Jackson-Weiss syndrome

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Abstract

*The Jackson-Weiss syndrome is characterized by tarsal and/or metatarsal coalitions and a (variable) craniosynostosis, accompanied by facial anomalies, broad halluces and normal hands. It has been described in two large families. The condition is inherited as an autosomal dominant trait with high penetrance and variable expression. Mutations in the fibroblast growth factor receptor 2 gene (*FGFR2*) have been identified as the cause of this syndrome. Treatment consists in a multiple-staged surgery.*

Keywords

Jackson-Weiss, craniosynostosis, cephalo-syndactyly, facial anomalies, *FGFR2* gene

Disease name / synonyms

Jackson-Weiss syndrome (OMIM #123150);
Craniosynostosis, midfacial hypoplasia and foot abnormalities;
JWS.

Definition

The Jackson-Weiss syndrome is an autosomal dominant condition with high penetrance and variable expression characterized by tarsal and/or metatarsal coalitions and craniosynostosis that can show a great intrafamilial variability; patients show facial anomalies, broad halluces and normal hands. The cause is a specific *FGFR2* mutation.

Clinical description

Jackson *et al*, 1976 (1) described a large family and observed craniosynostosis and facial anomalies with great variability in phenotypic expression. Midface hypoplasia and other symptoms that resemble Pfeiffer syndrome were found, next to patient without clear facial features. No thumb anomalies occur, like in Pfeiffer syndrome. The most consistent manifestations were found in the feet, both clinically or radiologically. Mild cutaneous syndactyly of second and third toes and broad great toes that deviated medially were frequently found. Radiological manifestations included short broad first metatarsal, abnormally shaped tarsal bones, calcaneocuboid fusion, and fusions

between first and second metatarsals. Some affected individuals showed neither clinical nor radiographic abnormalities of face and skull. There was no mental retardation.

Excluded diseases and differential diagnosis

Differential diagnosis includes other craniosynostosis syndromes such as Crouzon, Pfeiffer, Muenke and Apert syndromes.

Etiology

Jackson-Weiss syndrome was mapped to the 10q25-q26 region in the original family (2). Jabs *et al*, 1994 (3) identified a mutation in exon 7 of the fibroblast growth factor receptor-2 (*FGFR2*) gene (1031C->G transversion, resulting in an Ala344Gly amino acid substitution). Some other *FGFR2* mutations have been identified in individuals with Jackson-Weiss syndrome (4). FGFR2 is a member of the tyrosine kinase receptor superfamily, having a high affinity for peptides that signal the transduction pathways for mitogenesis, cellular differentiation and embryogenesis. Apert syndrome, Pfeiffer syndrome and Crouzon syndrome are also associated with *FGFR2* mutations.

Epidemiology

The condition has been described in two large families by Jackson and Weiss (1) and Escobar and Bixler, 1977 (5).

Diagnostic method

The diagnosis is based on the association of clinical and radiological features. Molecular genetic testing of the *FGFR2* gene may help to establishing the diagnosis in questionable cases.

Genetic counselling

Genetic counselling is according to autosomal dominant inheritance. Affected individuals have a 50% chance of passing the mutant gene to each child. The non-penetrance and wide variability in phenotype of affected persons should be discussed.

Prenatal diagnosis

Jackson-Weiss syndrome may be detected prenatally by ultrasound examination. Prenatal diagnosis using molecular genetic techniques is available for pregnancies at 50% risk.

Management including treatment

Treatment for this condition consists in a multiple-staged surgery.

Unresolved questions

The basis for the unusually wide variation in symptomatology of this syndrome remains to be determined.

References

1. Jackson CE, Weiss L, Reynolds WA, Forman TF, Peterson JA. Craniosynostosis, midfacial hypoplasia, and foot abnormalities: an autosomal dominant phenotype in a large Amish kindred. J Pediatr 1976;88:963-8.
2. Li X, Lewanda AF, Eluma F, Jerald H, Choi H, Alozie I, Proukakis C, Talbot CC Jr, Vander Kolk C, Bird LM, et al. Two craniosynostotic syndrome loci, Crouzon and Jackson-Weiss, map to chromosome 10q23-q26. Genomics 1994;22:418-24.
3. Jabs EW, Li X, Scott AF, Meyers G, Chen W, Eccles M, Mao JI, Charnas LR, Jackson CE, Jaye M. Jackson-Weiss and Crouzon syndromes are allelic with mutations in fibroblast growth factor 2. Nature Genetics 1994;8:275-9.
4. Heike C, Seto M, Hing A, Palidin A, Hu F, Preston RA, Ehrlich GD, Cunningham M. Century of Jackson-Weiss syndrome: further definition of clinical and radiographic findings in 'lost' descendants of the original kindred. Am J Med Genet 2001;100:315-24.
5. Escobar V, Bixler D. Are the acrocephalosyndactyly syndromes variable expressions of a single gene defect? BDOAS 1977;13(3C):139-54.