Association between migraine and aura, migrainous infarction and cortical laminar necrosis: a literature review

Associação entre enxaqueca e aura, enxaqueca por enfarte e necrose laminar cortical: uma revisão bibliográfica

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ABSTRACT

Introduction: Migraine infarction is one of the rare complications of migraine with aura, characterized by the persistence of aura symptoms for more than sixty minutes, associated with ischemic brain damage in the appropriate territory, demonstrated by neuroimaging examination. In spite of several cases reported in the literature correlate cerebral infarction with migraine, it is still unclear which magnetic resonance (MRI) pattern is associated with this condition. Cortical laminar necrosis (CLN) is a type of cortical infarction characterized by selective and late necrosis, especially in the third layer of the cerebral cortex, a region where there is greater vulnerability to metabolic stress. On MRI, CLN is characterized by an increase in cortical signal intensity on T1-weighted images with a typical curvaceous gyriform distribution. The goal of this study was to demonstrate, throughout a literature review, a possible association between migraine with aura, migraine infarction and cortical laminar necrosis without neuroimaging examination.**Methods**: A systematic research was performed in databases at the PubMed and Embase in February 2021. The search terms used for 'Migraine' or 'Migraine with aura' or 'Migrainous Infarction' combined with 'Cortical Laminar Necrosis', using their respective variations of the according as MeSH and Emtree. It was articles published in English, in pair reviewed journals, during any period and submitted to studies relevant to clinical questions, which revealed cases of Laminar Cortical Necrosis associated with migraine, were included. Studies that do not attempt the criteria, was excluded.**Results and Discussion**: The search for selected databases resulted in 24 articles. Excluding 14 articles were not chosen because they are not CLN, and 1 article published in conference abstracts that we did not choose for this review. Finally, 8 original studies were selected and critically analyzed in this review. There was a prevalence in hundred percent of the cases analyzed with migraine with aura (Table 1), and all of them manifested additional neurological symptoms. In two cases, the etiology was of familiar legacy of genetic origin, which consisted of a familial hemiplegic migraine. MR was performed days after the begining of symptoms, ranging from the 3rd to the 30th day. In all cases, was observed unilateral cortical hypersignal on axial T1-evaluation. Unilateral T1-evaluation cortical hyperintensity with Gadoliun and FLAIR was also identified in most of the cases. Less commonly, alterations to the DWI and ADC sequences are seen. **Conclusion**: Despite being a rare manifestation, this review demonstrates that CLN can be recognized as an attribute associated with migraine with aura, spread the spectrum of neuroimaging acts

correlated with migraine. Our goal was narrow the boundaries between neurovascular disease on imaging and a migraine with aura, helping neurologists to recognize this association. Before this scene of high predominance of migraines, further studies are needed to elucidate its relationship with CLN, as its pathophysiology and group of patients with risk factors, who may benefit from prophylactic treatment.

Keywords: migraine, migraine with aura, migraine infarction, cortical laminar necrosis.

