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LETTER TO THE EDITOR

Late-onset chorea after cerebral revascularization as a clinical manifestation of moyamoya disease

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Dear Editor,

Moyamoya disease is a cerebral arteriopathy with an incidence of 0.086 per 100,000 inhabitants [1], being more common in women and Asian population. It has a broad spectrum of clinical manifestations including movement disorders, which can occur more frequently at clinical debut. The following is an unusual case of late-onset chorea after cerebral revascularization, in medical literature only 3 cases like this have been described to our knowledge.

A 4-year-old girl was admitted in 2015 for focal seizures, with an unremarkable physical examination. She had no relevant data in her past pre-/perinatal history and the neurological development was normal. Brain magnetic resonance imaging (MRI) was negative to lesions. The patient was treated with carbamazepine and levetiracetam, with satisfactory seizure control. Three years later, she had acute alternating hemiparesis, and cerebral arteriography showed decreased caliber of the left middle cerebral artery and multiple small vessels of perimesencephalic and basal ganglia location. Moyamoya disease was diagnosed at that moment. Thereafter, an encephaloduroarteriosynangiosis (EDAS) was carried out obtaining a full recovery of the motor symptoms.

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At the beginning of the year 2020 at age 9, she was admitted for generalized choreic movements, prominent on the right side without other manifestations. Brain MRI showed no acute lesions; however, MR angiography showed persistence of dilated left lenticulostriate vessels (Fig. 1). The complete blood count, electrolytes, glucose, creatinine, bilirubin, and thyroid-stimulating hormone were within normal limits. Antinuclear antibodies, anti-DNA antibody, complement, Venereal Disease Research Laboratories test, Human Immunodeficiency Virus 1/2 test, and rapid strep test were also negative. The echocardiogram did not show any abnormality and rheumatic fever was ruled out. There was no temporal relationship with any drug or triggering event. It was concluded that the choreic syndrome was associated with moyamoya disease and treatment with oral haloperidol 0.5 mg every 12 h was initiated, resulting in partial improvement. We suggest tetrabenazine treatment, but patient's parents did not agree, because of potential adverse effects. During follow-up, the patient recovered, and now she is no longer on haloperidol. Patient's parents gave their informed consent to publish the case and the attached images.

Moyamoya disease is characterized by progressive occlusion of the terminal portion of the internal carotid artery and the proximal portion of the anterior and middle cerebral arteries. It was described by Takeuchi in 1961 [2], but since the work of Suzuki and Takaku in 1969, it is known as moyamoya disease ("Japanese expression for something hazy just like a puff of cigarette smoke drifting in the air") [3]. In cerebral arteriography, collateral blood flow is observed, provided by dilated leptomeningeal, thalamoperforator, and transdural vessels that irrigate distal areas to the occluded vessels [4].

In children, the most common clinical presentation is stroke, followed by transient ischemic attack, headache, and seizures [4–6]. Movement disorders can also occur with a frequency of 3–6%, with paroxysmal dyskinesia [1, 7, 8] and chorea [1, 9–12] mainly. Some case-series report a higher prevalence (47.4–54.9%) proposing a underestimation of movement disorders as a clinical manifestation of the disease [13–15]. Usually, chorea has been presented at the debut, and one hypothesis proposes that

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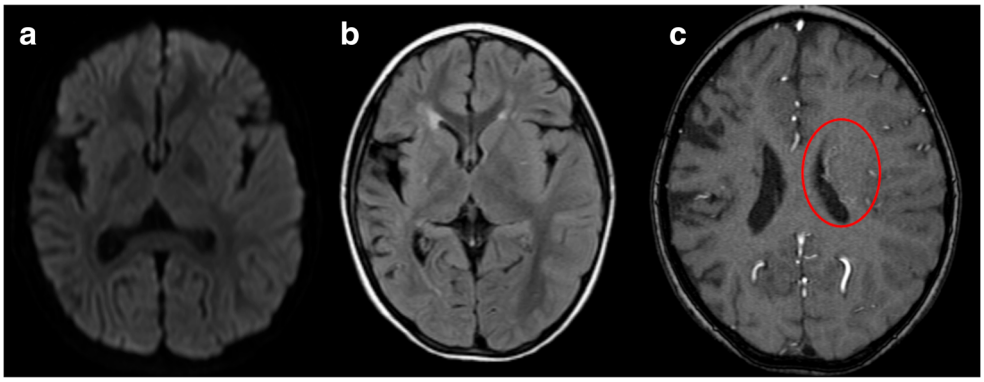

