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REPORTES DE CASO

# Ischemic stroke in a young patient due to protein S deficiency in the context of muscular dystrophy - case report

## Accidente cerebrovascular isquémico por déficit de proteína S en el contexto de distrofia muscular

## Acidente Vascular Cerebral Isquêmico em paciente jovem devido à deficiência de proteína S no contexto da distrofia muscular - relato de caso

**Juan David Vega-Padilla[1]*, Juan David Vivas-Suárez[2], Jorge Andrés Sánchez[3], Viviana Carolina Vargas-Quintana[4]**

[1] Hospital San José, Guachetá, Cundinamarca, Colombia

[2] Fundación Universitaria San Martín, Bogotá, Colombia

[3]Universidad de la Sabana, Chía, Colombia

[4] Hospital Universitario La Samaritana, Bogotá, Colombia

***Correspondencia: Dirección:** Calle 7 # 9 - 02 Saboyá, Boyacá **Celular:** 312 375 5426

**Correo electrónico:** ddavids89@hotmail.com

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## ABSTRAC

A 19-year-old woman with a 6-year history, consisting of frequent falls and weakness due to loss of strength in the lower extremities. During the last 10 hours, she presented a sudden episode of left hemiplegia, deviation of the labial commissure to the right, dysarthria and four emetic episodes. She was diagnosed with an ischemic stroke caused by a deficiency of the S-protein and, in addition, a muscular dystrophy. This case report may indicate a relationship between muscular dystrophy and ischemic stroke caused by a protein S deficiency.


**Key words**: stroke; thrombophilia; muscular dystrophies.

## RESUMEN

Mujer de 19 años con historia de 6 años de evolución consistente en caídas frecuentes y debilidad debido a la pérdida de fuerza en los miembros inferiores. Durante las últimas 10 horas, presentó un episodio repentino de hemiplejia izquierda, desviación de la comisura labial a la derecha, disartria y cuatro episodios eméticos. Ella fue diagnosticada con accidente cerebrovascular isquémico causado por una deficiencia de la proteína S y además con distrofia muscular. Este reporte de caso puede indicar una relación entre la distrofia muscular y el accidente cerebrovascular isquémico causado por una deficiencia de proteína S.


**Palabras clave:** Accidente cerebrovascular; trombofilia; distrofia muscular.

## RESUMO

Mulher de 19 anos com história de 6 anos, consistindo de quedas frequentes e fraqueza devido à perda de força nas extremidades inferiores. Durante as últimas 10 horas, apresentou episódio súbito de hemiplegia esquerda, desvio da comissura labial à direita, disartria e quatro episódios eméticos. Ela foi diagnosticada com um acidente vascular cerebral isquêmico causado por uma deficiência da proteína S e, além disso, uma distrofia muscular. Este relato de caso pode indicar uma relação entre distrofia muscular e acidente vascular cerebral isquêmico causado por deficiência de proteína S.


**Palavras-chave:** acidente vascular cerebral; trombofilia; distrofias musculares.

## BACKGROUND

Strokes are the second leading cause of mortality worldwide, originating 5.5 million deaths per year and in addition, they are the main cause of disability (1, 2). Ischemic stroke in young people is related to rare risk factors; such as cardiac embolism (2-3%), aortic dissection (10-25%), foramen ovale (24-50%), antiphospholipid syndrome (10%), factor V Leiden (3-7,5%), antithrombin III deficiency (5-8%), protein C deficiency (4-11%), protein S deficiency (6-23%), migraine (20-24%), pregnancy (7,5%), puerperium (7,5%), use of oral contraceptives (10-40%) and illicit drugs (9-20%) (3, 4). Only 2% of patients affected by a stroke have an early age (5) and its annual incidence is 2.4 per 100,000 people (6). In the literature, some cases of stroke have been described due to protein S deficiency in young patients (7) and this state of hypercoagulability occurs in one in 20,000 people (8). Muscular dystrophy has an incidence, in its most frequent form of 15.9 to 19.5 per 100,000 births (10), 6 cases of stroke have been reported in patients with muscular dystrophy and these were caused by embolism of cardiac origin (11). A case describing the presentation of stroke, S-protein deficiency and muscular dystrophy was not found in the literature search. The objective of this article is to describe the clinical case of a 19-year-old woman with a history of migraine and hypothyroidism who was admitted to an emergency department due to neurological deterioration and who is diagnosed with a stroke, protein S deficiency and muscular dystrophy.

