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(CASE REPORT)

Waardenburg syndrome type 1: A case report

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Abstract

Waardenburg syndrome (WS) is an autosomal dominant disorder caused by mutations in genes involved in the development of neural crest cells, affecting pigmentation, hearing, and craniofacial structures. This article presents a case of a 2-year-old girl diagnosed with WS type 1, who exhibited key characteristics such as a white forelock, heterochromia iridum, and dystopia canthorum, without hearing loss or other systemic abnormalities. The absence of hearing impairment does not exclude the diagnosis as this case highlights the variability in clinical presentation, making a comprehensive approach crucial for diagnosis and management. This case emphasizes also the need for early assessment, ongoing audiological monitoring, and multidisciplinary care to improve the patient's quality of life.

Keywords: Waardenburg syndrome; White forelock; Heterochromia iridum; Dystopia canthorum

1. Introduction

Waardenburg syndrome (WS) is a rare genetic disorder that affects the neural crest cells, leading to a variety of phenotypic manifestations, including pigmentary abnormalities, sensorineural deafness and defects in structures derived from neural crest cells. There are four subtypes (1–4), each associated with varying degrees of severity and distinct genetic mutations.

In this article, we present a case of a 2-year-old girl diagnosed with Waardenburg syndrome type 1, exhibiting the classical signs.

2. Case observation

A 2-year-old female child presented to our dermatology department with a white forelock on the anterior scalp, present since birth. The child was the second offspring of a non-consanguineous marriage, with a healthy sibling. There was no significant prenatal or perinatal history, and the child had normal developmental milestones according to her age. There was no family history of similar pigmentary or auditory abnormalities.

Upon clinical examination, the child had a centrally located white forelock over the frontal scalp. The white patch of hair was well-demarcated, with no associated depigmentation or hypopigmentation on the surrounding scalp or elsewhere on the body. The forelock itself was confined to the central part of the scalp, without any signs of progression or additional white patches **(Figure 1)**. Other dermatologic findings were unremarkable, and there were no signs of alopecia or other skin pigmentation abnormalities.

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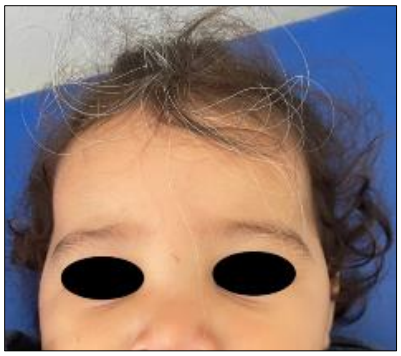

Figure 1 Centrally placed white forelock in frontal area without any associated depigmentation of the scalp

An otolaryngologic examination revealed no signs of hearing loss (the auditory screening test showed no evidence of sensorineural hearing impairment).

Ophthalmological evaluation revealed heterochromia iridum, characterized by different-colored irises. Additionally, dystopia canthorum**,** a condition in which the inner canthi of the eyes are widely spaced, was noted **(Figure 2)**. These craniofacial findings, in conjunction with the white forelock, raised suspicion for Waardenburg syndrome.

Figure 2 Heterochromia iridum with dystopia canthorum

Furthermore, abdominal and systemic examinations, including a full skeletal testing were recommended to assess for any skeletal or other associated anomalies, but the results were negative. No abnormalities were detected on X-ray or other imaging studies.

Given the constellation of features (white forelock, heterochromia iridum, and dystopia canthorum), and the absence of hearing loss or other systemic findings, the diagnosis of Waardenburg syndrome type 1 (WS1) was made. The patient's hearing status was monitored, and follow-up appointments were scheduled to assess for any changes.

3. Discussion

Waardenburg syndrome (WS) is a rare genetic disorder that primarily involves abnormal development of neural crest cells, resulting in a spectrum of clinical manifestations involving pigmentation, hearing and craniofacial structure [1]. It is typically inherited in an autosomal dominant pattern, with mutations in several genes critical to the development of pigment-producing cells (melanocytes) and structures of the inner ear [2]. The PAX3 gene is most commonly implicated in type 1 [3], whereas MITF and SNAI2 mutations are found in type 2 [4]. In some cases, SOX10**,** EDN3, or EDNRB mutations are responsible for the more severe manifestations seen in type 3 and 4, which may also involve musculoskeletal or gastrointestinal anomalies like Hirschsprung disease [5, 6]. Clinically, WS is characterized by congenital sensorineural hearing loss, pigmentary abnormalities (such as hypopigmentation of the hair and skin and heterochromia iridum), craniofacial features like synophrys (medial eyebrow flare), a broad nasal root, and dystopia canthorum which is an increased distance between the inner canthi of the eyes [7]. The syndrome is divided into four subtypes, each defined by specific clinical and genetic characteristics.

In our case, the patient presented with key features of Waardenburg syndrome type 1, especially a white forelock, heterochromia iridum and dystopia canthorum, which are pathognomonic signs for this subtype. Notably, the absence of hearing loss and other musculoskeletal abnormalities distinguishes this case and highlights the variability of the syndrome's clinical expression. Although sensorineural hearing loss is present in approximately 50% of individuals with WS 1 [8], its absence in our patient does not exclude the diagnosis, especially when the characteristic pigmentary and craniofacial signs are present. This emphasizes the importance of considering WS 1 even in the absence of hearing impairment, as other features of the syndrome, such as the white forelock and dystopia canthorum, can be quite distinct

and guide the diagnosis. Additionally, the lack of musculoskeletal abnormalities, typically seen in type 3 [9], further clarifies that our case is indeed a classic example of type 1.

This case is particularly significant because it underscores the necessity of early diagnosis and the need for a comprehensive approach to patient's management [9]. Even in the absence of hearing loss, children with Waardenburg syndrome should undergo a complete audiological evaluation, as hearing deficits can develop or become apparent later in life. Furthermore, the patient's physical features may have social and psychological implications, as children with visible craniofacial anomalies may experience challenges in terms of self-esteem and peer relationships [10].

4. Conclusion

While hearing loss is a prominent feature in many cases of Waardenburg syndrome type 1, this case highlights the importance of recognizing the full spectrum of clinical manifestations, including pigmentary and craniofacial signs, and reinforces the need for a multidisciplinary approach to care, including genetic counseling, monitoring for any emerging auditory issues, and providing psychological and educational support.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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