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Waardenburg syndrome: A rare genetic disorder

[1]Dr. Amandeep Singh, [2]Dr.C.L Nawal, [3]Dr. Radhey Shyam Chejara, [4]Dr.P.D.Meena, [5]Dr. Rajbeer Singh*, [6]Dr.Ram Kalyan Meena

[1,5]Resident Doctor, Department of Medicine, SMS Medical College, Jaipur

[2]Professor& Head, Department of Medicine, SMS Medical College, Jaipur

[3]Assistant Professor, Department of Medicine, SMS Medical College, Jaipur

[4]Professor, Department of Medicine, SMS Medical College, Jaipur

[6]Resident Doctor, Department of Otorhinolaryngology, SMS Medical College, Jaipur

Correspondence Author: Dr. Rajbeer Singh, Resident Doctor, Department Of Medicine, SMS Medical College, Jaipur, India.

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Abstract

Waardenburg syndrome is a genetic disorder named after a Dutch ophthalmologist who has first described the triad of hearing loss, dystopia canthorum and retinal pigmentary differences.[1] It was the first subtype among the four subtypes well known today. All races are affected equally without gender variations. It accounts from 2 to 5 % cases of peoples suffering from congenital deafness.[2]The pattern of inheritance is usually autosomal dominant.[3]We hereby reporting a case of Waardenburg syndrome type 2 with strong family history of Inheritance.

Keywords: Heterochromia, Deafness, Waardenburg syndrome (WS)

Introduction

Waardenburg syndrome is a rare heritable disorder defined as varying degrees of hearing loss and differences in the coloring (pigmentation) of the eyes, hair, and skin. Clinical features can vary both within and between families. WS has following clinical features.

Symptoms usually vary among different types of this syndrome but commonly they include:

- Heterochromia iridis as eyes with iris having two different colors.
- Premature graying of hair i.e poliosis.
- Laterally displaced medial canthi with dystopia of lacrimal puncta as well as blepharophimosis.
- Prominent broad nasal root.
- Hearing impairment ranging from moderate to profound

Different physical characteristic helps in determining the type of WS. Most common types among the four are type I and II.[4]

Table 1 Variants of Waardenburg syndrome [5, 6]

Waardenburg Type	Inheritance and Location	Auditory Phenotype	Associated Disorders
Type I	Autosomal dominant, 2q35	Congenital, variable sensorineural hearing loss	Craniofacial abnormalities, including dystopia canthorum; pigmentary abnormalities
Type 2	Autosomal dominant, 3p14.1-p12.3	Congenital, variable sensori neural hearing loss, may be progressive	Craniofacial abnormalities, without dystopia canthorum; pigmentary abnormalities
Type 2 with ocular albinism	Autosomal digenic, 3p14.1-p12.3 llq14-q21	Progressive sensorineural hearing loss	Ocular albinism
Type 3 (Klein- Waardenburg)	Autosomal dominant, 2q35	Sensorineural hearing loss	Craniofacial abnormalities, including dystopia canthorum; pigmentary abnormalities; musculoskeletal abnormalities
Type 4 (Shah- Waardenburg)	Autosomal recessive, 20qI3.2-q13.3	Sensorineural hearing loss	Craniofacial abnormalities, without dystopia canthorum; pigmentary abnormalities; Hirschsprung's disease

Case Report

A 27 year old right handed married Hindu female presented with history of decreased hearing from both ears, left more than right. On general physical examination, patient had pigmentation abnormality of the iris i.e. complete heterochromia iridum. The iris of right eye was blue in colour whereas that of left eye was brown. The nasal root was broad as well as high along with medial eyebrow flare (fig.1). There was no canthorum dystopia, no sinophrys, no skin pigmentation changes, and no deformities of the arms or leg. Otoscopy: Clean external auditory meatus, tympanic membrane with no perforations, translucent, further evaluating for the hearing loss, audiometry was done which was suggestive of bilateral sensorineural hearing loss, left more than right (fig 2).The patient did not have any other neurological defect and skin abnormality.