RESUMO

Introdução: O enxaqueca é uma das raras complicações da enxaqueca com aura, caracterizada pela persistência dos sintomas da aura durante mais de sessenta minutos, associada a danos cerebrais isquémicos no território apropriado, demonstrada pelo exame de neuroimagem. Apesar de vários casos relatados na literatura correlacionarem o enfarte cerebral com a enxaqueca, ainda não é claro qual o padrão de ressonância magnética (RM) que está associado a esta condição. A necrose laminar cortical (CLN) é um tipo de enfarte cortical caracterizado por necrose selectiva e tardia, especialmente na terceira camada do córtex cerebral, uma região onde existe uma maior vulnerabilidade ao stress metabólico. Na RM, o CLN é caracterizado por um aumento da intensidade do sinal cortical em imagens ponderadas em T1 com uma distribuição giroscópica curva típica. O objectivo deste estudo foi demonstrar, ao longo de uma revisão bibliográfica, uma possível associação entre enxaqueca com aura, enxaqueca por enxaqueca e necrose laminar cortical sem exame neuroimaginoso.**Métodos:** Foi realizada uma investigação sistemática em bases de dados no PubMed e Embase, em Fevereiro de 2021. Os termos de pesquisa utilizados para "Enxaqueca" ou "Enxaqueca com aura" ou "Enxaqueca com aura" combinados com "Necrose laminar cortical", utilizando as suas respectivas variações do segundo como MeSH e Emtree. Foram incluídos artigos publicados em inglês, em revistas revistas de pares, durante qualquer período e submetidos a estudos relevantes para questões clínicas, que revelaram casos de Necrose Cortical Laminar associada à enxaqueca. Foram excluídos os estudos que não tentam os critérios.**Resultados e Discussão:** A pesquisa de bases de dados seleccionadas resultou em 24 artigos. Excluindo 14 artigos não foram escolhidos porque não são CLN, e 1 artigo publicado em resumos de conferências que não escolhemos para esta revisão. Finalmente, 8 estudos originais foram seleccionados e analisados criticamente nesta revisão. Houve uma prevalência em 100% dos casos analisados com enxaqueca com aura (Tabela 1), e todos eles manifestaram sintomas neurológicos adicionais. Em dois casos, a etiologia era de herança familiar de origem genética, que consistia numa enxaqueca hemiplégica familiar. A RM foi realizada dias após o início dos sintomas, variando entre o 3º e o 30º dia. Em todos os casos, foi observado um hipersinal cortical unilateral na avaliação axial T1. A hipersintensidade cortical unilateral da avaliação T1 com Gadoliun e FLAIR também foi identificada na maioria dos casos. Menos frequentemente, são observadas alterações nas sequências DWI e ADC. **Conclusão:** Apesar de ser uma manifestação rara, esta revisão demonstra que o CLN pode ser reconhecido como um atributo associado à enxaqueca com a aura, espalhando o espectro de actos de neuroimagem correlacionados com a enxaqueca. O nosso objectivo era estreitar os limites entre a doença neurovascular por imagem e uma enxaqueca com aura, ajudando os neurologistas a reconhecer esta associação. Antes deste cenário de elevada predominância de enxaquecas, são necessários mais estudos para elucidar a sua relação com a CLN, como a sua fisiopatologia e grupo de pacientes com factores de risco, que podem beneficiar de tratamento profiláctico.

Palavras-chave: enxaqueca, enxaqueca com aura, enxaqueca com enxaqueca, necrose laminar cortical.