## CLINICAL CASE

### Anamnesis and physical examination:

A 19-year-old woman with a 6-year history, consisting of frequent falls and weakness due to loss of strength in the lower extremities. During the last 10 hours, she presented a sudden episode of left hemiplegia, deviation of the labial commissure to the right, dysarthria and four emetic episodes. 1 year ago, she had presented a similar episode that evolved spontaneously.

During the physical examination her blood pressure was 130/85 mm Hg, heart rate of 50 beats per minute, respiratory rate 22 per minute and temperature of 36.5 °C. In the neurological examination, she was sleepy, aware of person, time and place, with mechanical dysarthria, without alterations in the content or course of thought.
At the examination of the cranial nerves, the only positive finding was a deviation of the labial commissure to the right. When assessing the motor system muscle strength, it was evident 1/5 in the left hemi body and 3/5 in the right hemi body of the body predominantly proximal, hypotonia in the four extremities, generalized muscle tendinous reflexes + / ++++, left Babinsky, no me-

ningeal signs, no abnormal movements, the rest of the physical examination without alterations. Probable neurovascular syndrome and proximal weakness syndrome are diagnosed in the young patient under study.

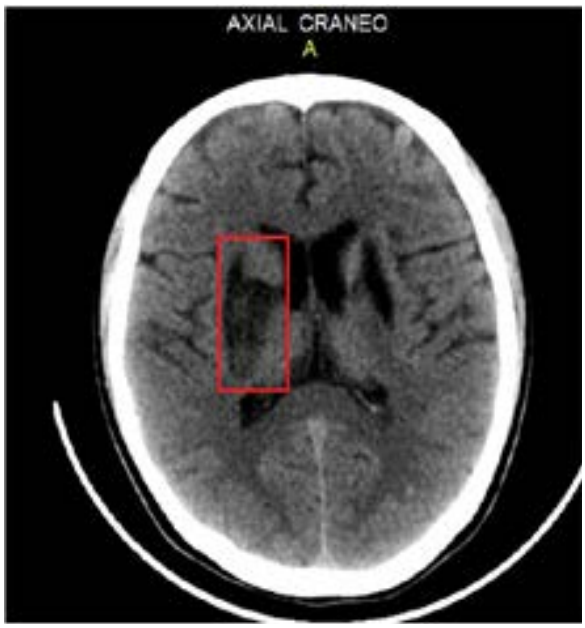
## DIAGNOSTIC AIDS

## DIAGNOSTIC IMAGING

### Cranial Computed Tomography (CT):

Lesion located towards the white matter depth, near the head of the caudate nucleus of approximately 23 x 17 x 18 mm, that does not produce mass effect. The image found in the nuclei of the left base is the Virchow Robin space and the other image in the nuclei of the base of the right side corresponds to a hypodense image of sub-acute characteristics that compromises the right internal capsule, wedge-shaped (See image 1).

