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ORIGINAL ARTICLE

Twig-like middle cerebral artery – pathophysiology and imaging approach

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Abstract

Objective: *A twig-like middle cerebral artery is an infrequent congenital disturbance that is difficult to distinguish from moyamoya disease. Cerebral angiography is essential for the differential diagnosis of stenotic-occlusive vasculopathies involving the middle cerebral artery.* **Methods:** *We explored the prevalence of the twig-like middle cerebral artery in our institution's angiography unit and reviewed the literature to clarify the imaging criteria.* **Results:** *The prevalence calculated in our anonymous database was 0.21%, which is in the frequency range described in the literature. Two cases that meet the diagnostic criteria and differ in clinical imaging characteristics are described in detail.* **Conclusions:** *Adequate imaging description allows precise diagnosis and approximation of the underlying etiopathogenic mechanism.*

Keywords: *Middle cerebral artery anomaly. Middle cerebral artery. Twig-like middle cerebral artery.*

Arteria cerebral media con variante tipo "rete" – fisiopatología y enfrentamiento imagenológico

Resumen

Objetivo: *La arteria cerebral media tipo "twig" o "rete" es una anomalía congénita infrecuente que es dificil de distinguir de la enfermedad de moyamoya. La angiografía cerebral es esencial para realizar el diagnóstico diferencial dentro de las vasculopatías esteno-oclusivas de arteria cerebral media.* **Métodos:** *Nosotros exploramos la prevalencia en nuestra base de datos anonimizada entre un total de 1428 angiografías diagnósticas realizadas entre enero del año 2010 y diciembre del 2023* **Resultados:** *La prevalencia resultó del 0.21%, lo cual está dentro del rango de lo reportado por la literatura internacional. Reportamos de forma detallada dos casos que reunen los criterios con diferencias clínicas-imagenológicas entre ellos.* **Conclusiones:** *La adecuada descripción imagenológica permite realizar un diagnóstico preciso y a través de la angio-arquitectura aproximarse al mecanismo etiopatogénico subyacente.*

Palabras clave: *Anomalía en arteria cerebral media. Arteria cerebral media tipo rete. Vasculopatía congénita.*

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Introduction

Twig-like middle cerebral artery (MCA) is a rare vascular anomaly in which a plexiform network of small vessels is seen to replace the M1 segment of the MCA[1]. The prevalence in the Latin American population has been described as around 0.088%[2]. This arteriopathy can cause both ischemic strokes as a result of hypoperfusion as well as intracranial hemorrhage due to the vulnerability of collateral circulation and the coexistence of aneurysms[3,4].

There are two hypotheses about the pathogenesis of the pathology, with different ages of presentation depending on the development mechanism. According to the congenital hypothesis, twig-like MCA results from a failure in the fusion of the multiple plexiform vessel networks constituting the primitive MCA[5]. The second hypothesis proposes that twig-like MCA is the secondary consequence of chronic MCA occlusion, and the adult age of diagnosis and clinical manifestations support this proposal[6].

The differential diagnosis of this entity includes slowly developing occlusive vasculopathy, and, in this regard, two essential entities, such as moyamoya disease (MMD) and moyamoya-like syndrome (MMS), should be considered[7,8].

Ischemic and hemorrhagic stroke may occur in patients with twig-like MCA, but also incidental diagnosis is possible[9].

Digital subtraction angiography is the gold standard in diagnosis[10]. It shows features of a plexiform network of vessels replacing the proximal trunk of the MCA, with distal branches of the MCA beyond this network being of normal caliber with anterograde flow[11]. Our study aimed to clarify the imaging concepts used in the twig-like diagnostic criteria that allow them to be differentiated from other vascular entities[12].

In addition, we provide cases and images from our hospital that support the concepts described.

Congenital etiopathogenesis

In the embryonic stage, the primitive MCA consists of multiple networks of plexiform vessels that fuse to transform into a normal MCA during development. As a result of the absence of the fusion process, a twig-like MCA presents a plexiform arterial network (PAN) of the M1 segment. As part of an alteration in embryonic development, there is a high coexistence with other intracranial vascular anomalies such as fenestrations, arterial duplications, or aneurysms[13].

