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Protein S Deficiency Revealed by Locked-In Syndrome: A Case Report

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Abstract **Case Report**

Locked-in syndrome (LIS) refers to patients with tetraplegia and lower cranial nerve paralysis but with intact consciousness. The main etiology of this syndrome is pontic ischemic stroke, but it may also be secondary to other less common mechanisms. We report the unusual case of a patient with a Locked-in syndrome following basilar arterial thrombosis related to protein S deficiency highlighting the key role of thrombophilia assessment to help with generally difficult diagnosis.

Keywords: Locked-in syndrome, Pontic ischemic stroke, Basilar arterial thrombosis, Protein S deficiency, Thrombophilia.

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INTRODUCTION

Locked-in syndrome is a rare clinical condition for which no incidence has been reported. It is most commonly caused by ischemic injury to the ventral pons [1]. Other mechanisms, such as hemorrhagic and traumatic injuries, can also be implicated to a lesser extent. The syndrome is characterized by tetraplegia and anarthria, with preserved consciousness. Patients retain vertical eye movement, enabling non-verbal communication and serving as evidence of intact consciousness. It is associated with a poor vital and functional prognosis.

We report the exceptional case of a patient presenting with Locked-in syndrome, attributed to a quantitative congenital protein S deficiency.

CASE PRESENTATION

Mr. C.H, a 52-year-old man with no significant personal or family medical history, was admitted to the emergency department for altered consciousness.

According to his family, the onset was abrupt, with no prior history of head trauma or seizure. Initial examination revealed a comatose patient with a Glasgow Coma Scale (GCS) score of 3/15 and normal pupillary reactivity. He was afebrile (temperature 36.8°C) with a capillary blood glucose level of 1.60 g/L. The patient was tachypneic, with a respiratory rate of 28 breaths per minute, an SpO_2 of 92% on room air, and coarse crackles on the right side, indicative of bronchial aspiration. His heart rate was 96 beats per minute, and his blood pressure was normal at 130/72 mmHg. An ECG showed a regular sinus rhythm with no conduction or repolarization abnormalities.

After intubation and stabilization, an initial brain CT scan was performed, but no abnormalities were detected. Similarly, a lumbar puncture yielded normal results. A second CT scan performed 24 hours later suggested the presence of an ischemic stroke in the right cerebellar territory. Further evaluation with brain magnetic resonance imaging (MRI) confirmed the findings of the second CT scan (Figure 1). An angiographic CT of the supra-aortic trunks revealed a complete thrombosis of the basilar artery (Figure 2, 3).

As part of the etiological workup, viral and syphilitic serologies were negative. Immunological tests also showed no abnormalities. A thrombophilia panel revealed a quantitative protein S deficiency (60% of the normal value), confirmed on a second test performed after two months of hospitalization (53% of the normal value), consistent with a class III protein S deficiency.

Sedation was discontinued on the third day of hospitalization. Neurological re-evaluation showed a conscious patient presenting with tetraplegia and anarthria. Communication was possible through vertical

eye movements, defining the classic Locked-in syndrome.

The clinical course was marked by persistent severe neurological deficits, accompanied by complications from prolonged immobility, including infections, muscle atrophy, pressure ulcers, and depression. The patient died after eight months of hospitalization due to septic shock.

