British Journal of Medicine & Medical Research

21(9): 1-5, 2017; Article no.BJMMR.32921
ISSN: 2231-0614, NLM ID: 101570965

Waardenburg Syndrome in an 8 Year Old African Child: Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. Author VO designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors IOC and NC proof read the initial manuscript. Authors VO and NC managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2017/32921
Editor(s):
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Complete Peer review History: http://www.sciencedomain.org/review-history/19189

Case Report

Received 23rd March 2017
Accepted 10th May 2017
Published 25th May 2017

ABSTRACT

Aim: Waardenburg syndrome is a very rare condition, inherited autosomally with genetic heterogeneity and characterized by deafness, hair discoloration, iris discoloration and eyelid changes.
Case Report: We report a case of an 8 year old female child with a history of a striking difference between the eyes since birth. Ocular examination revealed slightly widened medial canthal distances and hypertelorism. There was a lateral displacement of the right inner canthi [Dystopia Canthorum]. The Iris was hypopigmented and bluish in colour in the right eye, whilst the left Iris was brown and darkly pigmented.
Discussion: The diagnosis of WS is considered if there are 2 major or 1 major and 2 minor criteria

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according to Waardenburg consortium. Our patient had 2 major criteria viz pigmentary disturbances of the iris and dystopia canthorum. Waardenburg syndrome is sub classified into 4 types. The management of Waardenburg's syndrome, comprises early detection and referral to the appropriate unit including audiology, correction for refractive error and use of cosmetic contact lenses.

Conclusion: Waardenburg syndrome is a rare disease. In all suspected patient, hearing impairment, severe musculoskeletal contractures and Hirschsprungs disease should be ruled out.

Keywords: Waardenburg syndrome; dystopia; hypertelorism; Hirschsprungs.

1. INTRODUCTION

Waardenburg syndrome is a very rare condition, inherited autosomally with genetic heterogeneity. The most frequent characteristic features are deafness, hair discolouration, iris discolouration and eyelid changes. Prevalence in the population is 1:42000, while the incidence is 1:270000 births [1]. The diagnosis of WS is considered if there are 2 major or 1 major and 2 minor criteria.

The major criteria include congenital sensorineural deafness, pigmentary disturbance of the iris, white forlock, dystopia canthorum and an affected first degree relative.

The minor criteria are congenital leucoderma, medial eyebrow flare, broad and high nasal root, hypoplasia of alae narsi, and premature greying of the hair.

We present a case of an 8 year old female child, with Waardenburg syndrome presenting to an ophthalmic unit.

2. CASE REPORT

Ms A, an 8 year old female child was referred to our unit with a history of a striking difference between the eyes since birth. The mother confirmed the pregnancy was full term, with no significant events during gestation. Birth was a normal, spontaneous vaginal delivery. The milestones were not delayed, and the child was currently enrolled in full time education with no apparent concerns. The patient was the 4th of 5 siblings. No other member of the family has Heterochromia Irides. The mother was 40 years of age, whilst the father was 43 years old. Examination revealed well child, not small for age. The general examination did not reveal any abnormality, physically or mentally. The child's hearing was grossly normal. Ocular examination revealed slightly widened medial canthal distances and hypertelorism. There was a lateral displacement of the right inner canthi [Dystopia Canthorum]. The Iris was hypopigmented and bluish in colour in the right eye, whilst the left Iris was brown and darkly pigmented. Fundal examination was normal. No significant refractive error was found. The disease was diagnosed based on the presence of 2 major criteria as proposed by the waardenburg consortium viz; pigmentary disturbances of the iris and dystopia canthorum.

Fig. 1. Ocular appearance at presentation

Because of taunting from other children in school and comments about her appearance, the parents were more particular about the eye appearance and sought medical help. The options of management were discussed with the parents including a cosmetic contact lens. Following a successful contact lens trial in clinic, she was subsequently fitted with an 8.3 base curve, plano, hand painted contact lenses with a clear pupil and high DK lenses to enable extended wear [David Thomas UK Ltd].

3. DISCUSSION

Waardenburg Syndrome is a genetic disorder that may be evident at birth. The range and

severity of the symptoms vary greatly from case to case. However Iris discolouration, congenital deafness and hair changes are common features. Waardenburg syndrome is sub classified into 4 types according to the Waardenburg consortium.

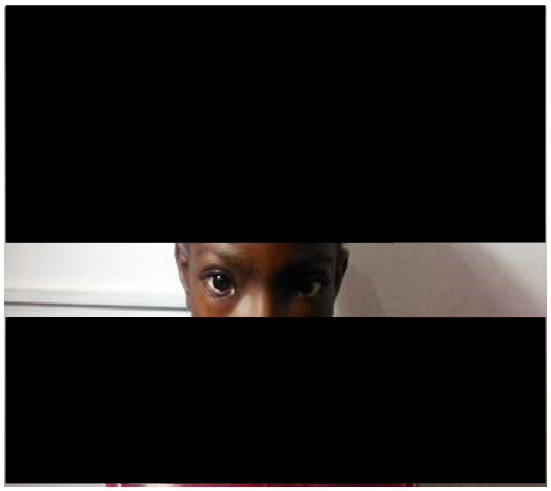

Fig. 2. Ocular appearance after contact lens fitting

In type 1: Waardenburg syndrome type I (WS1) is an auditory-pigmentary disorder comprising congenital sensorineural hearing loss and pigmentary disturbances of the iris, hair, and skin, along with dystopia canthorum (lateral displacement of the inner canthi). The hearing loss in WS1, observed in approximately 60% of affected individuals, is congenital, typically non-progressive, either unilateral or bilateral, and sensorineural. Congenital leukoderma is frequently seen on the face, trunk, or limbs. [2] Type 1 is inherited as an autosomal dominant trait with variable penetrance and expressivity.

