Seronegative neuromyelitis optica spectrum disorder in primary familial brain calcification with PDGFB variant

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Dear Editor,

Primary familial brain calcification (PFBC) was previously known as idiopathic basal ganglia calcification or Fahr's disease. This disorder is characterized by calcification of the basal ganglia, thalamus, and the dentate nucleus of the cerebellum. The symptoms include parkinsonism, cerebellar ataxia, psychiatric symptoms, and cognitive impairment. Fahr disease, platelet-derived growth factor subunit B (PDGFB) and blood-brain barrier have been implicated in altered aquaporin-4 (AQP4) function. This case describes the second case of PFBC with NMOSD. A common mechanism in PFBC with PDGFB variants is possibly the BBB disruption due to PDGFB dysfunction, resulting in the influx of plasma proteins and mineralization.

In conclusion, we report a case of seronegative NMOSD in a patient with PFBC and a PDGFB variant. This finding suggests a novel approach for NMOSD. PDGFB variant may affect AQP4 without antibody-mediated effects and frontal lobe dysfunction but no headache or parkinsonism. Genetic testing by the Sanger method, performed at 42 years of age, revealed a point mutation in exons 5 of PDGFB (c.356C > T, p.Leu119Pro). The same variant was found in his mother and brother, and we diagnosed them with PFBC associated with a PDGFB variant.

In this case, the PDGFB variant may be associated with NMOSD development. PDGFB is a member of the PDGF gene family of mitogenic factors in mesenchymal cells. In the CNS, PDGFB is secreted from endothelial cells undergoing vasculogenesis, which mobilizes PDGF-receptor β (PDGFRB)-expressing pericytes surrounding the lumen. The pericytes contribute to BBB, stimulating endothelial cells to form tight junctions. The cause of brain calcification in PFBC with PDGFB variants is possibly the BBB disruption due to PDGFB dysfunction, resulting in the influx of plasma proteins and mineralization.

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may be involved in pathogenesis. However, there are some limitations. The other two cases in the same family of our proband did not develop optic neuritis or myelitis; the mother had parkinsonism, and the brother presented schizophrenia-like symptoms and parkinsonism. In addition, the fact that steroid therapy and PE were each partially effective suggests the involvement of both an inflammatory mechanism and some immune mechanism, but the details are unknown. The clinical spectrum between NMOSD and PDGFB.

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Fig. 1. Findings of head CT and MRI and spinal cord MRI.

(A) The CT shows bilateral symmetrical calcification of the basal ganglia and thalamus. (B) T2-weighted image shows a high-intensity lesion in the area postrema (arrowhead).

(C) T2-weighted image shows high-intensity lesions in the area postrema (arrowhead) and at the level of C3 (arrow).

(D) T2-weighted image shows high-intensity lesions at the level of T5 and T8 (arrows).