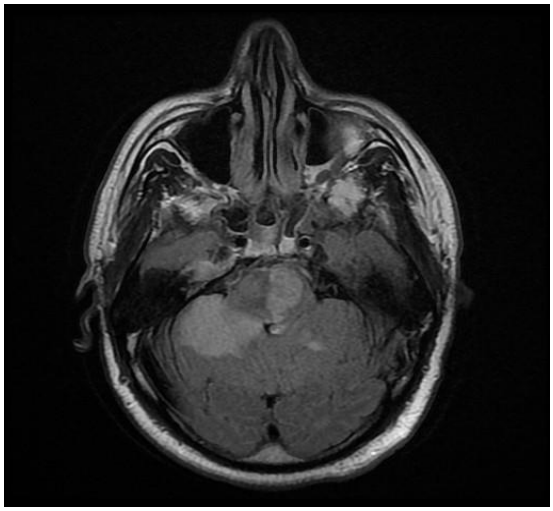

Figure 1: Brain MRI: Right cerebellar AVCI

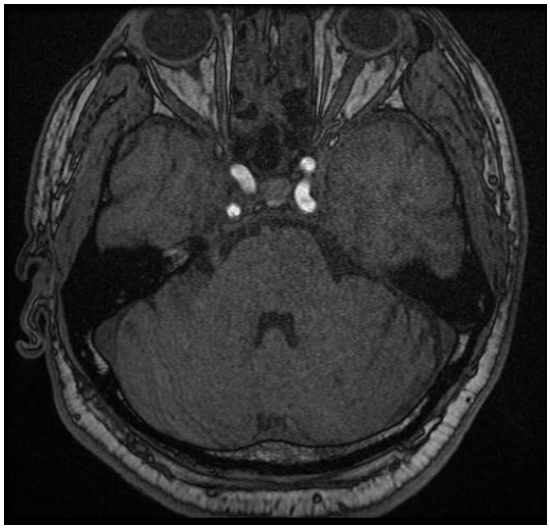

Figure 2: MRI angiography: complete thrombosis of the basilar trunk

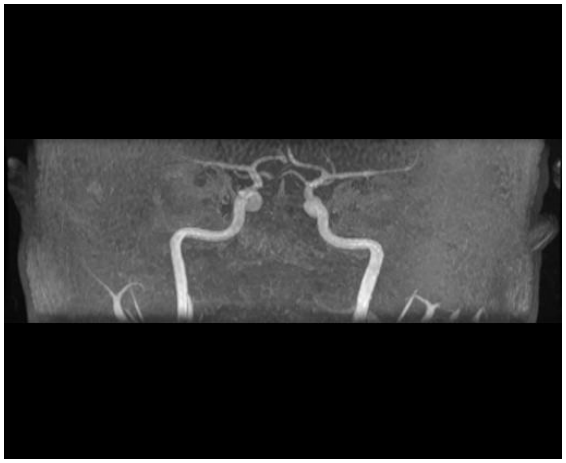

Figure 3: MRI angiography: complete thrombosis of the basilar trunk

DISCUSSION

Occlusion of the basilar artery, the main vessel of the posterior cerebral circulation, can produce nonspecific symptoms [2] such as headache, dizziness, cranial nerve paralysis, hemiplegia, Locked-in syndrome [3], or even coma.

In our case, a constitutional protein S deficiency was identified as the factor responsible for the ischemic stroke secondary to basilar artery occlusion.

Protein S, first described in Seattle in 1977, is a vitamin K-dependent glycoprotein with anticoagulant properties. Protein S is primarily synthesized in hepatocytes but is also produced by endothelial cells, osteoblasts, and smooth muscle cells. This glycoprotein circulates in plasma in two forms: approximately 40% as a free form and 60% bound to C4 binding protein (C4BP), a regulatory protein of the complement system. Protein S has two anticoagulant mechanisms of action:

- A protein C-activated (PCA)-dependent mechanism: Protein S acts as a cofactor to PCA, enhancing PCA binding to membrane phospholipids and accelerating PCA inhibition of coagulation factors Va and VIIIa.
- A PCA-independent mechanism: Even in the absence of PCA, protein S can exert a direct anticoagulant effect. In vitro studies have shown that protein S directly inhibits activated factor X and prothrombinase complexes (composed of factor Xa coupled with factor Va) that convert prothrombin into thrombin. Additionally, protein S promotes fibrinolysis by inhibiting thrombin-activatable fibrinolysis inhibitor (TAFI), a proenzyme that, when activated by thrombin, inhibits fibrinolysis.

Thus, a protein S deficiency primarily results in increased factors Va and VIIIa, leading to a prothrombotic state.

Hereditary protein S deficiency is considered an independent risk factor for venous thrombosis. Clinical manifestations most commonly include deep vein thrombosis of the lower limbs or pulmonary embolism. More rarely, venous thrombosis can occur at other sites (brain, upper limbs, or viscera).

However, the association between protein S deficiency and arterial thrombosis remains controversial. This link has been suggested in several case reports describing ischemic strokes (IS) or arterial thrombosis in patients with protein S deficiency as the sole explanation [4-6]. In a study of 36 young adults with unexplained cerebral infarction, five patients (13.8%) had protein S deficiency [7].