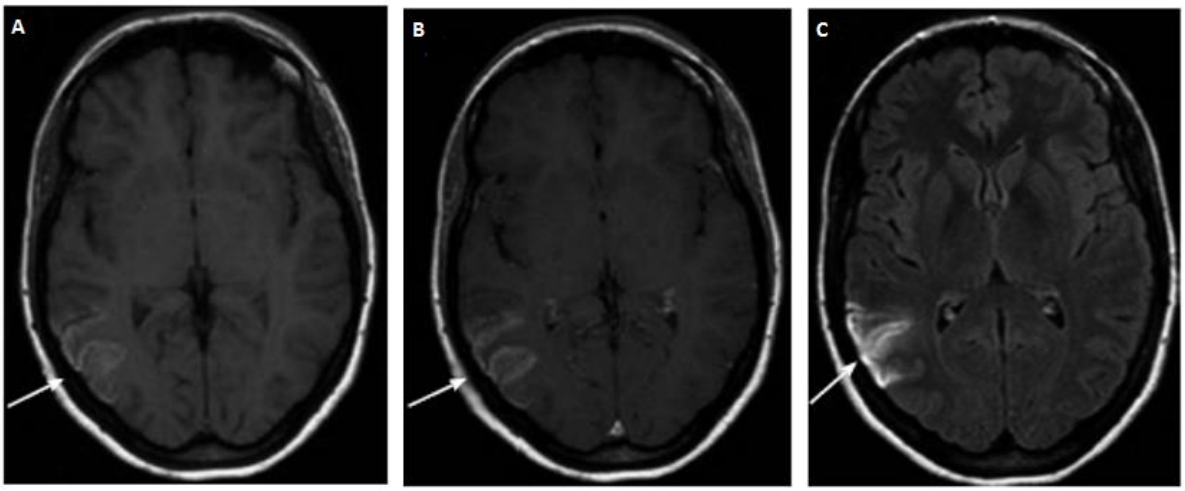
1 INTRODUCTION

Migraine infarction is a rare complication of migraine with aura, characterized, according to the criteria of the International Classification of Headache Disorders, 3rd edition (ICHD-3), by the persistence of two symptoms of the aura for more than sixty minutes, associated with brain damage ischemic in appropriate territory, demonstrated by neuroimaging examination, in the absence of potential causes of ischemic stroke.[1,2,3] The pathophysiology of migrant infarction has not been fully elucidated, however, it is proven that Possible mechanisms include cerebral hemodynamic changes, with increased vascular resistance, glutamatergic neuronal hyperexcitability, interruption of neural ion homeostasis, release of neuroinflammatory mediators, endothelial dysfunction related to reduced bioavailability of vasodilator-inducing vasodilators and increased vasodilator-inducing bioavailability. can be a cause and an effect Despite several cases reported in the literature correlating cerebral infarction with migraine, it is still not clear which MRI pattern is associated with each other, with descriptions of cerebrovascular accidents (CVAs) with multiple small lesions, isolated lesions in posterior or anterior circulation, most of the time, cortico-subcolor

Cortical laminar necrosis (CLN) is a type of cortical infarction characterized by selective and delayed necrosis, mainly in the third layer of the cerebral cortex, a region where there is greater vulnerability to metabolic stress.[1] The lesion is usually greater in the depths and sides of the sulci of the brain. than on the crest of the gyri, and there is relative and absolute preservation of the underlying white matter.[1,5] This condition represents an increasingly recognized neuropathological endpoint, being observed in the context of hypoglycemic and hypoxic encephalopathy, status epilepticus, metabolic and immunological disorders, toxic and infectious. However, it is a very uncommon type of cerebral infarction correlated with the spectrum of migraine.[2, 7] In magnetic resonance imaging (MRI), CLN is characterized by an increase in cortical signal intensity on T1-weighted images, with a typical curvilinear giriform distribution (Fig. 1A).[1,2] Contrast enhancement on T1-weighted gadolinium-based images can be seen in the subacute and late phases (Fig. 1B), and is due to the breakdown of the blood-brain barrier.[1,2] Finding these phase changes Acute symptoms are particularly challenging as they usually appear two weeks after ischemia, peak in intensity around a month and then slowly disappear over 3 months to 2 years, and cortical atrophy may appear in the chronic phase. [1,7,8,9,10] Some studies have shown that T1 hypersignal reflects the presence of substances such as hemoglobin, lipid-laden macrophages, melanin, paramagnetic substances or protein-rich fluid, therefore, not being sec. undone to hemorrhagic transformation of cerebral ischemia.[1,9] Fluid-attenuated inversion recovery-weighted (FLAIR) images may also demonstrate signal

hyperintensity, which appears later (Fig. 1C).[1,4] Only a few case reports have evaluated diffusion-weighted imaging (DWI) abnormalities in the acute phase of CLN.[10] Thus, this entity still has several unexplored characteristics, with a significant gap in knowledge regarding the acute phase of CLN.

Figure 1 (A-C): Cortical laminar necrosis demonstrated in brain RMI in migrainous stroke on D20 after stroke: (A) Axial T1 demonstrating cortical hypersignal in the right temporal lobe. (B) Axial T1 demonstrating post-contrast cortical highlights. (C) Axial FLAIR demonstrating cortical hypersignal in corresponding area.[13]



2 OBJECTIVE

Is to demonstrate, through a literature review, the possible association between migraine, migrainous infarction and cortical laminar necrosis in the neuroimaging exam.

3 METHODS

A systematic literature search was carried out in the PubMed and Embase databases during February 2021. The search terms used were 'Migraine' or 'Migraine with Aura' or 'Migrainous Infarction' combined with 'Cortical Laminar Necrosis ', using their respective variations according to MeSH and Emtree. We only include articles published in English, in peer-reviewed journals, during any period. Only studies relevant to the clinical question, which described cases of CLN associated with migraine, were included. After the initial screening, to determine which articles met the inclusion criteria, two independent researchers initially analyzed the title of the studies. If it was still unclear, the abstracts and full texts were carefully analyzed. Studies that did not meet the inclusion criteria were excluded. All articles included were case reports. Inclusion was based on agreement between the two reviewers, and there were no cases of non-consensus.

