Painful callosities in a young boy

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A 9-year-old boy was first evaluated at 4 years of age with fragile hair since the first months of life (Figure 1), thin nails, onychomadesis, and koilonychia. By the age of 2, he had plantar erythema in areas of pressure that evolved with hyperkeratosis and intense local pain. His mother had had similar lesions on the plantar surface since childhood. Physical examination showed rounded hyperkeratotic plaques at plantar pressure sites with an erythematous halo (Figure 2). The hairs were examined under optic microscopy and evidenced trichorrhexis nodosa (Figure 3). He was started on acitretin, and the hyperkeratosis and pain decreased initially, but he needed an increase in dosage at follow-up because the pain intensified. A pediatric orthopedist evaluated him and recommended orthopedic insoles and physiotherapy, but there was no improvement in the pain. At follow-up, the hyperkeratosis had worsened and progressed to the entire anterior portion of the soles and part of the heels (Figure 4), with severe pain even with the use of topical and systemic antiinflammatories, analgesics, and opioids.

WHAT IS THE DIAGNOSIS?
Diagnosis: Olmsted syndrome

DISCUSSION

He underwent a genetic study, which found a mutation in the transient receptor potential vanilloid-3 cation channel (TRPV3) gene, specifically in p.G573Cys amino acid residue, confirming the diagnosis of Olmsted syndrome (OS). There are seven dominant (p.Gly573Ser, p.Gly573Cys, p.Gly573Ala, p.Gln580Pro, p.Leu673Phe, p.Trp692Gly, and p.Trp692Cy) and three recessive (p.Trp521Ser, p.Gly568Cys, p.Gln216-Gly262d) gain-of-function mutations reported in TRPV3 amino acid residues, resulting in heterogeneous genotypes and phenotypes of OS.1 The TRPV3 gene is involved in hair growth and skin keratinization once it regulates differentiation, proliferation and apoptosis of the keratinocytes present in hair follicle and interfollicular areas.2 These gain-of-function mutations promote calcium influx and apoptosis, with consequent skin hyperkeratosis.1,3 Mutations in the membrane-bound transcription factor protease site 2 enzyme were identified in a recessive X-linked form of OS.1

Olmsted syndrome is a rare genodermatosis. The signs and symptoms begin in the neonatal period or childhood and are permanent and progressive.1,4 In this case, the patient had initial lesions that were classically distributed on the pressure points, which with time began to affect a large part of the soles. Half of patients with OS have pain in the plantar hyperkeratotic sites that can vary from mild to severe and lead to disability to walk. Hair disorders are frequent in this syndrome, with curly and fragile hair, and trichorrhexis nodosa may be present microscopically, as well as pill torti, longitudinal ridges, and transverse fractures of the hair shaft. Nail disorders (including onychodystrophy, thin and brittle nails) are also frequent.1 The absence of periorificial keratotic plaques is a rare phenomenon, and in the majority, it is difficult to control the hyperkeratosis even with systemic treatments, which results in intense pain.1

The differential diagnosis includes other severe forms of palmoplantar keratodermas, such as Clouston syndrome, Haim-Munk syndrome, mal de Meleda, pachyonychia congenita, Papillon-Lefèvre syndrome, tyrosinemia type II, and Vohwinkel syndrome.3 Genetic study can help in the diagnosis of Haim-Munk syndrome and clinically related diseases, such as Papillon-Lefèvre syndrome, in which a mutation in the lysosomal protease cathepsin C gene is identified.1,5 Periorificial hyperkeratosis may confirm the diagnosis, but because of the clinical variability of cutaneous lesions, genetic study should be considered for diagnostic confirmation.2

Genetic study allowed diagnosis of the disease in the mother and child presented herein, allowing a specific review of the therapeutic possibilities. The available treatments are not fully effective in the control of hyperkeratosis and pain and do not change the course of the disease.1 In this patient, neither emollients, keratolytics, and acitretin (considered in the literature to be a good therapeutic option) or high doses of potent analgesics and opioids alleviated the hyperkeratotic plaques and severe pain, leading to a serious compromise in his and his family’s quality of life. Identification of the genes responsible for OS is promising in the search for a specific therapy for cases with great morbidity.

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REFERENCES