**Image 1.** Cranial Computed Tomography (CT).

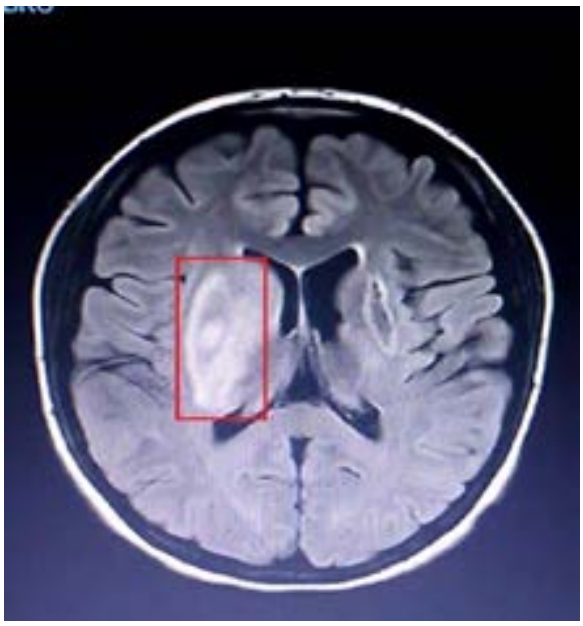



Lesion located towards the white matter depth, near the head of the caudate nucleus of approximately 23 x 17 x 18 mm, that does not produce mass effect.

### Simple And Contrasted Brain *Magnetic Resonance Imaging* (MRI):

Simple and contrasted brain magnetic resonance imaging where a right extensive basal nucleus infarction without hemorrhagic transformation was observed with cystic malacia zone in the territory of lenticulostriate arteries of the lateral group in the left basal nucleated region (image 2).

**Image 2.** Simple Brain Magnetic Resonance Imaging



Simple brain magnetic resonance imaging where a right extensive basal nucleus infarction without hemorrhagic transformation was observed with cystic malacia zone in the territory of lenticulostriate arteries of the lateral group in the left basal nucleated region.

## Brain Panangiography

Image in which an occlusion of the right middle cerebral arterial was identified in its M1 segment, with retrograde perfusion through the pial anastomoses (Image 3).

**Image 3.** Brain panangiography

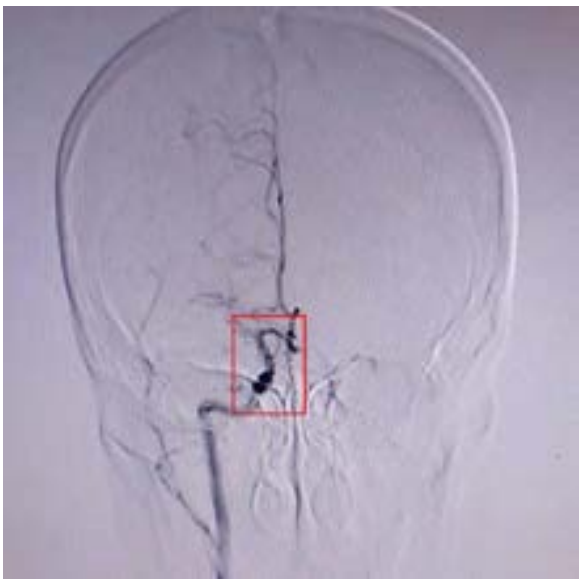


Image in which an occlusion of the right middle cerebral arterial was identified in its M1 segment, with retrograde perfusion through the pial anastomoses.

Additionally, other diagnostic images were requested, such as the angioresonance of the vessels of the neck that were normal, the transthoracic echocardiogram that showed strong dilation of right cavities with severe triscuspidea insufficiency without cardiac malformations, short circuits or vegetations.

## Laboratory test:

In the study of the etiology of ischemic cerebrovascular accident, infectious causes (syphilis, HIV and endocarditis), autoimmune (SLE, vasculitis), cardiac (short circuits, arrhythmias), carotid vascular origin were ruled out and within the hypercoagulable state the protein S deficit was confirmed, in table 1 all the requested laboratories, their results and reference values are reported.

**Table 1.** Labs requested in Ischemic stroke in a young patient.

| Laboratory | Reference value | Result | Interpretation |
|---|---|---|---|
| **Circulating anticoagulant lupus** | -- | 40,4 seconds | Negative for lupus anticoagulant |
| **Protein C Coagulation** | 70 to 140 % | 80% | Negative for protein C deficit |
| **Protein S coagulation** | 63 to 149 % | **19,5%** | **Positive for protein S deficiency** |
| **Total CK Creatin Kinase** | 38 to 234 IU/L | 133 IU/L | Negative for rhabdomylosis |
| **Glycoprotein Beta 2 IgM** | 0 to 20 | 6,15 | Negative for antiphospholipid antibody syndrome |
| **ANAS, ENAS and Anti DNA** | -- | -- | Negatives for autoimmune pathology (SLE, etc) |
| **Blood picture, Glycemia, Creatinine, urine and electrolytes test** | -- | -- | Hemogram, basic chemistry and normal renal function |
| **HLA genetic study with NGS-Illumina method** | ---- | Negative | The result does not confirm Fabry's disease |