4 RESULTS AND DISCUSSION

The search in selected databases resulted in 24 articles. There was no duplicate article. 14 ineligible papers were excluded because they were not CLNs, and 1 article published in congress abstracts that did not contain eligible data for this review. Finally, 8 original studies that met the inclusion criteria were selected and were critically analyzed in this review. From the analysis of the cases, considering their individualities, it was possible to see agreements between the reported cases and, thus, to make some possible associations related to the objective of this review.

At first, considering migraine, which was the main complaint of the reported patients, some recurrent and more relevant aspects were noted. There was a prevalence, in one hundred percent of the cases analyzed, of migraine with aura (Table 1). In two cases, the etiology was of familial origin of genetic order, which consisted of familial hemiplegic migraine.[11,12] In the other studies, there was no association that could explain the etiology of the. All reported cases met ICHD-3/ International Headache Society (IHS) diagnostic criteria for migraine-induced cerebral infarction, and two cases had their pain period prolonged for more than 72 hours, characterizing another complication of the disease, migranous status. From the 5 female cases, only two had a history of oral contraceptive use, one of which was associated with heavy smoking as a risk factor for migraine with aura and stroke. The age of the patients ranged between 14 and 57 years, confirming the trend towards a lower incidence of migraine complications in the elderly. All cases showed additional neurological symptoms superimposed on migraine with typical aura. There was a higher prevalence of symptoms such as dysarthria, ataxia and hemiparesis, surrounding a suggestive spectrum of brainstem aura and hemiplegic aura.[2,13,14,15] Also described, in three cases, were unilateral myoclonic facial movements and hemifacial spasms, suggesting a pathophysiological interposition with movement disorders, involving cortical, thalamic and brainstem regions stimuli and hyperexcitation.[4,12,13]

Table 1: Recurrent and more relevant aspects reported patients

Articles	Gender	Age of migraine diagnosis	Age	Previous illnesses	Medications in use	Habits	Other neurological symptoms during a migraine attack	Migraine type	Migraine complications	Migraine family history	Changes in the MRI exam	Time of appearance of CLN on MRI
Black DF et al. (2004)	M	18	51	NA	NA	NA	Right hemiparesis; cerebellar ataxia	Familial hemiplegic migraine (FHM)	Migrainous infarction	Yes	hypervascularity in the left hemispheric cortex on FLAIR, T1 and T2, showing post-contrast enhancement on T1.	14th day
Liang Y et al. (2007)	F	NA	57	No other diseases	Unused	NA	Left homonymous hemianopsia; Tinnitus, and left arm and leg paresthesias	Migraine with visual aura	Migrainous infarction. Migrainous Status	No	Hyperintense signal on FLAIR, T1, T2 and DWI, hyposignal on ADC, in the right hemispheric cortex, showing post-contrast enhancement on T1. MRV was negative for dural sinus thrombosis.	14th day
Arboix A et al. (2013)	F	21	29	Anxiety disorder	Oral contraceptive; Alprazolam 0.5 mg/day	Heavy smoking (20 cigarettes/day in the last 4 years)	Dysarthria, left brachial hemiparesis and hemihypoesthesia (NIH = 2) and brief and autolimited left clonic facial movements.	Migraine with and without typical aura (visual)	Migrainous infarction. Migrainous Status	No	Increased signal on FLAIR, T1, T2 and DWI in the right temporo-parietal cortex, showing a post-contrast enhancement on T1. MRA was normal and negative for dural sinus thrombosis	20th day
Reid JM et al. (2014)	M	NA	56	NA	NA	NA	Neglect, dysphasia, mild left hemiplegia, gait ataxia, focal left facial twitching	Familial hemiplegic migraine (FHM)	Migrainous infarction	Yes	Cortical laminar necrosis in the right temporo-parietal area	30th dia
Khardenavis V et al. (2018)	F	Adolescence	27	No other diseases	Unused	NA	dysarthria, right hemiparesthesias (NIH = 4)	Migraine with and without typical aura (visual)	Migrainous infarction	Yes	Gyral enhancement in the left temporoparietal region	14th dia
Morais R et al. (2018)	F	18	37	Anxiety disorder. Homozygous for the PAI gene mutation (PAI 4G / 5G and PAI G / A-844). Von Willerbrand factor slightly increased by 204% (normal value 70-120%)	Oral contraceptive; Propranolol 20 mg/day	NA	left homonymous superior quadrantanopsia, which persisted after 90 days	Migraine with typical aura (visual)	Migrainous infarction	No	Cortical increased signal with gyriform appearance on T1, T2 and FLAIR involving occipitotemporal gyrus and lingual gyrus (along the collateral sulcus). MRV was negative for dural sinus thrombosis.	30th day
Sharma SR et al. (2019)	F	20	27	No other diseases	Unused	NA	dysarthria, right hemiparesthesias, brief and autolimited left–clonic facial movements.	Migraine with and without typical aura (visual)	Migrainous infarction	Yes	Gyral T2/T1/FLAIR hyperintensity involving the left superior parietal lobule	15th day
Messina LM et al. (2017)	M	NA	14	No other diseases	Unused	NA	dysarthria, aphasia and visual disturbances	Migraine with typical aura (visual)	Migrainous infarction	No	Cortical laminar necrosis on supramarginal gyrus in the left cerebral hemisphere	3th day