Acquired etiopathogenesis

There is a broad description of cases in which the clinical manifestations and diagnosis are made in late adulthood. These cases are unlikely due to a persistent alteration since embryonic development but rather to an acquired anomaly associated with hypertension and atherosclerosis that, as a secondary consequence, ends in a unilateral chronic occlusion of the proximal segment of the MCA, with adjacent development of a plexiform network with preservation of the normal caliber of the distal M1 segment[14].

Methodology

The present study, conducted with meticulous care, aimed to determine the prevalence of certain clinical characteristics from an anonymized database, using a retrospective and descriptive approach. A total of 1,428 diagnostic angiographies performed between January 2010 and December 2023 at our diagnostic center were included.

The data were processed and anonymized to ensure patient privacy.

The analysis was performed using specialized statistical software to identify the prevalence of significant findings, both descriptively and inferentially.

Epidemiology

The prevalence rate of rete MCA in Asian and European literature has been reported between 0.1 and 0.67%[11,12,15].

All diagnostic angiographies performed at our center between January 2010 and December 2023 were reviewed. Only those in which a complete anterior circulation study had been performed were included. Three cases met all clinical imaging criteria, resulting in a prevalence of 0.21%.

Clinical manifestations

Our literature review identified 82 cases of twig-like MCA in 15 previous studies. Among 56% of the patients were female, with a mean age of 48 years ± 21.2 years. Most published cases were symptomatic at diagnosis (72/82, 87%). Headache was the most common presenting symptom, reported in 47% of patients, followed by paresis contralateral to the steno-occlusive artery in 23 patients (28%). Intracranial hemorrhage was more frequent than ischemic stroke, which was seen in 38%

and 27%, respectively. The coexistence of an intracranial aneurysm was described in 38% of cases[1,11,14,15].

Diagnostic imaging

At present, the gold standard test for a twig-like MCA remains the DSA[10]. However, in a complementary way, the computed tomography (CT) perfusion study can be useful to identify areas of hypoperfusion and detect areas of the MCA territory where compensatory mechanisms maintain adequate cerebral flow, providing indirect information on vascular reserve[11]. In addition, including magnetic resonance imaging (MRI) of the intracranial vessel wall, combined with magnetic resonance angiography, may further aid in the differential diagnosis of other unilateral intracranial vasculopathy, such as those causing MMS[7,8].

Angiographic criteria in the diagnosis of twig-like MCA

Angiographically, an abnormal PAN with multiple channels and a steno-occlusive change is observed in the proximal M1 segment of the affected MCA. Adjacently, the lenticulostriate arteries (LSA) arise from the PAN, whereas the distal branches of the MCA beyond the network maintain a normal vessel caliber with anterograde blood flow[11]. About the differential diagnosis, it is essential to highlight that in twig-like MCA, there is unilateral involvement of the MCA without involvement or progression toward the contralateral side[12].

Case reports

Here, we report two cases whose age of clinical presentation differs widely, suggesting a different pathogenic mechanism.

Case 1

The patient was a 52-year-old female with hypertension. She referred three episodes of focal seizures with alteration to the state of consciousness in the last year, so brain MRI and MR angiography were performed, finding an absence of the M1 segment of the left MCA with the persistence of plexiform network from LSA (Figs. 1 and 2), for which requests DSA under suspicion of moyamoya syndrome. DSA showed the presence of twig-like left MCA involving the entire M1 tract with anterior and posterior M2 branches

