What Is Your Diagnosis?

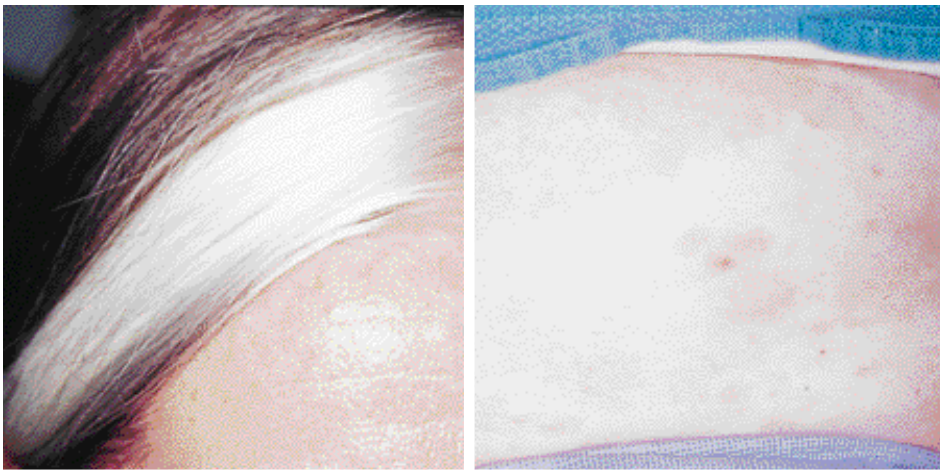

Figure not available online

This patient has a daughter with partial deafness.

PLEASE TURN TO PAGE 45 FOR DISCUSSION

Dirk M. Elston, MD, Departments of Dermatology and Laboratory Medicine, Geisinger Medical Center, Danville, Pennsylvania.

The Diagnosis: Waardenburg Syndrome

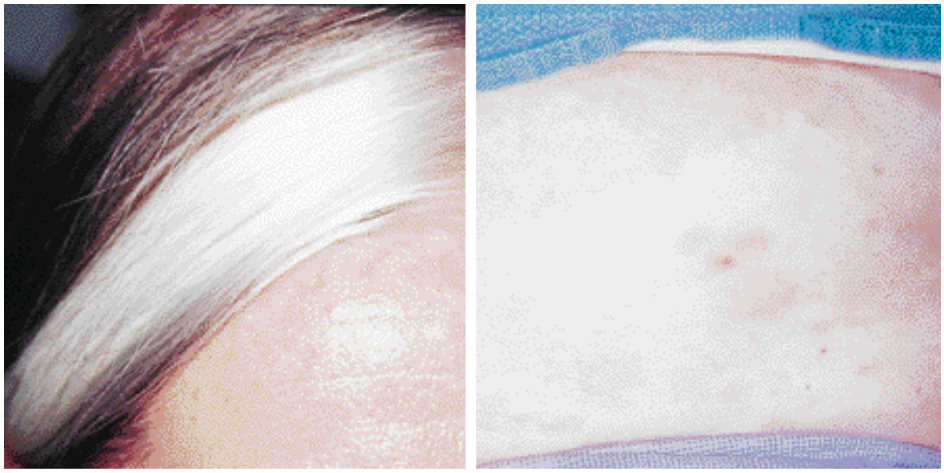

Figure not available online

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.[1] 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.[2] Partial anodontia, myelomeningocele, facial palsy, and lingua plicata have been reported.[3-5] Lateral displacement of the inner canthi is characteristic of Waardenburg syndrome type I; normally located inner canthi are characteristic of type II.[6] Type III represents an extreme presentation of type I with arm abnormalities. Most patients with Waardenburg syndrome type III are homozygous for the trait.[7] Patients with Waardenburg syndrome type IV have an absence of colonic ganglia (Hirschsprung disease).[8]

Waardenburg syndrome is the most common syndromal cause of deafness.[9] Most affected individuals probably have some inner ear abnormalities, but the incidence of clinically apparent hearing loss is highly variable.[10] Children with this condition should be evaluated early because hearing loss

The author reports no conflict of interest.
The images are in the public domain.

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

1. Nayak CS, Isaacson G. Worldwide distribution of Waardenburg syndrome. *Ann Otol Rhinol Laryngol*. 2003;112:817-820.
2. Suyugul Z, Tuysuz B, Tukenmez F, et al. Waardenburg syndrome: variable phenotypic expression in monozygotic twins. *Clin Dysmorphol*. 1998;7:77-78.
3. Bandyopadhyay S, Prasad S, Singhania PK. Partial anodontia in a case of Waardenburg's syndrome. *J Laryngol Otol*. 1999;113:672-674.
4. Nye JS, Balkin N, Lucas H, et al. Myelomeningocele and Waardenburg syndrome (type 3) in patients with interstitial deletions of 2q35 and the PAX3 gene: possible digenic inheritance of a neural tube defect. *Am J Med Genet*. 1998;75:401-408.
5. Dourmishev AL, Dourmishev LA, Schwartz RA, et al. Waardenburg's syndrome with facial palsy and lingua plicata: is that a new type of disease? *Cutis*. 1999;63:139-141.
6. Wang C, Kim E, Attaie A, et al. A PAX3 polymorphism (T315k) in a family exhibiting Waardenburg syndrome type 2. *Mol Cell Probes*. 1998;2:55-57.
7. Read AP, Newton VE. Waardenburg syndrome. *J Med Genet*. 1997;34:656-665.
8. Syrris P, Carter ND, Patton MA. Novel nonsense mutation of the endothelin-B receptor gene in a family with Waardenburg-Hirschsprung disease. *Am J Med Genet*. 1999;87:69-71.
9. Sculerati N. Analysis of a cohort of children with sensory hearing loss using the SCALE systematic nomenclature. *Laryngoscope*. 2000;110:787-798.
10. Liu XZ, Newton VE. Distortion product emissions in normal-hearing and low-frequency hearing loss carriers of genes for Waardenburg's syndrome. *Ann Otol Rhinol Laryngol*. 1997;106:220-225.
11. Oysu C, Baserer N, Tinaz M. Audiometric manifestations of Waardenburg's syndrome. *Ear Nose Throat J*. 2000;79:704-709.
12. Bondurand N, Pingault V, Goerich DE, et al. Interaction among SOX10, PAX3 and MITF, three genes altered in Waardenburg syndrome. *Hum Mol Genet*. 2000;9:1907-1917.
13. Potterf SB, Furumura M, Dunn KJ, et al. Transcription factor hierarchy in Waardenburg syndrome: regulation of MITF expression by SOX10 and PAX3. *Hum Genet*. July 2000;107:1-6.
14. Cheng Y, Cheung M, Abu-Elmagd MM, et al. Chick sox10, a transcription factor expressed in both early neural crest cells and central nervous system. *Brain Res Dev Brain Res*. 2000;121:233-241.
15. DeStefano AL, Cupples LA, Arnos KS, et al. Correlation between Waardenburg syndrome phenotype and genotype in a population of individuals with identified PAX3 mutations. *Hum Genet*. 1998;102:499-506.
16. Smith SD, Kelley PM, Kenyon JB, et al. Tietz syndrome (hypopigmentation/deafness) caused by mutation of MITF. *J Med Genet*. 2000;37:446-448.