COL6A2 Mutation and Cerebral Moyamoya-like Disease: A Case Suggesting a Shared Extracellular Matrix Pathogenesis

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Introduction

Collagen VI-related myopathies are a group of genetic disorders caused by mutations in COL6A1, COL6A2, or COL6A3, typically characterized by progressive muscle weakness, joint contractures, and distal joint hyperlaxity. While primarily affecting skeletal muscle, emerging evidence suggests potential vascular involvement. The association between COL6A2 mutations and cerebrovascular abnormalities resembling moyamoya vasculopathy is rare and not well characterized

Case report

Clinical Presentation

49-year-old woman with 10-year progression of lower limb weakness, gait disturbance, and balance impairment. Two brief, self-limited episodes of right-sided facial and brachial paresthesias.

Physical features: Short stature, small/stubby extremities

Neurological examination:

Waddling gait, positive Gowers' sign, inability to walk on heels. Mild proximal weakness (iliopsoas, gluteals), moderate distal weakness (anterolateral leg compartments), bilateral Achilles tendon contractures, hypoesthesia in the left hand

EMG: Findings consistent with **primary myopathy**

Brain MRI: Extensive hyperintensities in the right periventricular, frontal, and parietal white matter. Involvement of bilateral subcortical regions.

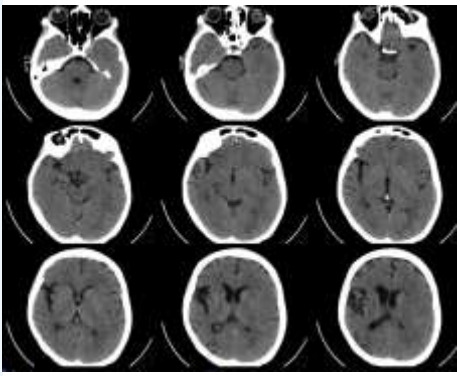
Lumbar Puncture (CSF Analysis): Presence of **oligoclonal bands** in both serum and CSF (Type 4 pattern)

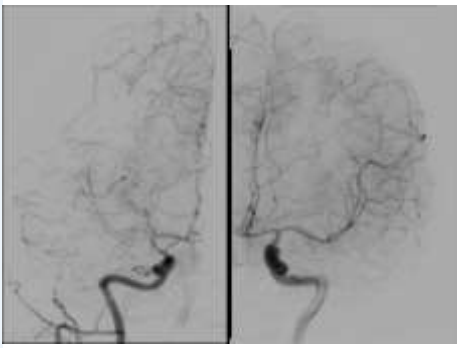
Muscle biopsy (biceps brachii): nonspecific myopathic changes

Cerebral Angiography: Moyamoya-like vasculopathy: Severe narrowing of the right supraclinoid and terminal ICA, absence of right M1, and involvement of right A1. Collateral circulation via perforating and leptomeningeal vessels. Moderate narrowing of left supraclinoid ICA with early collateralization

Genetic Analysis Two heterozygous pathogenic variants in **COL6A2**: **c.1832>A, c.1970-9G>A**

Confirms diagnosis of a **Collagen VI-related myopathy**





Conclusion

This case reports a novel association between COL6A2-related myopathy and moyamoya-like vasculopathy. While COL6A2 mutations typically affect muscle, this suggests possible cerebrovascular involvement. Similarities with COL4A1/2-related vasculopathies point to a shared extracellular matrix-related mechanism. Although causality is unproven, the findings warrant further study and broader diagnostic consideration in atypical neuromuscular cases.

References

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