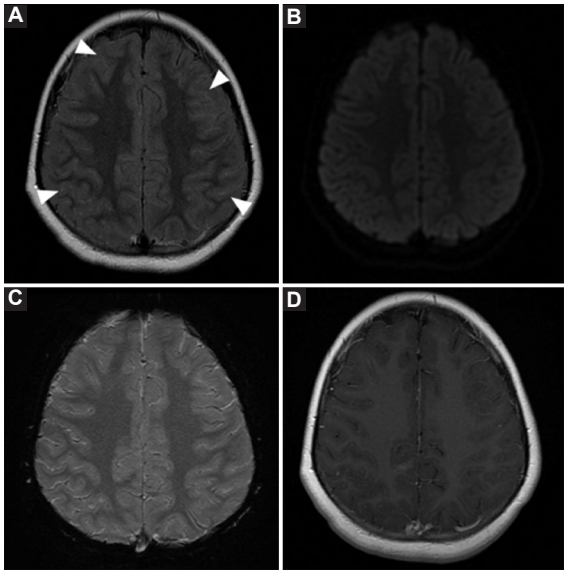

Figure 1. Brain magnetic resonance imaging. **A:** axial T2 fluid-attenuated inversion recovery shows subtle diffuse sulcal hyperintensity (white arrowheads), without parenchymal lesions. No abnormalities in **B:** diffusionweighted image; **C:** GRE T2-weighted image, and **D:** gadolinium-enhanced T1-weighted image.

arising independently of the network (Fig. 3). No polymorphism associated with MMD was identified, particularly without ring finger protein 213 mutation. A test for antinuclear antibodies was positive at a titer of 1:160 with a homogeneous-speckled pattern, but the remainder of the antinuclear-antibody screening (anti-double-stranded DNA, anti-Ro/SSA, anti-La/SSB, and anti-ENA) was negative. An antineutrophil cytoplasmic antibody test, rheumatoid factor, anticardiolipin antibodies immunoglobulin G and immunoglobulin M, venereal disease research laboratory, and HIV were all negative. Cerebrospinal fluid analysis was within normal limits.

Case 2

The patient was an 8-year-old male child. He presented a syncopal episode; upon regaining consciousness, weakness in the right lower extremity was evident for an hour and a half, with complete recovery. CT angiography showed an irregularity of the right proximal MCA, so he was referred for a complementary imaging study. DSA revealed a rete MCA anomaly at the right M1 (Fig. 4), and CTP showed hypoperfusion of the right hemisphere.

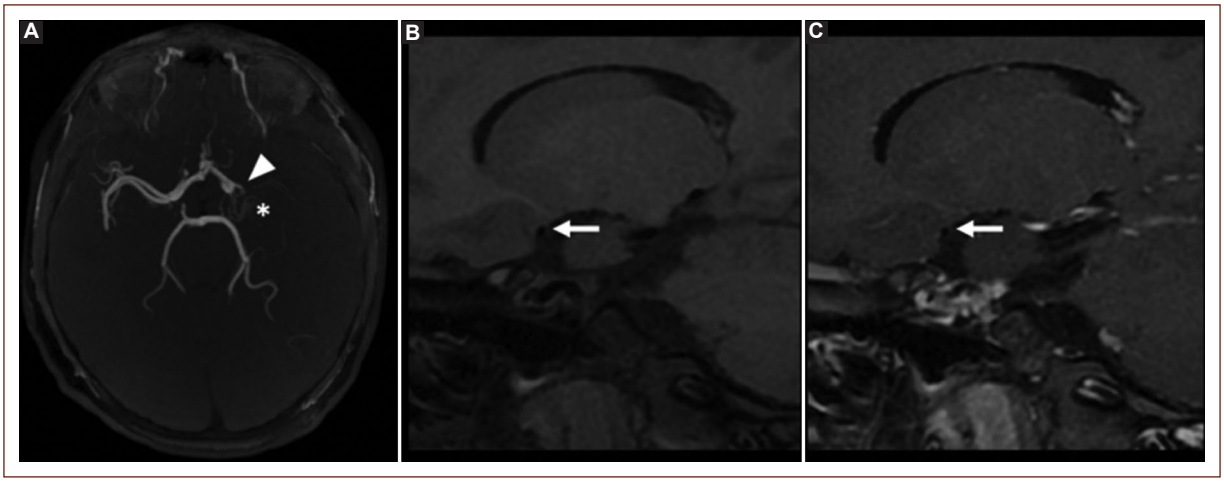

Figure 2. Magnetic resonance imaging. **A:** axial 3D time of flight maximum intensity projection image shows flow signal absence in the M1 segment of the left cerebral media artery (white arrowhead), associated with fine vessels forming a rete mirabilis (white asterisk). Three-dimensional (3D) variable-flip-angle turbo-spin-echo (CUBE) T1-weighted sequence with fat suppression, before **(B)** and after gadolinium administration **(C)**, shows no enhancement of the left cerebral media artery wall (white arrow).