Figure 1: Congenital Heterochromia Iridis, Broad Nasal Root, Medial Eyebrow Flare

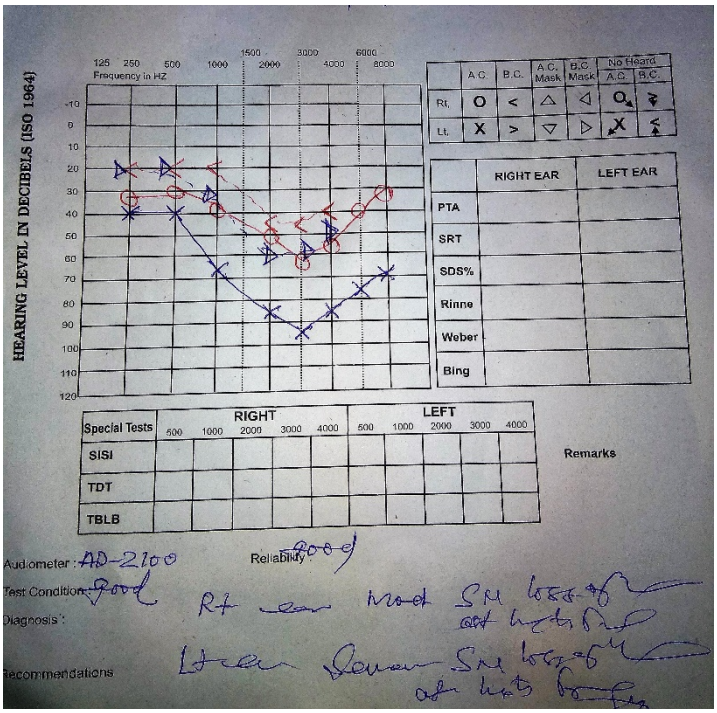
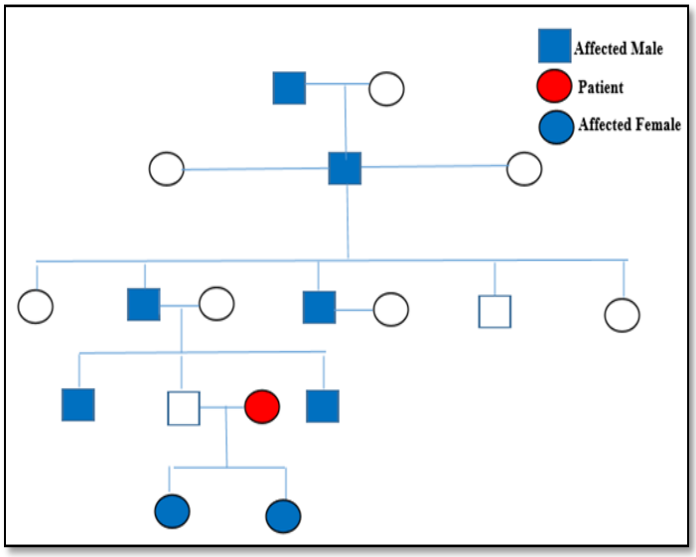


Figure 2: Pure Tone Audiometry

Enquiring about her family history, she had significant family history of the same features. The pattern of inheritance is Autosomal Dominant. The pedigree is as follows.



All above features fulfills criteria for diagnosing Waardenberg Syndrome Type 2.

Discussion

Waardenburg syndrome is a heritable disorder having incidence of 1 in 40,000 that manifests with sensorineural deafness, pigmentary defects of the skin, hair and iris and various defects of neural crest-derived tissues. Mutations in the EDN3, EDNRB, MITF, PAX3, SNAI2, and SOX10 genes leads to different types of Waardenburg syndrome.[7]Waardenburg syndrome (WS) is diagnosed clinically. The Waardenburg Consortium in 1992 had proposed the diagnostic criteria. Both major as well as minor criteria were included. For diagnosing WS type 1, among the following criteria given below, either 2 major criteria should be present or 1 major along with 2 minor of the following criteria are required. [8, 9] ,

Major criteria

- Congenital sensorineural type of hearing loss (present from birth)
- Heterochromia iridis (either complete or segmental); isohypochromia iridis (pale blue eyes); or defective pigmentation in fundus.
- Hair pigmentation like white forelock or loss of colour of hairs.
- Dystopia canthorum (It is characteristically seen in WS types 1 and 3)
- 1st degree relative with Waardenburg syndrome

Minor criteria

- Leukoderma from birth
- Synophrys or medial eyebrow flare
- Nasal bridge is broad or high(uppermost part of the nose) Hypoplasia of the nostrils
- Premature gray hair (Age <30)

WS type 2 has same features as type 1, no dystopia canthorum) . WS type 3 has musculoskeletal abnormalities such as hypoplasia of muscles, flexion contracture, syndactyly or fused fingers.

WS type 4 although similar to WS type 2, but associated with Hirschsprung disease.

There should be multidisciplinary approach for treating the syndrome. It includes ophthalmology, Otorhinolaryngology as well as genetic councelling. Diagnosis at childhood allows efficient audiological approach by which quality of life can be improved.[10]Treatment with cochlear implants provides excellent results along with proper hearing rehabilitation.[11]

Conclusion

Waardenburg is a rare disorder. Diagnosing the disease early will improve hearing defects which are most important for overall development of children with this disease. Genetic counseling of the family is all a good initiative to be taken.

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