21. Eisenmenger LB, Rivera-Rivera LA, Johnson KM, Drolet BA. Utilisation of advanced MRI techniques to understand neurovascular complications of PHACE syndrome: a case of arterial stenosis and dissection. BMJ Case Rep 2020;13:e235992.
22. Pavlakis SG, Schneider S, Black K, Gould RJ. Steroid-responsive chorea in moyamoya disease. Mov Disord 1991;6:347-9.
23. Sugita Y, Funaki T, Takahashi JC, Takagi Y, Fushimi Y, Kikuchi T, et al. Reversible striatal hypermetabolism in chorea associated with moyamoya disease: a report of two cases. Childs Nerv Syst 2016;32:2243-7.
24. Demartini Z Jr, Teixeira BCA, Cardoso-Demartini AA. Choreoathetosis in Moyamoya Disease. World Neurosurg 2021;156:103-4.
25. Maheshwari S, Anthony A, Kushwaha S, Singh S, Desai R, Madan D. Moyamoya Disease Presenting as Alternating Hemiparesis with Relapsing Remitting Hemichorea: An Unusual Manifestation. J Pediatr Neurosci 2018;13:514-6.
26. Hara S, Hori M, Murata S, Ueda R, Tanaka Y, Inaji M, et al. Microstructural Damage in Normal-Appearing Brain Parenchyma and Neurocognitive Dysfunction in Adult Moyamoya Disease. Stroke 2018;49:2504-7.
27. Gatti JR, Torriente AG, Sun LR. Clinical presentation and stroke incidence differ by moyamoya etiology. J Child Neurol 2021;36:272–80.
28. Lu J, Xia Q, Yang T, Qiang J, Liu X, Ye X, et al. Electroencephalographic features in pediatric patients with moyamoya disease in China. Chin Neurosurg J 2020;6:3.
29. M. Srinivasan HL, Hausman-Kedem M, Smith ER, Constantini S, Roth J. Current trends in pediatric moyamoya: a survey of international practitioners. Childs Nerv Syst 2021;37:2011-23.
30. Kim T, Oh CW, Bang JS, Kim JE, Cho WS. Moyamoya Disease: Treatment and Outcomes. J Stroke 2016;18:21-30.
31. Yamada S, Oki K, Itoh Y, Kuroda S, Houkin K, Tominaga T, et al. Research Committee on Spontaneous Occlusion of Circle of Willis (Moyamoya Disease). Effects of Surgery and Antiplatelet Therapy in Ten-Year Follow-Up from the Registry Study of Research Committee on Moyamoya Disease in Japan. J Stroke Cerebrovasc Dis 2016;25:340-9.
32. Hao F, Gao G, Guo Q, Liu S, Wang M, Chang Z, et al. Risk Factors for Massive Cerebral Infarction in Pediatric Patients With Moyamoya Disease. Pediatr Neurol 2024;153:159-65.