Research Article

Waardenburg Syndrome: A Case Report with Clinical and Audiological Correlation

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Abstract

Waardenburg syndrome (WS) is a rare genetic disorder characterized by varying degrees of sensorineural hearing loss and pigmentary abnormalities involving the skin, hair, and eyes. First described in 1951, it encompasses a spectrum of phenotypic expressions linked to defects in neural crest cell development. This publication presents a case of a 7-year-old girl exhibiting classic clinical features including hypopigmented patches, dystopia canthorum, and congenital sensorineural hearing loss. The report highlights the importance of early diagnosis through clinical recognition and genetic understanding. A brief review of the literature is included, focusing on the classification, global distribution, and genetic basis of the syndrome. Early identification and multidisciplinary management are crucial for improving quality of life and preventing complications associated with hearing impairment.

Keywords: Waardenburg syndrome; Dystopia canthorum; Hypopigmentation; Sensorineural hearing loss; Genetic disorder; Neural crest.

1. Introduction

Waardenburg syndrome (WS) is a genetically heterogeneous condition primarily affecting neural crest-derived tissues. It was first described by Petrus Johannes Waardenburg in 1951, who identified a constellation of features including lateral displacement of the inner canthi, pigmentary disturbances, and congenital deafness [1]. The syndrome is inherited in an autosomal dominant pattern in most cases, although sporadic mutations have also been reported. Its estimated prevalence varies globally, with studies suggesting it accounts for approximately 2–5% of all cases of congenital deafness [3].

The pathogenesis of WS is linked to mutations in genes involved in neural crest cell migration and differentiation, such as PAX3, MITF, SOX10, and EDNRB [2]. These mutations disrupt melanocyte development, leading to pigmentation anomalies and auditory dysfunction. Clinical manifestations vary widely, even among affected members of the same family, indicating variable expressivity and incomplete penetrance.

WS is classified into four major types (I–IV) based on clinical presentation and genetic findings. Type I is characterized by dystopia canthorum, whereas Type II lacks this feature. Type III (Klein–Waardenburg syndrome) includes musculoskeletal abnormalities, and Type IV (Shah–Waardenburg syndrome) is associated with Hirschsprung disease [4]. Among these, Types I and II are the most common.

Common clinical features include heterochromia iridis, white forelock, premature graying, hypopigmented skin patches, and sensorineural hearing loss. Dystopia canthorum, a hallmark of Type I, is defined as lateral displacement of the inner canthi with normal interpupillary distance [4]. The diagnosis is largely clinical, based on established major and minor criteria, although molecular testing can confirm the underlying mutation.

Despite its rarity, awareness of WS is important for early diagnosis, genetic counseling, and management. This report presents a classical case of Waardenburg syndrome in a young child, emphasizing key diagnostic features and reviewing relevant literature.

2. Case report

A 7-year-old girl came to the outpatient department with complaints of decreased hearing since birth and noticeable skin discoloration. She was born of a non-consanguineous marriage, with no significant perinatal complications. Family history revealed no similar condition.

On clinical examination, the child exhibited multiple hypopigmented patches distributed over the trunk and upper limbs [Figure 2]. Facial examination revealed dystopia canthorum, characterized by increased distance between the medial canthi with normal interpupillary distance [Figure 1]. The nasal root appeared broad. No limb abnormalities were observed.

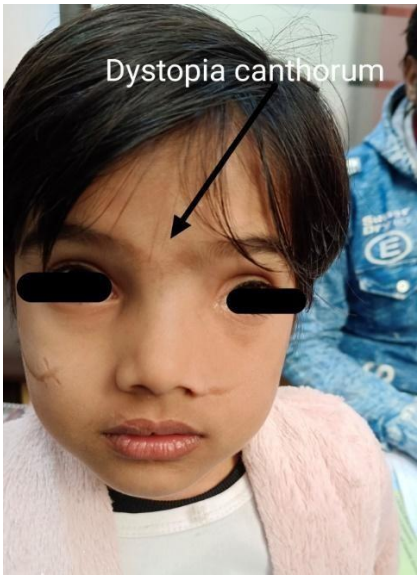

Figure 1: Exhibits dystopia canthorum, characterized by increased distance between the medial canthi with normal interpupillary distance

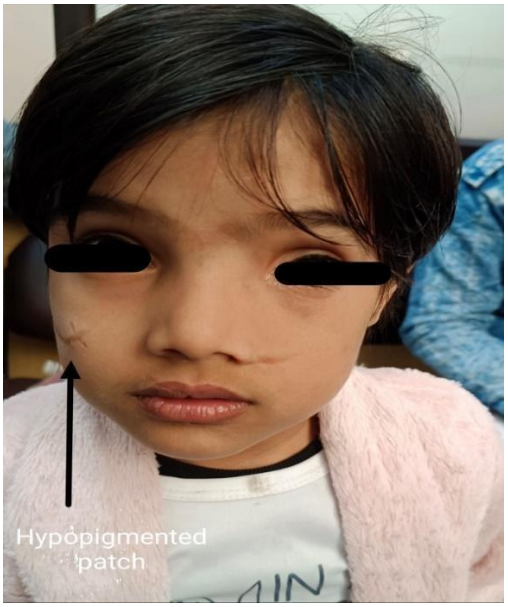

Figure 2: Exhibits hypopigmented patch on the right side of cheek

Ophthalmologic examination did not reveal heterochromia, but mild iris hypopigmentation was noted. Audiological evaluation using pure tone audiometry confirmed bilateral sensorineural hearing loss of moderate severity [Figure 3].