A prospective study in Sweden among patients under 65 years old with a history of stroke showed that 4 of 66 patients (6%) with transient ischemic attack (TIA) or stroke had low levels of free protein S [8]. Conversely, many studies demonstrate a weaker association between protein S deficiency and stroke [9-11].

There is no clear answer or current consensus on which stroke patients should be screened for coagulation abnormalities or which specific tests should be performed. A general consensus suggests that the yield of thrombophilia testing is low and that the decision to pursue such investigations should be individualized until larger studies provide more data.

The best available treatment for basilar artery occlusion is intra-arterial thrombolysis, although its long-term benefits have not yet been proven [12].

CONCLUSION

Hereditary protein S deficiency is rarely implicated in ischemic stroke and even less frequently in basilar artery thrombosis. This exceptional case of Locked-in syndrome due to protein S deficiency highlights the diagnostic challenges, underscores the key role of thrombophilia testing in aiding diagnosis, and emphasizes the poor prognosis associated with this syndrome.

Conflicts of Interest: The authors declare no conflicts of interest.

REFERENCES

1. Smith, E., & Delargy, M. (2005). Locked-in syndrome. *Bmj*, *330*(7488), 406-409. doi: 10.1136/bmj.330.7488.406.
2. Schonewille, W. J., Wijman, C. A., Michel, P., Rueckert, C. M., Weimar, C., Mattle, H. P., ... & Algra, A. (2009). Treatment and outcomes of acute basilar artery occlusion in the Basilar Artery International Cooperation Study (BASICS): a prospective registry study. *The Lancet Neurology*, *8*(8), 724-730. doi: 10.1016/S1474-4422(09)70173-5.
3. Aryasinghe, L., Kazim, Y., Obeid, H. F., & Hashim, H. (2016). The hyperdense basilar artery sign: a case of locked-in syndrome. *International Journal of Emergency Medicine*, *9*(1), 1-3. doi: 10.1186/s12245-016-0104-9.
4. Martinez, H. R., Rangel-Guerra, R. A., & Marfil, L. J. (1993). Ischemic stroke due to deficiency of coagulation inhibitors. Report of 10 young adults. *Stroke*, *24*(1), 19-25.
5. Gonthier, A., & Bogousslavsky, J. (2004). Cerebral infarction of arterial origin and haematological causation: the Lausanne experience and a review of the literature. *Revue neurologique*, *160*(11), 1029-1039.
6. Girolami, A., Simioni, P., Lazzaro, A. R., & Cordiano, I. (1989). Severe arterial cerebral thrombosis in a patient with protein S deficiency

(moderately reduced total and markedly reduced free protein S): a family study. *Thrombosis and haemostasis*, *61*(01), 144-147.

7. Barinagarrementeria, F., Cantu-Brito, C., De La Pena, A., & Izaguirre, R. (1994). Prothrombotic states in young people with idiopathic stroke. A prospective study. *Stroke*, *25*(2), 287-290.
8. Vrethem, M., Dahle, C., Lindahl, T., & Ernerudh, J. (1998). Association between deficiency of free protein S and anticardiolipin antibodies in patients≤ 65 years of age with acute ischemic stroke and TIA. *European Journal of Neurology*, *5*(5), 491-497.
9. Adams, H. P., Kappelle, L. J., Biller, J., Gordon, D. L., Love, B. B., Gomez, F., & Heffner, M. (1995). Ischemic stroke in young adults: experience in 329 patients enrolled in the Iowa Registry of stroke in young adults. *Archives of neurology*, *52*(5), 491-495.
10. Kristensen, B., Malm, J., Carlberg, B., Stegmayr, B., Backman, C., Fagerlund, M., & Olsson, T. (1997). Epidemiology and etiology of ischemic stroke in young adults aged 18 to 44 years in northern Sweden. *Stroke*, *28*(9), 1702-1709.
11. Mayer, S. A., Sacco, R. L., Hurlet-Jensen, A., Shi, T., & Mohr, J. P. (1993). Free protein S deficiency in acute ischemic stroke. A case-control study. *Stroke*, *24*(2), 224-227.
12. Powers, W. J. (2007). Intra-arterial thrombolysis for basilar artery thrombosis: trial it. *Stroke*, *38*(2), 704-706.
13. Schäfer, H. P., & von Felten, A. (1989). Protein-S deficiency in young patients with thrombotic brain infarction. *Schweizerische medizinische Wochenschrift*, *119*(16), 489-492.