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Cohen Syndrome

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Definition

Cohen syndrome is a rare autosomal recessive disease with diversified clinical manifestations. Patients with this syndrome may present neutropenia, hypotonia, microcephaly, mental retardation, short stature, obesity, and characteristic facial features (Rezaei et al. 2009; Duplomb et al. 2014; El Chehadeh-Djebbar et al. 2013; Chandler et al. 2003; Kolehmainen et al. 2004).

The syndrome was first described by Cohen et al. in 1973 in a few patients with hypotonia, obesity, and facial dysmorphisms (Chandler et al. 2003).

Introduction

Cohen syndrome is caused by homozygous or compound heterozygous mutations in the *COH1* gene (Rezaei et al. 2009; Duplomb et al. 2014; Chandler et al. 2003; Kolehmainen et al. 2004), also known as *VPS13B* (Duplomb et al. 2014; El Chehadeh-Djebbar et al. 2013).

COH1 gene encodes a protein whose function is unclear but that seems to be a potential transmembrane protein that may be involved in protein sorting and intracellular protein transport (Rezaei et al. 2009; Duplomb et al. 2014). Patients who suffer from Cohen syndrome have defective glycosylation, which appears by the accumulation of galactosylated fucosylated structures and asialyted fucosylated structures (Wintergerst et al. 2017).

Therefore, patients with this syndrome may present heterogeneous and variable clinical manifestations (Rezaei et al. 2009; Duplomb et al. 2014; Chandler et al. 2003).

Clinical Presentation

Cohen syndrome is a multisystem disorder. Patients may present progressive retinochoroidal dystrophy and high myopia, microcephaly, moderate to profound psychomotor retardation, hypotonia, joint hypermobility, truncal obesity, short stature, and characteristic facial features, such as smooth and short philtrum, thick hair and eyebrows, wave-shaped eyelids, long eyelashes, hypotonic appearance, prominent upper central incisors, and high nasal bridge (Rezaei et al. 2009; El Chehadeh-Djebbar et al. 2013; Chandler et al. 2003; Kolehmainen et al. 2004; Wintergerst et al. 2017).

Besides that, neutropenia is also observed in these patients, in association with recurrent infections. Severe infections are unusual in patients

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with Cohen syndrome; however, gingivitis, periodontitis, aphthous ulcers, and cutaneous infections may be seen in some patients (Rezaei et al. 2009; Chandler et al. 2003).

Laboratory Findings and Diagnostic Testing

The diagnosis of Cohen syndrome can be suspected based on the clinical phenotype of the patients (Wintergerst et al. 2017).

Therefore, the diagnosis of the syndrome is based on clinical findings and molecular genetic tests to identify mutations in *COH1* (Chandler et al. 2003*;* Kolehmainen et al. 2004*)*, but there is not a consensus about clinical diagnostic criteria yet (Chandler et al. 2003).

For example, Kolehmainen et al. (2004) proposed the following criteria for diagnosis of Cohen syndrome – presence of at least six of the following eight cardinal features: retinal dystrophy and high myopia, microcephaly, developmental delay, joint hypermobility, typical Cohen syndrome facial characteristic, truncal obesity with slender extremities, overly sociable behavior, and neutropenia (Kolehmainen et al. 2004). However, Chandler et al. proposed another criteria for the diagnosis of the syndrome, such as the presence of at least two of the following features in a child with learning difficulties: facial dysmorphism (thick hair, eyelashes, and eyebrows, wave-shaped and downward slanting palpebral fissures, short and upturned philtrum with grimacing expression on smiling, prominent nose), pigmentary retinopathy, and neutropenia (Wintergerst et al. 2017).

A common laboratory finding in patients with Cohen syndrome is the neutropenia, generally intermittent (Rezaei et al. 2009; Kolehmainen et al. 2004).

Generally, the diagnosis of this syndrome is confirmed just after school age, when visual disorders are identified and the patients are forwarded to investigation because of that (El Chehadeh-Djebbar et al. 2013; Chandler et al. 2003). However, the diagnosis of certainty is only possible through genetic analysis (Wintergerst et al. 2017).

Treatment and Prognosis

A multidisciplinary intervention is important not only for the patient with Cohen syndrome but also for the family, such as physical, occupational, and speech therapy to approach psychomotor developmental delay, hypotonia, and joint hypermobility (Chandler et al. 2003).

Patients with neutropenia may use granulocyte colony-stimulating factor (GCSF), and in cases of recurrent infections, standard therapy depending on the infection may be necessary (Rezaei et al. 2009).

Some surgical procedures can also be necessary to correct facial dysmorphism (Wintergerst et al. 2017).

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