NIH: Institutes of Health Stroke Scale (NIHSS); NA: Not available; MRI: Magnetic Resonance Imaging; MRV: Magnetic Resonance Venography; MRA: Magnetic Resonance Angiography; ADC: Apparent diffusion coeficiente

After the migrainous clinical picture, it is of fundamental importance to describe the findings of the neuroimaging exams of the patients described in the mentioned works, which aim, above all, to understand the different manifestations of migraine. In this sense, there is a report, in 5 of the 8 cases, of hypersignal on T1 with contrast on MR, involving the affected cortical areas, implying a rupture of the blood-brain barrier. This phenomenon may be related to the hypoperfusion described in Leão's cortical spreading depression (CAD), where a triphasic

vasomotor response occurs, evolving from vasoconstriction and hyperemia to a prolonged period of hypovolemia with subsequent reduction in cerebral blood flow, which may progress to infarction. This imaging finding favors hypoperfusion as one of the triggers for the rupture of the blood-brain barrier.[2,5,11,13,15,16] MR was performed days after the beginning of symptoms, ranging from the 3rd to the 30th day. In all cases, cortical hypersignal was observed on axial, unilateral T1-axial, which was variably located in the temporal, parietal and occipital regions. Unilateral cortical hyperintensity in FLAIR consideration was also identified in most cases. Under these circumstances, those images were suggestive of edema followed by signs of migrainous infarction in cortex's regions, with preservation of the inner layers of white substance. It is also worth considering that the studies in this review have shown that brain imaging tests can identify areas of CLN within four months after the acute crisis in the migraine with aura, and that, in some cases, CLN is also demonstrated by alterations in the DWI and ADC sequences, areas correlated to cytotoxic edema, seen through the MR.[5,13]

Finally, in the reports considered for this review, an enthusiasm in looking for possible pathophysiological mechanisms that explain CLN was noticed. In this context, it can be said that all researchers, without exception, admitted the absence of well-established knowledge about these mechanisms. However, there were agreements between the articles in some plausible aspects, highlighting vascular alterations resulting from CAD, which denotes a self-propagating wave of neuronal and glial depolarization that spreads through the cerebral cortex, leading to a molecular cascade of events involving mediator release pro-inflammatory, low arterial perfusion culminating in the triphasic vasomotor response, previously mentioned.[16,17,18] Besides, recurrent focal CAD may be responsible for persistent aura, increasing the probability of infarction in this area. The presence of hypercoagulation disorders, such as increased von Willebrand factor, has also been correlated with the possible etiopathogenesis of NCL.[1,18] Oxidative stress, a mechanism attributed to ischemic events, was also mention as a likely factor in which it would induce a response. inflammatory and would facilitate the production of clots.[1] However, they were unable to fully describe the pathogenesis of this migraine complication. In the end, the etiopathogeny of migrainous infarction and NCL can be explained by an interaction of metabolic, hypoxic and cellular factors correlated to the pathophysiology of migraine with aura that lead to endothelial dysfunction, ischemia and infarction.