A muscle weakness study was performed through a electromyography and nerve conduction studies of all four limbs, which reported pattern of proximal myopathy in lower limbs. Muscle biopsy reported: skeletal muscle with strong variation in size of the fibers with the presence of some hyaline fibers that increased in size and others of atrophic appearance, together with myopathy changes with degeneration and myofibral regeneration. There is endomysial fibrosis and infiltrates by adipose tissue, the morphology described is compatible with muscular dystrophy.

**Treatment:**

The patient was treated by a team of specialists, and received support from the services of internal medicine, neurology, nutrition, psychiatry and physiotherapy. The anticoagulation was initiated with Enoxaparin 1 mg per kg twice a day and warfarin 2.5 mg orally once a day, upon reaching the therapeutic levels of INR (between 2 and 3) the low molecular weight heparin was suspended. She was discharged 2 weeks later and continued the controls every 3 months with internal medicine and neurology.

**Follow-up:**

After more than 1 year of treatment, she presents left hemiplegia, moves in a wheelchair, regained speech. Within the renal function, a persistent proteinuria was developed in nephrotic range, ascites with hypertensive gradient portal, she is in treatment with warfarin 2.5 mg orally once a day, furosemide 40 mg orally once a day and physical therapy.

## DISCUSSION

The cerebrovascular stroke in a young patient can be defined as the one that is presented up to the age of 55 years and one of its biggest challenges is to establish the triggering cause, being cardioembolic origin and arterial dissection the most frequent. In addition, when these etiologies are ruled out, other more rare entities should be searched for through angiography, cerebrospinal fluid study, vasculitis and thrombophilia tests , and genetic studies among others (12).

Half of hereditary thrombophilias are due to a mutation of factor V Leiden and the mutation of the prothrombin gene, the rest of the cases are explained by alterations of antithrombin III, protein C and S (13). The alterations in the protein S can be quantitative or qualitative and their presence means an increased risk of thrombotic events. They are classified into three groups: type I, when there are low levels of total protein S, free protein S and protein activity S; type II when there are normal levels of total protein S and free protein S with low levels of protein S activity; and, type III, when there are low levels of free protein S and

activity of protein S with normal levels of total protein S (14).

Muscular dystrophy is characterized muscle weakness that usually affects certain groups depending on the type, leading in time to a greater or lesser degree of disability and among its diagnostic methods we have electromyography, genetic studies and muscle biopsy (15).

In the present case, it was observed the onset of symptoms in adolescence with loss of strength in the proximal muscle groups, findings that were confirmed with the electromyography and biopsy. Additionally during the course of her myopathy, she presented symptoms and signs of a cerebrovascular stroke. In the study of its etiology, the protein S deficiency was confirmed, due to the rare coexistence of these three diseases. The disclosure of this case is important with the aim of contributing to the development of new knowledge and although the case reports do not allow to establish causality, it is possible to generate some questions such as: Are myopathies a risk factor for the development of hypercoagulability events and/or thrombosis? Thrombotic events in patients with muscular dystrophy have been caused by cardiomyopathy; nevertheless, in this case report, protein S deficiency was described as the main cause of stroke. In the review of the literature we found a study that described an alteration in the coagulation markers in 96% of the patients with muscular dystrophy, this may suggest that in addition to the cardiomyopathy and the loss of mobility, the alterations in the markers of coagulation are frequent in patients with muscular dystrophy and also a risk factor for thrombotic events. This question may be answered in the future with other higher category research designs such as a case-control study.

