Thalamic stroke in a patient with membranous interventricular septal aneurysm☆

Infarto talámico en un paciente con aneurisma del septo interventricular

Dear Editor:

Membranous interventricular septal aneurysms are rare congenital heart defects associated with increased risk of embolic stroke. However, this association cannot be clearly established due to the low incidence of this type of aneurysm.

We present the case of a 66-year-old man who was referred to our department due to left thalamic stroke presenting with instability, poor coordination, and language alterations; symptoms lasted 5 hours and improved progressively, with the patient presenting no sequelae. The patient reported history of heart disease (although no medical records were available) and no other relevant history. Physical examination revealed systolic murmur at the left sternal border and systolic and diastolic murmurs in the aortic area. An electrocardiography study displayed sinus rhythm with right bundle branch block and left anterior fascicular block.

Brain MRI revealed no alterations. We performed several screening tests, including an ultrasound study of the supra-aortic trunks, a study of hypercoagulability disorders (protein C or protein S deficiency, antithrombin III, factor V Leiden, prothrombin G20210A, lupus anticoagulant, and anticardiolipin antibodies), an echocardiogram, and Holter monitoring to rule out any arrhythmia with high embolic potential, such as atrial fibrillation. All tests yielded normal results, with the exception of transthoracic echocardiogram, which revealed an aneurysm in the membranous interventricular septum with perimembranous interventricular communication (Fig. 1), moderate aortic insufficiency, and mild left ventricular hypertrophy, with normal left ventricular global and segmental systolic function.

These findings were confirmed with a transoesophageal echocardiogram, which revealed an aneurysm protruding towards the right ventricular outflow tract and a perimembranous ventricular septal defect with left-to-right shunt. We did not detect any other possible causes of embolism, such as patent foramen ovale, interatrial septal aneurysm, thrombi in the left atrial appendage, or atherosclerotic plaques in the aortic arch.

In summary, our patient was a 66-year-old man with stroke who did not present atrial fibrillation, patent foramen ovale, hypercoagulability disorders, or evidence of artery disease at other levels. As he presented few cardiovascular risk factors, we hypothesise that the pathogenic mechanism of stroke was a thrombus originating in the membranous interventricular septal aneurysm.

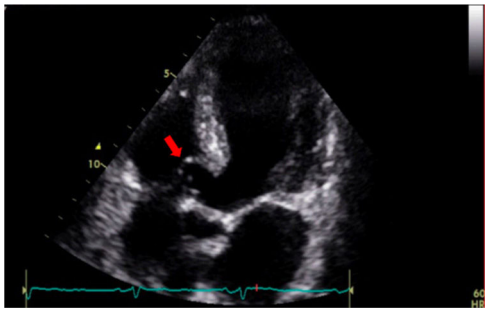

Figure 1 Transthoracic echocardiogram showing a membranous interventricular septal aneurysm (arrow).

Membranous interventricular septal aneurysms are recognised as a possible cause of embolism.[1] In the case presented here, embolism seems to have been the cause of thalamic stroke, which usually causes pure sensory or atypical lacunar syndromes.[2]

The incidence of this heart defect is estimated at 0.2%—3% in the general population.[3] In most cases, the aneurysm is a benign, incidental finding,[4] although it can cause aortic or tricuspid regurgitation, right ventricular outflow tract obstruction, infective endocarditis, aneurysm rupture, atrioventricular block, or thromboembolism.[5] Individuals with asymptomatic membranous interventricular septal aneurysms should be followed up to detect any of these complications.[6] Patients presenting unexplained embolic events should be thoroughly assessed to rule out presence of this rare heart defect.

Differential diagnosis of membranous interventricular septal aneurysms includes sinus of Valsalva aneurysms, abscesses, and ischaemic or traumatic aneurysms.[7] Our patient's clinical history, the absence of infection and history of surgery or myocardial infarction, and the location of the aneurysm suggest that this heart defect was caused by spontaneous partial closure of the interventricular communication; this is in fact the most frequent cause of membranous interventricular septal aneurysms.

Treatment options for patients with stroke include surgical excision and repair of the aneurysm and anticoagulant treatment. Less frequently, patients may benefit from percutaneous closure, although this technique is more challenging when applied to membranous interventricular septal aneurysms than to other types of heart defects.[8] In our case, we informed the patient about the possible management strategies; as he was unwilling to undergo surgery, we started anticoagulation with acenocoumarol. After 3 years of follow-up, the patient has presented no further embolic events or complications.

Membranous interventricular septal aneurysms, though rare, may potentially cause severe complications. Given that the most appropriate management strategy in these patients is yet to be established, we deemed it interesting to report this case of satisfactory progression with conservative treatment.

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Paucisymptomatic hyperCKaemia due to a mutation in the *ANO5* gene☆

HiperCKemia paucisintomática secundaria a mutación en el gen ANO5

Dear Editor:

Asymptomatic/paucisymptomatic hyperCKaemia is a frequent reason for consultation at neuromuscular disorders units. Elevated creatine kinase (CK) levels, or hyperCKaemia, may be caused by multiple factors, including hereditary myopathies. One such hereditary myopathy is anoctaminopathy secondary to mutations in the *ANO5* gene (11p14.3). Recessive *ANO5* mutations cause a wide range of clinical phenotypes, including limb-girdle muscular dystrophy type 2 L, Miyoshi myopathy 3, and isolated hyperCKaemia or hyperCKaemia associated with exercise intolerance.[1]

We present the case of a 41-year-old man with no relevant medical history except for hyperCKaemia of 6 years' progression, detected in a routine blood test (1200—4500 U/L). He practised both aerobic and anaerobic exercise, and had developed exercise intolerance over the previous year. He had never presented choluria or rhabdomyolysis. The examination revealed no muscle weakness, amyotrophy, or myotonia. An electromyography study showed motor unit potentials with myopathic features in the muscles of both lower limbs, with no pathological spontaneous activity. A muscle MRI scan revealed asymmetric fatty infiltration in the semimembranosus and medial gastrocnemius muscles (Fig. 1), with myoedema in the semimembranosus, biceps femoris, and gastrocnemius muscles on STIR sequences (Fig. 2), despite the lack of clinical evidence of weakness. A transthoracic echocardiogram and Holter electrocardiography found no alterations. A muscle biopsy revealed a dystrophic pattern, with variations in fibre size, marked nuclear internalisation, and signs of necrosis and regeneration. An immunohistochemical study and Western blot analysis detected no alterations in dystrophin, sarcoglycans, calpain, dysferlin, or caveolin.

In view of the nonspecific dystrophic alterations revealed by the MRI and biopsy studies, we requested a next-generation sequencing analysis of a panel of genes associated with neuromuscular disorders. The analysis identified a homozygous variant, c.1982 T > C, in exon 8 of *ANO5* (reference sequence: NM_213599), which causes amino acid substitution p.Leu661Pro. This variant is registered in the gnomAD database with a frequency of 0.00003230, but had not previously been associated with any disease. A genetic study of the patient's relatives revealed that both parents were heterozygous carriers of the mutation. After over 8 years of follow-up, the patient has developed no further symptoms besides mild exercise intolerance.

We present a case of paucisymptomatic hyperCKaemia secondary to a mutation in the *ANO5* gene; diagnosis was reached with massive DNA sequencing of a pre-established group of genes associated with our patient's symptoms. As mentioned previously, the aetiology of hyperCKaemia is multifactorial. Several diagnostic algorithms can be used, which include different complementary tests[2,3]; gene panel sequencing is not currently included. Among the initial tests performed in our patient, muscle MRI and biopsy

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