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IMAGES IN METABOLIC MEDICINE

Herpetiform keratitis and palmoplantar hyperkeratosis: warning signs for Richner-Hanhart syndrome

Diogo C. Soares[1] · **Mariana N. Stroparo**[2] · **Yu C. Lian**[2] · **Cristina Y. Takakura**[3] · **Sabrina Wolf**[4] · **Regina Betz**[4] · **Chong A. Kim**[1]

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Abstract Richner-Hanhart syndrome (RHS, tyrosinemia type II) is a rare, autosomal recessive inborn error of tyrosine metabolism caused by tyrosine aminotransferase deficiency. It is characterized by photophobia due to keratitis, painful palmoplantar hyperkeratosis, variable mental retardation, and elevated serum tyrosine levels. Patients are often misdiagnosed with herpes simplex keratitis. We report on a a boy from Brazil who presented with bilateral keratitis secondary to RHS, which had earlier been misdiagnosed as herpes simplex keratitis.

Case report

A 2-year-old boy from Brazil, born from a consanguineous marriage, presented with photophobia at 2 months of age. At 1 year, he developed painful plantar hyperkeratosis that affected his ability to walk. He was diagnosed with herpetiform keratitis by an ophthalmologist and treated with acyclovir eye ointment, which did not result in improvement of symptoms. The patient was subsequently sent to a reference center and prescribed oral acyclovir for 14 days. No improvement was observed, and he was hospitalized for investigation.

Dermatological examination revealed sharply demarcated, yellowish hyperkeratotic plaques localized at pressure bearing areas on both plantar surfaces and the palmar surface of his fingertips (Fig. 1). After 7 days, a worsening of his skin lesions was observed and betamethasone and gentamicin were prescribed. In addition, serology and PCR were performed to detect HSV, both of which came back negative. The patient presented neurocognitive development appropriate for age. His parents and his 7-year-old sister did not show any skin or eye symptoms and have normal neurocognitive development.

Oculocutaneous tyrosinemia was suspected, which was supported by his elevated blood tyrosine levels (blood tyrosine level: 1004.4 μmol/L, normal: ≤ 165.5 μmol/L) measured at baseline. After informed written consent was given by the parents, sequencing of the coding region of the *TAT* gene in the patient and his mother revealed the known mutation c.177_178insT;V60Cfs*33. The mutation was identified in a homozygous state in the patient and in a heterozygous state in his mother. The father's DNA was not accessible and therefore was not sequenced. This result confirmed the diagnosis of oculocutaneous tyrosinemia. Richner-Hanhart syndrome (RHS, tyrosinemia type II) is a rare, autosomal recessive inborn error of tyrosine metabolism caused by tyrosine aminotransferase deficiency [Natt et al 1992, Huhn et al 1998]. It is characterized by photophobia due to keratitis, painful palmoplantar hyperkeratosis, variable mental retardation, and elevated serum tyrosine levels. Patients are often misdiagnosed with herpes simplex keratitis [Buist et al 1995, Macsai et al 2001, Krol and Siegel 2012].

A low-protein diet (<0.6 g/kg/day) was implemented. The parents of the patient reported significant improvement of his

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✉ Diogo C. Soares
diogo.soares@hc.fm.usp.br

[1] Clinical Genetics Unit, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, Av. Dr. Eneas Carvalho de Aguiar, 647, São Paulo 05403-000, SP, Brasil

[2] Instituto de Infectologia Emílio Ribas, São Paulo, SP, Brasil

[3] Nutrition Unit, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, SP, Brasil

[4] Institute of Human Genetics, University of Bonn, Bonn, Germany

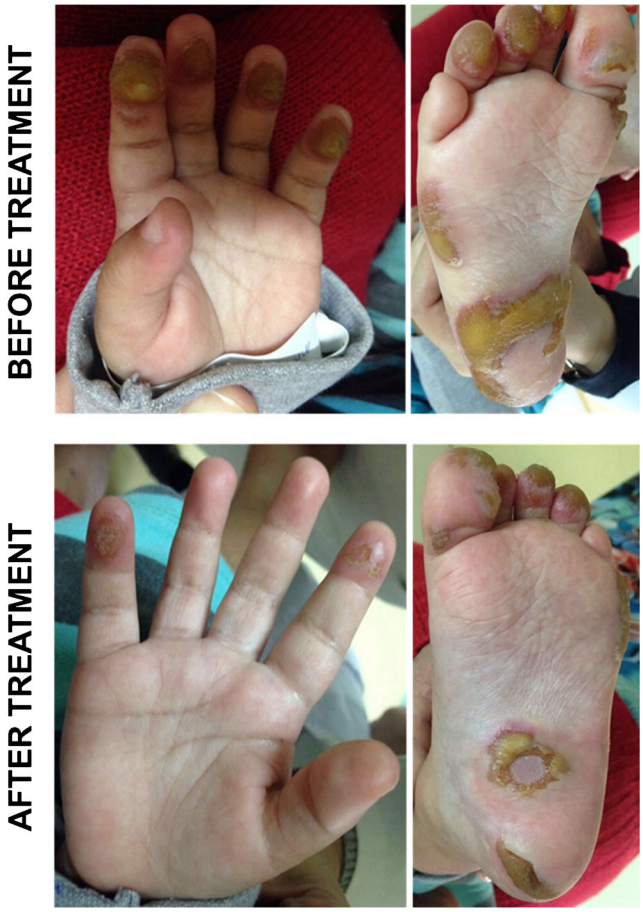

Fig. 1 Plaques on the fingertips, showing regression 3 weeks after the patient started a low-protein diet (Natt et al 1992; Huhn et al 1998; Buist et al 1995; Macsai et al 2001; Krol and Siegel 2012)

skin lesions and pain within the first week of treatment. At the 3-week follow-up, evident regression of the hyperkeratotic plaques was noticeable (Fig. 1). Three months after diagnosis, a reduction of blood tyrosine levels (711.9 μmol/L/, normal: ≤ 165.5 μmol/L) was observed. Sixteen months after diagnosis, the patient has largely adhered to the recommended diet and remained symptom-free. The blood tyrosine levels remain stable (607 μmol/L, normal: ≤ 165.5 μmol/L).

Compliance with ethical standards

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Conflicts of interest None.

Informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from the patient's mother for being included in the study.

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