Waardenburg syndrome type III

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Creation Date: December 1997
Updated: May 2003
April 2005

Scientific Editor: Professor Didier Lacombe

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Keywords
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Differential diagnosis
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Abstract
Waardenburg syndromes are deafness syndromes associated with pigmentary disturbances. Their incidence is 1/270,000 births/year. They are distinguished by their autosomal dominant transmission and their irregular depigmentation. Wardenburg syndrome type III is the rarest form. The diagnostic criteria include the association of limb anomalies - hypoplasia of the musculoskeletal system, flexion contractures, fusion of the carpal bones, syndactylies - and, in common with type I, facial dysmorphism including dystopia canthorum, pigmentary disturbances and deafness. The molecular diagnosis consists in searching for mutations in the PAX3 gene. Management combines hearing aids and limbs physiotherapy. Skin and eyes photoprotection is highly recommended.

Keywords
deafness, pigmentary disorder, limb anomalies, facial dysmorphism, PAX3 gene

Name of the disease and synonyms
Waardenburg syndrome type III (WS III)
Waardenburg–Klein syndrome
Waardenburg syndrome with limbs anomalies

Excluded diseases
Waardenburg syndrome type I (WS I);
Waardenburg syndrome type II (WS II);
Other neurocristopathies.

Diagnostic criteria/Clinical description
WS III is an extreme in severity and rarity presentation of Waardenburg syndrome type I (WS I).

WS III is characterized by the presence of musculoskeletal abnormalities in association with clinical features of WS I:
- Limb anomalies: hypoplasia of the musculoskeletal system, flexion contractures, fusion of the carpal bones, syndactylies.
- Facial dysmorphism, pigmentary anomalies and deafness in common with WS I. The dystopia of the canthi, as in type I, is also present.

Differential diagnosis
The diagnosis is based on the presence of limb anomalies together with the other classical features of WS.
Incidence
The incidence of WS III has not been estimated, but is much less frequent than the other types.

Management and treatment
Hearing aids and limbs physiotherapy are recommended. Skin and eyes photoprotection is highly recommended.

Etiology
The syndrome is the result of a primary abnormality of melanocytes affecting the ears, eyes, hair and skin. Heterozygous mutation in the PAX3 gene (paired box gene 3; encoding transcription factors) localized on chromosome 2q37 is found in approximately 50% of the patients. Homozygous mutations have been described in some individuals with WS III.

Molecular diagnosis
Search for mutations in the PAX3 gene.

Genetic counseling
WS III is usually transmitted following an autosomal dominant pattern of inheritance with variable inter- and intrafamilial expressivity. The same family can harbor features of WS I and WS III.

Prenatal diagnosis
It is possible if the familial PAX3 mutation has been identified.

Unresolved questions and comments
A homozygous pax3 mutation in mice is responsible for intrauterine or neonatal death and severe abnormalities of closure of the neural crest, which is not seen in humans.

References