Fig. 1 **a** Axial DWI b1000 shows no acute ischemic lesion in the basal ganglia. **b** Axial FLAIR imaging shows periventricular microangiopathic leukoencephalopathy and encephalomalacia of the right temporal lobe. **c** Magnetic resonance angiography shows persistence of dilated left lenticulostriate vessels (red circle)

it is secondary to ischemia or hypoperfusion of the basal ganglia, subthalamus, and fronto-parietal cortical/subcortical areas [13]. Cerebral angiography has shown hypertrophied lenticulostriate arteries with damage in vascular autoregulation [14, 16], and the same image was seen in our patient (Fig. 1c). The last is associated with hypermetabolism of the striatum and could generate activation of the direct pathway and the thalamus-cortical motor circuit (evidenced in 18F-fluorodeoxyglucose positron emission tomography) [16]. In other hand, existence of areas with greater membrane excitability and release of excitatory neurotransmitters is also proposed. For those reasons, chorea could result from dysfunction in network and functional connectivity and not from a focal lesion. It has been reported that, after revascularization and normalization of cerebral perfusion and autoregulation, chorea resolves without recurrence [1, 17]; in fact, surgical revascularization has been suggested in patients in early stages because of the excellent prognosis [5]. After 2 years of EDAS, our patient presented generalized chorea not associated with cerebral infarction, which leads us to suspect that cerebral areas with alteration of perfusion and metabolism still persist; unfortunately, this could not be proven with functional images due to the limitation of diagnostic resources [18], but the limited information available supports our hypothesis [14, 16]. Recently, EDAS has been described as a technique that restores satisfactorily blood flow in only a limited area, with SPECT studies demonstrating the persistent abnormal cerebral blood flow [19].

Table 1 Summary of case reports about patients with moyamoya disease and chorea-onset after cerebral revascularization

Reference	Sex age	Clinical-radiological findings		Outcome
		Preoperative	Postoperative	
[14]	Female 11 years old	Transient ischemic attack (no more data reported). - MRI showed hypertrophied collateral vessels within the basal ganglia. - MR angiography showed extensive network of collateral vessels coursing through the basal ganglia.	Right hemichorea-onset 3 years after cerebral revascularization - Cerebral angiography demonstrated development of surgical collateral vessels and persistence of a large left thalamoperforating artery.	No treatment reported. Hemichorea resolution after 2 days
[16]	Female 17 years old	Transient numbness and weakness on the left side of the body - Cerebral angiography revealed severe stenosis in the terminal portion of the bilateral internal carotid artery with extensive development of abnormal collateral vessel networks.	Left hemichorea-onset 5 years after cerebral revascularization - MRI showed a small ischemic lesion in the right frontal white matter. - MR angiography showed a dilated and extended lenticulostriate artery passing through the right striatum and connecting to the medullary artery in the periventricular area. - SPECT showed normal cerebral blood flow. - 18F-FDG PET showed markedly elevated glucose metabolism in the right striatum.	Treatment with oral haloperidol (doses not reported). Hemichorea resolution after 2 months
[16]	Female 10 years old	Transient motor weakness of the left leg - Cerebral angiography revealed severe stenosis in the terminal portion of the bilateral internal carotid artery with extensive development of abnormal collateral vessel networks.	Right hemichorea-onset 3 months after cerebral revascularization - MR angiography showed a dilated and extended lenticulostriate artery in the left striatum. - SPECT showed hypoperfusion in the left basal ganglia. - 18F-FDG PET showed elevation of glucose metabolism in the left striatum.	Treatment with oral haloperidol (doses not reported). Hemichorea resolution (time not reported)

18F-FDG PET 18F-fluorodeoxyglucose positron emission tomography, *MRI* magnetic resonance imaging, *SPECT* single-photon emission computed tomography

The treatment recommendations of chorea in moyamoya disease are based on case reports, with haloperidol being more frequently used, without ruling out the possibility of using other antipsychotics. Similar to the previously reported cases [14, 16], the patient used haloperidol with partial response but achieving improvement in her functionality. Tetrabenazine could be a good option, but in this case, that was not evaluated. Another surgical intervention that improves cerebral blood flow was not considered because of the risks.

The 3 patients reported previously have characteristics similar to our patient: all are women, with persistence of dilated lenticulostriate vessels, and all responded to haloperidol treatment (Table 1). The prognosis in these patients was good; it has been considered that duration of chorea is about 1.35 years [14], and the mortality rate is 4.3% [1].

In conclusion, this is a case of atypical presentation of moyamoya disease. The late-onset chorea despite cerebral revascularization suggests persistence of alteration in perfusion and metabolism of certain brain areas. Further studies are required to evaluate the physiopathological hypothesis mentioned and thus to propose a more effective therapeutic intervention in the future.

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Author contribution Pilar Enríquez-Ruano MD: data collection, case description, analysis of the case, review of literature, writing the draft.

Cristian Eduardo Navarro MD MSc: conceptualization, review of literature, writing, and editing the manuscript.

Natalia Penagos MD: revision of the manuscript.

Oscar Mauricio Espitia MD: conceptualization, editing the manuscript.

Data availability Not applicable

Code availability Not applicable

Declarations

Ethical approval Ethics approval was given for case report by Fundación Hospital Pediátrico La Misericordia - HOMI.

Consent to participate The patient's parents gave their informed consent to participate in this study.

Consent for publication The patient's parents gave their informed consent to publish the case and the attached images.

Conflict of interest The authors declare no competing interests.

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