Waardenburg Syndrome

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Keywords: genetic conditions

1. Introduction

Waardenburg syndrome is a group of genetic conditions that can cause hearing loss and changes in coloring (pigmentation) of the hair, skin, and eyes. Although most people with Waardenburg syndrome have normal hearing, moderate to profound hearing loss can occur in one or both ears. The hearing loss is present from birth (congenital). People with this condition often have very pale blue eyes or different colored eyes, such as one blue eye and one brown eye. Sometimes one eye has segments of two different colors. Distinctive hair coloring (such as a patch of white hair or hair that prematurely turns gray) is another common sign of the condition. The features of Waardenburg syndrome vary among affected individuals, even among people in the same family.

There are four recognized types of Waardenburg syndrome, which are distinguished by their physical characteristics and sometimes by their genetic cause. Types I and II have very similar features, although people with type I almost always have eyes that appear widely spaced and people with type II do not. In addition, hearing loss occurs more often in people with type II than in those with type I. Type III (sometimes called Klein-Waardenburg syndrome) includes abnormalities of the arms and hands in addition to hearing loss and changes in pigmentation. Type IV (also known as Waardenburg-Shah syndrome) has signs and symptoms of both Waardenburg syndrome and Hirschsprung disease, an intestinal disorder that causes severe constipation or blockage of the intestine.

2. Frequency

Waardenburg syndrome affects an estimated 1 in 40,000 people. It accounts for 2 to 5 percent of all cases of congenital hearing loss. Types I and II are the most common forms of Waardenburg syndrome, while types III and IV are rare.

3. Causes

Mutations in the *EDN3*, *EDNRB*, *MITF*, *PAX3*, *SNAI2*, and *SOX10* genes can cause Waardenburg syndrome. These genes are involved in the formation and development of several types of cells, including pigment-producing cells called melanocytes. Melanocytes make a pigment called melanin, which contributes to skin, hair, and eye color and plays an essential role in the normal function of the inner ear. Mutations in any of these genes disrupt the normal development of melanocytes, leading to abnormal pigmentation of the skin, hair, and eyes and problems with hearing.

Waardenburg syndrome types I and III are caused by mutations in the *PAX3* gene. Mutations in the *MITF* or *SNAI2* gene can cause Waardenburg syndrome type II.

Mutations in the *SOX10*, *EDN3*, or *EDNRB* gene can cause Waardenburg syndrome type IV. In addition to melanocyte development, these genes are important for the development of nerve cells in the large intestine. Mutations in one of these genes result in hearing loss, changes in pigmentation, and intestinal problems related to Hirschsprung disease.

In some cases, the genetic cause of Waardenburg syndrome has not been identified.

3.1 The genes associated with Waardenburg syndrome

- EDN3
- EDNRB

- MITF
- PAX3
- SNAI2
- SOX10

4. Inheritance

Waardenburg syndrome is usually inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person has one parent with the condition. A small percentage of cases result from new mutations in the gene; these cases occur in people with no history of the disorder in their family.

Some cases of Waardenburg syndrome type II and type IV appear to have an autosomal recessive pattern of inheritance, which means both copies of the gene in each cell have mutations. Most often, the parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition.

5. Other Names for This Condition

- Waardenburg's syndrome

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