5 CONCLUSION

This is the first review to describe the association of CLN with migraine infarction and migraine with aura. This work demonstrates that CLN can be recognized as a characteristic

associated with migraine with aura, extending the spectrum of neuroimaging findings correlated with migraine. Our objective was to narrow the existing boundaries between neurovascular findings on imaging exams and migraine with aura, helping neurologists to recognize this association. Few cases are reported in the scientific literature and given a scenario of high prevalence of migraine, more studies are needed to elucidate the relationship of CLN and migraine with aura, as well as its pathophysiology and the group of patients with risk factors, which may benefit from prophylactic treatment.

REFERENCES

1. Lattanzi S, Rinaldi C, Dobran M, et al. Cortical Laminar Necrosis and Migrainous Stroke. J Neurosci Rural Pract 2019; 10(3):563-4.

2. Khardenavis V, Karthik DK, Kulkarni S, et al. Cortical laminar necrosis in a case of migrainous cerebral infarction. BMJ Case Rep. 2018; doi:10.1136/bcr-2017-221483.

3. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (ICHD-3). Cephalalgia 2018; 38: 1–211.

4. Sharma SR, Massaraf H, Das S, et al. Cortical Laminar Necrosis as a Presenting Manifestation of Migraine in an Apparently Normal Patient: a rare case report. J Neurosci Rural Prect. 2019; 10(3):559-562.

5. Morais R, Sobral F, Gil Cunha G, et al. Advanced MRI study of migrainous infarction presenting as cortical laminar necrosis: Case report and literature review. Clinical Neurology and Neurosurgery 2018; 82-85.

6. Wolf ME, Szabo K, Griebe M, Förster A, Gass A, Hennerici MG, Kern R. Clinical and MRI characteristics of acute migrainous infarction. Neurology. 2011 May 31;76(22):1911-7.

7. Finsterer J. Laminar cortical necrosis in mitochondrial disorders. Clin Neurol Neurosurg. 2009; 111(8):655-8. doi: 10.1016/j.clineuro.2009.07.010. Epub 2009 Aug 6. PMID: 19664878.

8. Komiyama M, Nishikawa M, Yasui T. Cortical laminar necrosis in brain infarcts: chronological changes on MRI. Neuroradiology 1997; 39(7): 474-9.

9. Allen LM, Hasso AN, Handwerker J, et al. Sequence-specific MR imaging findings that are useful in dating ischemic stroke. Radiographics 2012; 32(5): 1285-97.

10. Cannella R, Sparacia G, Lo Re V, et al. Advanced magnetic resonance imaging of cortical laminar necrosis in patients with stroke. Neuroradiol J. 2019; 32(6):431-7.

11. Black DF , Kung S, Sola CL, et al. Familial hemiplegic migraine, neuropsychiatric symptoms, and Erdheim-Chester disease. Headache 2004; 44(9):911-915.

12. Reid JM, Tyagi A, Nazir F. Familial Hemiplegic Migraine and Focal Status Epilepticus Causing Cortical Laminar Necrosis. J Neurol Neurosurg Psychiatry 2009; 80:452–466.

13. Arboix A, González-Peris S, Grivé E, et al. Cortical laminar necrosis related to migrainous cerebral infarction. World J Clin Cases 2013; 1(18): 256-259.

14. Morais R, Nunes C, Pereira D, et al. Migrainous infarction: cortical laminar necrosis Neuroradiology 2013; 55: 1455-1511.

15. Liang Y, Scott TF. Migrainous infarction with appearance of laminar necrosis on MRI. Clin Neurol Neurosurg 2007; 109(7):592-596.

16. Leão AAP. Spreading depression of activity in the cerebral cortex. J. Neurophysiol 1944; 7(6):359-90.

17. Leão AAP. Pial circulation and spreading depression of activity in cerebral cortex. J Neurophysiol 1944; 7(6):391-6

18. Charles A. Advances in the basic and clinical science of migraine. Ann Neurol 2009; 65(5):491-8.