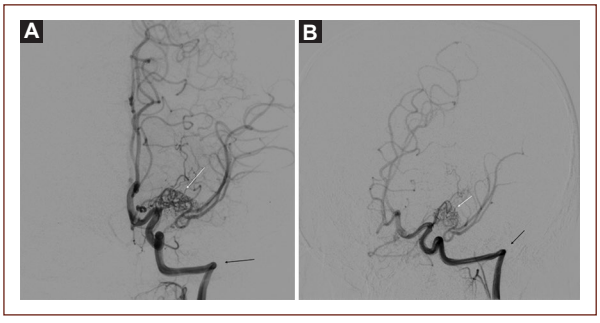

Figure 3. Digital subtraction angiography. **A:** antero-posterior proyection. **B:** oblique proyection, twig-like rete in M1 segment with normal Silvian distal (white arrow) and aberrant internal carotid artery (black arrows).

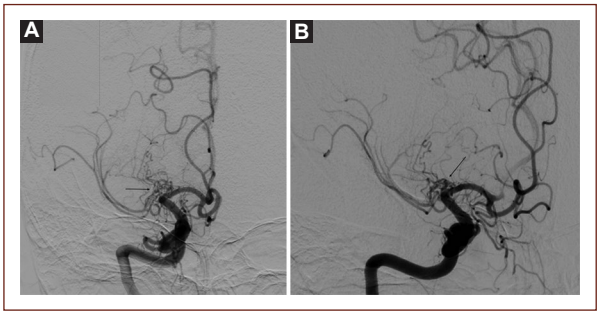

Figure 4. Digital subtraction angiography from a right internal carotid artery injection in anterior-posterior **(A)**, and oblique views **(B)**, showing right twig-like middle cerebral artery and the lateral lenticulostriate arteries arising from the network (black arrows).

Discussion

Knowledge of the variations of MCA, its incidence, and natural history is essential to make the appropriate diagnosis, in which DSA is clarifying, showing a more precise resolution of the anatomy, demonstrating an absence of internal carotid terminus and posterior cerebral artery involvement[1]. This will aid in distinguishing it from moyamoya angiopathy that may be present, thereby guiding the management of subsequent care and necessary treatment. Conversely, it helps in steering clear of ineffective and hazardous procedures[14].

The reason for requesting the angiographic procedure in 100% of the cases was moyamoya-like or moyamoya syndrome. This diagnosis was suspected by the referring doctor after a non-invasive imaging study, so it seems essential to disseminate the differentiating criteria within these pathological entities[15].

In our small case series, we present the broad age spectrum in which a twig-like MCA can be detected, highlighting one of the cases of younger age at the time of diagnosis, which increases the probability that it is associated with a congenital etiopathogenic mechanism. Diagnosis at an early age requires follow-up during the different stages of life since the compensatory mechanisms that develop during the embryonic stage and childhood could falter with the dynamic changes in circulation over time. Non-invasive monitoring makes it possible to predict claudication of the hypoperfused territory and to be able to perform a timely intervention[16]. It also seems essential to

identify concomitant vascular anomalies, especially aneurysms, since these have a higher prevalence in patients diagnosed at an early age, which correlates with a high cumulative incidence of hemorrhagic complications[17,18].

The prevalence calculated in our anonymized database was 0.21%, which is within the range described in the literature for Asian populations and noticeably different from other Latin–American studies. This variation may be attributed to the ethnic heterogeneity between the Argentinian and Chilean populations. Argentina experienced significant European migration between 1857 and 1960, primarily from Italy and Spain, which contributed to a genetic makeup comprising approximately 76% European, 17% Native American (NA), and 4% African ancestry in the Buenos Aires sample population[19]. In contrast, the Valparaiso, Chile sample population (our study site) consists of 57.11% European, 40.43% NA, and 1.97% African ancestry[20,21].

Interestingly, if we consider that NA populations originated primarily from Siberia and, as recent findings indicate, also from East China based on mitochondrial DNA lineage D4h studies, the higher NA component in our population could explain the observed prevalence being closer to that of Asian populations[22].

Conclusion

Twig-like MCA is a rare vascular anomaly whose prevalence in our series is similar to that reported in the literature. DSA is essential for diagnosing and approaching this pathology's etiopathogenesis.

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The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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