H syndrome: When skin hyperpigmentation is a sign of a multifaceted rare genetic disorder.

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Introduction

H syndrome is an autosomal recessive disorder characterized by hyperpigmented, hypertrichotic, indurated cutaneous patches with multisystemic manifestations including hepatosplenomegaly, hearing loss, heart anomalies and hypogonadism. H syndrome is a monogenic genodermatosis resulting in different clinical presentations ranging from mild to very severe phenotype. Thus, a highly variable expressivity is noted for this syndrome and the diagnosis suspicion is based mainly on the localization of the hyperpigmentation on the inner thighs. In fact, the hyperpigmentation can be extended over the entire surface of the lower limbs but constantly sparing the knees. H syndrome is caused by mutations in the *SLC29A3* gene.

Objective

The aim of our work was to conduct a clinical and genetic investigation in five unrelated patients with suspected H syndrome.

Method

This study included five Tunisian patients. Their ages ranged 4–39 years, without any familial history. After written informed consent was obtained from all participants or their guardians, peripheral blood samples were collected. Genomic DNA was extracted from the samples according to standard techniques. Genetic analysis of the *SLC29A3* gene was performed using direct sequencing of PCR products was performed with the ABI prism 3500 DNA Genetic Analyzer (Applied Biosystems, Foster City, CA, USA), using the ABI Prism Big Dye Terminator v3.1 Cycle Sequencing Ready Reaction Kit (Applied Biosystems).

Results

We identified recurrent mutations in the *SLC29A3* gene (p.R363Q and p.P324L) in the sixth exon, which harbors the majority of the mutations and a novel frame-shift mutation in exon 2, p.S15Pfs*86, which has a likely pathogenic influence on the hENT3 protein function through *in silico* analysis. Moreover, we reported extremely variable dermatological phenotypes of the studied patients.

Conclusion

Our study extends the mutation spectrum of H syndrome by reporting a novel frame-shift mutation, the p.S15Pfs*86 in exon 2 of SLC29A3 gene and emphasizes the relevance of genetic testing for its considerable implications in early diagnosis and clinical management.

Biography

Dr. Hager Jaouadi is a geneticist, graduate of PhD degree from University Tunis el Manar, Tunisia. She worked at Pasteur Institute of Tunis and Marseille Medical Genetics in France, mainly on rare to ultra-rare genetic skin disorders and heart diseases. Her main areas of expertise are human genetics and next generation sequencing for cardiogenetics diagnosis. Currently, she obtained a position of postdoctoral research scientist in Columbia University Medical Center at New York, United States.

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