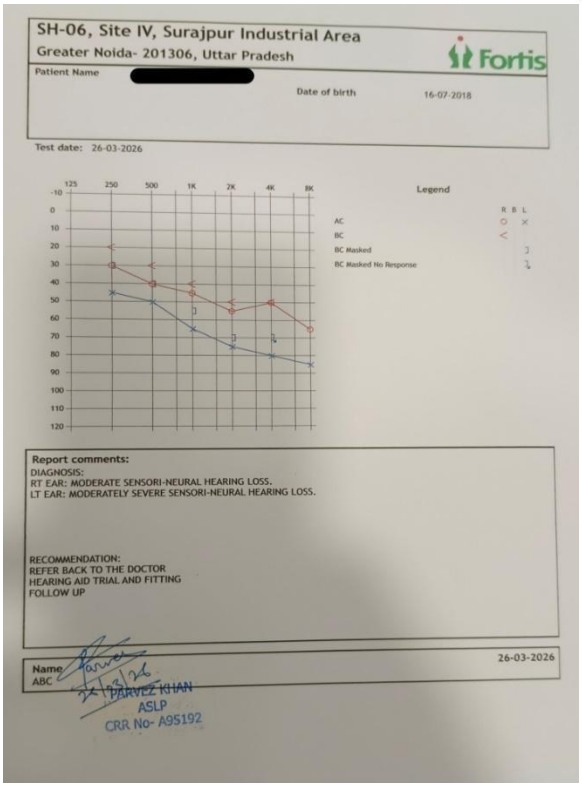

Figure 3: Audiometry finding showing Sensorineural hearing loss

Based on the presence of dystopia canthorum, hypopigmented skin patches, and congenital sensorineural hearing loss, a clinical diagnosis of Waardenburg syndrome Type I was made. The patient was referred for genetic counseling and audiological rehabilitation, including hearing aids and speech therapy.

3. Discussion

Waardenburg syndrome is primarily characterized by abnormalities arising from defective neural crest cell development. These abnormalities affect melanocyte distribution, leading to pigmentary changes in the eyes, hair, and skin, as well as defects in the stria vascularis of the cochlea, resulting in sensorineural hearing loss [2,4].

Key clinical manifestations include heterochromia iridis (complete or segmental), brilliant blue eyes, white forelock, premature graying of hair, dystopia canthorum, and cutaneous hypopigmentation. Hearing impairment is a major clinical concern and may range from mild to profound. Craniofacial features such as a broad nasal root and hypoplastic alae nasi are also commonly observed [1,4].

The diagnosis of Waardenburg syndrome is primarily clinical and is based on a combination of major and minor criteria [1,4].

Major criteria include:

- Congenital sensorineural hearing loss
- Pigmentary disturbances of the iris (complete heterochromia iridis, segmental heterochromia, or hypoplastic blue iris)
- White forelock or hair hypopigmentation (poliosis)
- Dystopia canthorum
- First-degree relative previously diagnosed with WS

Minor criteria include:

- Congenital leukoderma (patches of hypopigmented skin)
- Broad and high nasal root
- Hypoplasia of alae nasi
- Premature graying of hair (before 30 years of age)

A diagnosis is established when two major criteria or one major plus two minor criteria are present. In the present case, the patient fulfilled multiple major criteria, including sensorineural hearing loss, iris pigmentary abnormalities, white forelock, and dystopia canthorum, along with minor criteria such as a broad nasal root and hypoplastic alae nasi, supporting the diagnosis of Type I WS [1,4].

WS is divided into four subtypes:

- **Type I:** Presence of dystopia canthorum (most common)
- **Type II:** Similar features without dystopia canthorum but higher incidence of hearing loss
- **Type III (Klein–Waardenburg syndrome):** Includes musculoskeletal abnormalities
- **Type IV (Shah–Waardenburg syndrome):** Associated with Hirschsprung disease [4]

The heterogeneity of WS arises from mutations in genes such as PAX3, MITF, and SOX10 [2,5]. Although diagnosis remains largely clinical, genetic testing can aid in confirmation and subtype classification.

Early diagnosis is crucial for timely intervention, particularly for hearing impairment, which significantly affects speech and cognitive development. Management requires a multidisciplinary approach involving audiological rehabilitation, speech therapy, ophthalmologic evaluation, and genetic counseling [3,4].

4. Conclusion

Waardenburg syndrome is a rare but clinically significant genetic disorder with distinctive phenotypic features. Recognition of key signs such as dystopia canthorum, hypopigmentation, and sensorineural hearing loss is essential for early diagnosis. Classification into subtypes aids in understanding prognosis and associated anomalies. Early intervention, particularly for hearing deficits, can greatly improve developmental outcomes. Increased awareness among clinicians is vital for prompt diagnosis and appropriate management.

- **Financial Support and Sponsorship:** None
- **Presentation at a Meeting:** None
- **Competing Interest Statement by All the Authors:** The authors declare that they have no competing interest.
- **Authorship Statements by All Authors:** All authors of this article declare that we qualify for authorship as defined by ICMJE. each author has participated sufficiently in work and takes public responsibility for appropriateness of content of this article**.**
- **Ethical Approval:** Not required
- **Consent:** Written informed consent has been taken by the patient

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