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Images of Interest / Imagens de Interesse

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy

Arteriopatia Cerebral Autossómica Dominante com Infartos Subcorticais e Leucoencefalopatia

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Abstract

CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) is a genetic disorder caused by mutations in the NOTCH3 gene, leading to recurrent subcortical infarcts, migraine with aura, early dementia, and psychiatric disorders. Diagnosis is confirmed by genetic testing and MRI. Treatment is symptomatic, with a focus on stroke prevention. Clinical presentations can vary, and early genetic testing is crucial for diagnosis and management. This case is of particular relevance as it highlights the importance of early genetic testing in the diagnosis of CADASIL, emphasizing the role of genetic confirmation in atypical cases where clinical features might initially suggest other diagnoses. We present a case of a 46-year-old woman with progressive difficulty walking, vertigo, severe headache, and transient paresthesia. She had a long history of recurrent neurological symptoms, including syncope and chronic headaches, and recently experienced memory deficits. MRI showed characteristic hyperintense white matter lesions and a lacunar infarct, leading to a diagnosis of CADASIL, confirmed by the presence of a NOTCH3 mutation on genetic testing.

Keywords

CADASIL; Central nervous system; Magnetic Resonance Imaging; Diagnosis.

Resumo

CADASIL (Arteriopatia Cerebral Autossómica Dominante com Infartos Subcorticais e Leucoencefalopatia) é uma doença genética causada por mutações no gene NOTCH3, levando a infartos subcorticais recorrentes, enxaqueca com aura, demência precoce e distúrbios psiquiátricos. O diagnóstico é confirmado por testes genéticos e ressonância magnética. O tratamento é sintomático, com foco na prevenção de derrames. As apresentações clínicas podem variar, e o teste genético precoce é crucial para o diagnóstico e manejo. Este caso é particularmente relevante, pois destaca a importância do teste genético precoce no diagnóstico de CADASIL, enfatizando o papel da confirmação genética em casos atípicos, onde as características clínicas podem inicialmente sugerir outros diagnósticos. Apresentamos o caso de uma mulher de 46 anos com dificuldade progressiva para caminhar, vertigem, dor de cabeça severa e parestesia transitória. Ela tinha um longo histórico de sintomas neurológicos recorrentes, incluindo síncope e dores de cabeça crónicas, e recentemente apresentou déficit de memória. A ressonância magnética mostrou lesões características de substância branca hiperatenuantes e um infarto lacunar, levando ao diagnóstico de CADASIL, confirmada pela presença de uma mutação NOTCH3 ao teste genético.

Palavras-chave

CADASIL; Sistema nervoso central; Imagem por ressonância magnética; Diagnóstico.

Case Presentation

A 46-year-old woman presented with progressive difficulty walking and vertigo, associated with severe headache and paresthesia in the left lower limb, perioral region, and tongue. These symptoms were transient, resolving the following day, leaving only persistent headache. She had a long history of recurrent paresthesia, paresis, syncope, and chronic headaches for over 15 years, with recent memory deficits affecting her ability to perform calculations.
Physical examination revealed bilateral nystagmus, a shuffling gait, and hyperreflexia. MRI demonstrated hyperintense foci in the subcortical and deep white matter, including the external capsule and temporal poles, along with a lacunar infarct in the right gangliocapsular region, consistent with CADASIL. Genetic testing confirmed the presence of a NOTCH3 mutation.

Discussion

CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) is a genetic disorder caused by mutations in the NOTCH3 gene located on chromosome 19. It is characterized by recurrent subcortical infarcts, migraine with aura, early dementia, and psychiatric disorders. The diagnosis is confirmed by genetic testing for mutations in the NOTCH3 gene, which has shown near 100% sensitivity and specificity for the condition. MRI typically reveals white matter hyperintensities in the temporal lobe and external capsule, as well as lacunar infarcts.[1]

This pathology, though initially considered rare, has an estimated prevalence of 1.3 to 4.1 per 100,000, with recent studies suggesting a higher rate in the general population, especially among Asians.[2] Despite its association with stroke and dementia, the clinical manifestations and progression of CADASIL can be variable, often presenting with episodes of recurrent ischemic stroke, cognitive decline, and psychiatric symptoms. Management is largely symptomatic, with antiplatelet therapy used to prevent strokes and secondary prevention focusing on managing cerebrovascular risk factors.[3]

The differential diagnosis of CADASIL includes conditions such as sporadic subcortical atherosclerotic encephalopathy, MELAS, and primary CNS angiitis. Although migraine with aura is a common presenting symptom, its treatment can be complex, as therapies like acetazolamide and valproate may interfere with cerebral vasoreactivity in CADASIL patients.[4] This case deviates from the typical presentation, as the patient did not initially present with migraines.

Prospective studies on CADASIL are limited, but historical data suggest a median age of diagnosis around 40 years, with an average age of death around 56 years.[4] This case aligns with these figures. Additionally, CADASIL may present atypically, including cases of asymptomatic individuals and rare complications such as intracerebral hemorrhage.[4] Given the complexity of CADASIL and its potential for atypical manifestations, it is crucial for clinicians to consider a thorough family history and perform genetic testing for accurate diagnosis and management.

CADASIL poses diagnostic challenges due to its variable clinical presentation. This case highlights the importance of family history and early genetic testing for patients presenting with unexplained strokes or dementia. While the treatment approach remains largely symptomatic, continued research is essential to improve therapeutic strategies and outcomes for affected individuals.

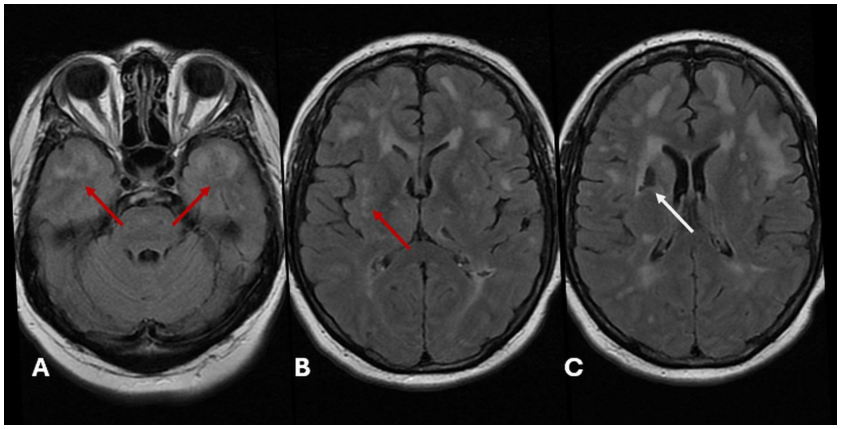

Figure 1 – Brain MRI on axial FLAIR sequence (A-C). Few scattered FLAIR hypersignal foci in the subcortical and deep/periventricular white matter of both cerebral hemispheres, including the external capsule and temporal poles - two regions of specific involvement (red arrows). Additionally, there was a chronic lacunar infarct in the right gangliocapsular region (white arrow).

Ethical Disclosures / Divulgações Éticas

Conflicts of interest: The authors have no conflicts of interest to declare.

Conflitos de interesse: Os autores declaram não possuir conflitos de interesse.

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Confidentiality of data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Confidencialidade dos dados: Os autores declaram ter seguido os protocolos do seu centro de trabalho acerca da publicação dos dados de doentes.

Protection of human and animal subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Protecção de pessoas e animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial.

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