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The authors

## CONFLICTS OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## REFERENCES

1. Vega, Juan-David, et al. Factores asociados al ataque cerebrovascular isquémico entre los a-os 2013 a 2016: estudio de casos y controles. Rev. Colomb. Cardiol. 2017;24(6): 574-82. doi: 10.1016/j.rccar.2017.04.001.

2. Boehme, Amelia K; Esenwa, Charles; Elkind, Mitchell SV. Stroke risk factors, genetics, and prevention. Circulation Research. 2017 Feb;120(3):472-95. doi: 10.1161/CIRCRESAHA.116.308398.

3. Maaijwee, Noortje Amm, et al. Ischaemic stroke in young adults: risk factors and long-term consequences. Nature Reviews Neurology. 2014 Jun;10(6):315-25. doi: 10.1038/nrneurol.2014.72

4. O'donnell, Martin J, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. The Lancet. 2010 Jul;376(9735):112-23. doi: 10.1016/S0140-6736(10)60834-3.

5. Rolfs, Arndt, et al. Acute cerebrovascular disease in the young. Stroke. 2013 Feb;44(2):340-49. doi: 10.1161/STROKEAHA.112.663708.

6. Putaala J, Metso AJ, Metso TM, Konkola N, Kraemer Y, Haapaniemi E, et al. Analysis of 1008 consecutive patients aged 15 to 49 with first-ever ischemic stroke: the Helsinki young stroke registry. Stroke. 2009 Apr;40(4):1195-1203. doi: 10.1161/STROKEAHA.108.529883.

7. Zamora-González, Yaneth; Agramonte-Llanes, Olga M.; Rodríguez-Pérez, Loreta. Deficiencia de proteínas C y S: marcadores de riesgo trombótico. Revista cubana de hematología, inmunología y hemoterapia [Internet]. 2013 [citado 12 de marzo de 2019];29(1):40-47. Disponible en: http://scielo.sld.cu/pdf/hih/v29n1/hih05113.pdf.

8. Lietz K, Kuchling SE, Parkhurst JB. Hemorrhagic stroke in a child whit protein S and factor VII deficiencies. Pediatr. Neurol. 2005 Mar;32(3):208-10. doi: org/10.1016/j.pediatrneurol.2004.08.008.

9. Emery, Alan eh. The muscular dystrophies. The lancet. 2002 Feb;359(9307):687-95. doi: 10.1016/S0140-6736(02)07815-7.

10. Ryder, S., et al. The burden, epidemiology, costs and treatment for Duchenne muscular dystrophy: an evidence review. Orphanet J Rare Dis. 2017 Apr;12(1):79. doi: 10.1186/s13023-017-0631-33

11. Dorman, Guido, et al. Ataque cerebrovascular cardioembólico en paciente con distrofia muscular. Neurología Argentina. 2016 April–June;8(2):118-21. doi: 10.1016/j.neuarg.2015.10.001.

12. Ferro, José M.; Massaro, Ayrton R.; MAS, Jean-Louis. Aetiological diagnosis of ischaemic stroke in young adults. Lancet Neurol. 2010 Nov;9(11):1085-96. doi: 10.1016/S1474-4422(10)70251-9.

13. Hollenhorst, Marie A.; Battinelli, Elisabeth M. Thrombosis, Hypercoagulable States, and Anticoagulants. Primary Care: Clinics in Office Practice. 2016 Dec;43(4):619-35. doi: 10.1016/j.pop.2016.07.001.

14. Anderson, Julia AM; Weitz, Jeffrey I. Hypercoagulable states. Clin. Chest Med. 2010 Dec;31(4):659-73. doi: 10.1016/j.ccm.2010.07.004.

15. Mercuri, Eugenio; Muntoni, Francesco. Muscular dystrophies. The Lancet. 2013 Feb;381(9869):845-60. doi: 10.1016/S0140-6736(12)61897-2.

16. Cobos, Everardo; Phy, Michael; Keung, Yi Kong. Thrombotic risk of muscular dystrophy: protein C deficiency, factor V Leiden, and myotonic dystrophy. Clinical and Applied Thrombosis/Hemostasis. 1999 Jul;5(3):185-86. doi: 10.1177/107602969900500308.