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COMMENT

A commentary on band-like calcification with simplified gyration and polymicrogyria: report of 10 new families and identification of five novel *OCLN* mutations

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There are evidences suggesting that mutations in occludin (*OCLN*) gene (5q13) are associated with the development of band-like calcification with simplified gyration and polymicrogyria (BLC-PMG) (OMIM#251290), and some cases has been described [1–3]. In 2010, this disorder has been included in the pseudo-TORCH spectrum (PTS) [1]. The PTS phenotypes mimics congenital infections with major cerebral malformations, including mainly: congenital microcephaly, intracranial calcification in a heterogeneous pattern, seizures, enlarged ventricles, and severe neurodevelopmental disorder [1–3].

On the volume 62, issue 5 of this periodical, Abdel-Hamid and collaborators [3] conducted a study on the aforementioned gene in patients with BLC-PMG of 10 consanguineous families. They reported that pathogenic mutations in this gene are related to development of neurological and clinical manifestations present in the individuals studied. Phenotypically, the patients presented progressive microcephaly, brain calcification and areas of polymicrogyria, leading to a severe mental retardation, and seizures.

OCLN gene encodes for a tight-junction protein (occludin) whose loss of functions might affect the permeability of the blood–brain barrier (BBB) [1]. Considering the genetic landscape for the development of calcifications, the authors cited that *Ocln* knockout (KO) mouse has extracranial manifestations, such as chronic gastritis, thinning of compact bone, and testicular atrophy [4]. We would like to highlight that the *Ocln* KO also presents brain calcification, reinforcing the association with the phenotype reported in humans.

Few disorders, such as primary brain calcification (PBC) and type 1 interferonopathy (a PTS disorder), exhibits brain calcification located most commonly in basal ganglia and/or thalamus, similar to BLC-PMG [5, 6]. The PFC is a rare neuropsychiatric condition that might be inherited in an autosomal dominant pattern or even caused by de novo mutations. Four different genes (*SLC20A2*, *PDGFB*, *PBGFRB*, and *XPR1*) have been associated with the development of this disorder [6–8]. More recently, patients with type 1 interferonopathy are being linked to mutations in *USP18* gene and also presents calcifications in some areas of the brain [5].

Additionally, homozygous for pathogenic variants in *ISG15* gene present a interferonopathy and bilateral and symmetric calcifications, such as in PBC [9]. Nicolas et al. [10] have reported the association between patients with severe neurodevelopmental deficit that presented spots of brain calcification and a homozygous *PCDH12* variant. Intriguingly, mice with hippomorphic *Pdgfb* and *Slc20a2* KO mice shows focus of brain calcification, such as *Ocln* KO mice, and patients with BLC-PMG [3, 7, 8].

Altogether, we attempt to demonstrate the clinical importance and susceptibility of some areas of the brain to calcify, and the overlap of several phenotypes and diseases. We also called attention to the studies in animal models that may represent, at least in part, an important factor that contribute to understand the outcomes seen in patients.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no competing interests.

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