Type 2: Waardenburg syndrome type 2 (WS2) is a type of Waardenburg syndrome characterized by varying degrees of deafness and pigmentation (coloring) abnormalities of the eyes, hair and/or skin. WS2 differs from WS1 and some other types of WS by the absence of dystopia canthorum (lateral displacement of the inner canthi of the eyes). [3,4] Sensorineural hearing loss occurs in the majority of people with WS2, and heterochromia iridis (differences in eye coloring) occurs in about half. WS2 may be caused by changes (mutations) in any of several genes, but in many cases the genetic cause is unknown. While inheritance is usually autosomal dominant, sometimes WS2 is not inherited, occurring for the first time in someone with no family history of the condition. Treatment may include the use of hearing aids and/or cosmetic products (if desired) for skin hypopigmentation [3].

Type 3: Klein-Waardenburg syndrome; Waardenburg syndrome, type 3; Waardenburg syndrome with upper limb anomalies; White forelock (poliosis) syndrome with multiple congenital malformations. Inheritance is by autosomal dominance.

Type 4: Waardenburg syndrome type 4, also known as Waardenburg-Shah syndrome, is a genetic condition that can cause hearing loss; changes in coloring (pigmentation) of the hair, skin, and eyes; and Hirschsprung disease, an intestinal disorder that causes severe constipation or blockage of the intestine. Waardenburg syndrome type 4 is further divided into types 4A, 4B, and 4C based on their genetic cause. Type 4A is caused by mutations in the *EDNRB* gene, mutations in *EDN3* cause 4B, and mutations in *SOX10* cause type 4C. This condition is usually inherited in an autosomal dominant fashion; however, some cases of type 4 appear to have an autosomal recessive pattern of inheritance [5,6].

Other occasional associations reported are cleft lip and palate, EEG abnormalities, epilepsy, microphthalmia, anterior lenticonus and high refractive errors [1,7].

In some cases there may be no family history, indicating new mutant gene. Also the condition may be associated with advancing age of the father [Paternal age factor], [8] as noted by Onabolu et.al in their report of a case.

Waadenburg syndrome type 1 is believed to be caused by PAX3 gene on the long arm of chromosome 2 [2q35].

Recent genetic studies on Waardenburg syndrome revealed that Waardenburg anophthalmia syndrome caused by a *SMOC1* variant in a Pakistani population.[9] Other recent findings was a heterozygous missense variation in EDNRB following performance of exome sequencing in a WS2 index case.[10] Interestingly, homozygous (and very rare heterozygous) EDNRB mutations are already described in type IV WS (i.e., in association with Hirschsprung disease [HD]) and heterozygous mutations in isolated HD. Furhtermore, N Felah et al. [11] suggest that *SOX10* duplication can cause disorders of sex development and PCWH,

supporting the hypothesis that *SOX10* toxic gain of function rather than dominant negative activity underlies PCWH(Peripheral Demyelinating Neuropathy, Central Dysmyelinating Leukodystrophy, Waardenburg Syndrome, and Hirschsprung Disease).

Amoni et.al reported 2 cases; one with dystopia canthorum and the other without [12]. Also Omolase et.al reported a recent case of congenital heterochromia iridis in a 6 month old, which however appears to be bilateral hypopigmentation of the iris [13].

Other potential causes of congenital heterochromia should be considered on presentation, including Horner's syndrome, Hirschsprungs disease, incontinentia pigmenti and Parry-Romberg's syndrome. Charrow J. reported an 18 month old African boy with type 1 disease but no hearing loss [14]. 50% of cases do not have hearing impairment. In those that have deafness; it may be unilateral or bilateral, variable in severity and non-progressive but profound.

The management of Waardenburg's syndrome, comprises early detection and referral to the appropriate unit including audiology. In our patient the cosmetic and psychological factors prompted presentation to the eye department. Genetic counselling may have a role especially in situations where consanguinity is an associated factor [15].

4. CONCLUSION

Waardenburg syndrome is a very rare condition characterized by deafness, hair discolouration, iris discolouration and eyelid changes. In all suspected patient, hearing impairment, severe musculoskeletal contractures and Hirschsprungs disease should be ruled out. Early detection and referral to appropriate unit is vital in management.

CONSENT

All authors declare that 'written informed consent was obtained from the parents for publication of this paper and accompanying images'.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/19189