What Is Your Diagnosis?

This patient has a daughter with partial deafness.

Figure not available online

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Waardenburg syndrome is an autosomal-dominant disorder that affects 1 in 40,000 individuals and accounts for more than 2% of cases of congenital deafness. Manifestations include lateral displacement of the inner canthi; heterochromia of the irides; white forelock; and other sites of poliosis, piebaldism, and sensorineural deafness. Expression of the disease is variable, even between monozygotic twins. Partial anodontia, myelomeningocele, facial palsy, and lingua plicata have been reported. Lateral displacement of the inner canthi is characteristic of Waardenburg syndrome type I; normally located inner canthi are characteristic of type II. Type III represents an extreme presentation of type I with arm abnormalities. Most patients with Waardenburg syndrome type III are homozygous for the trait. Patients with Waardenburg syndrome type IV have an absence of colonic ganglia (Hirschsprung disease).

Waardenburg syndrome is the most common syndromal cause of deafness. Most affected individuals probably have some inner ear abnormalities, but the incidence of clinically apparent hearing loss is highly variable. Children with this condition should be evaluated early because hearing loss

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may result in poor performance in school. This patient was unaware of her diagnosis, and her daughter had been classified as borderline retarded until her hearing deficit was discovered. All affected families should be evaluated by an audiologist. Otoacoustic emissions may be necessary to provide optimal fitting of hearing aids, especially in children.11

Waardenburg syndrome types I and III are associated with mutations in the PAX3 gene. Some type II cases are associated with the microphthalmia-associated transcription factor gene. The type IV phenotype can result from mutations in the endothelin-B receptor gene, the gene for its ligand (endothelin-3), or the SOX10 gene.12 All of these genes are functionally interrelated and contribute to the formation of the nervous system.13,14 Specific mutations in the PAX3 gene correlate with the expression of different features of Waardenburg syndrome.15

Tietz syndrome is associated with congenital profound deafness and generalized hypopigmentation and is inherited as a fully penetrant autosomal-dominant trait. Tietz syndrome is associated with mutations of the MITF gene, a gene also associated with Waardenburg syndrome type II. In contrast to Tietz syndrome, depigmentation in Waardenburg syndrome is patchy, and hearing loss is variable.16

REFERENCES