

Case Report

Juvenile type II Waardenburg syndrome: a rare case report in Kerala

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ABSTRACT

Rare diseases are many in number but their treatments are less, as most of these rare diseases are genetical and there is no complete cure for a genetic disorder. Waardenburg syndrome (WS) is one among that type of rare genetic disorder thus the treatment is limited but the number of cases are increasing. This was the case report of a newborn baby showing major symptoms of WS. The patient got it through paternally. To make a final conclusion, various diagnostic tests were conducted including the family history as the patient's father had premature grey hairs and white patches on the body. Even though there is no complete cure for this disease condition, the sign and symptoms can be controlled before making it into a major disability. This case report typically dealt with the major types, clinical presentation, diagnosis and supportive therapy for a patient diagnosed with WS. Also showed the crucial role of consanguineous parents on this syndrome because the children affecting this rare syndrome are increasing. This report showed that further studies are required to check how the colour of the hair is changing in WS patients and what is happening to the gene involved in the production of melanin. Also, studies are required the find why WS typically affecting the major sensory organs such as eyes, ears, nose and skin.

Keywords: White forelock, Brilliant blue iris, Dystopia canthorum

INTRODUCTION

The unusual observations are the gemstones of inventions. Many diseases and their treatments are yet to be discovered. WS is one among that, which is a group of rare genetic conditions that are characterized by unusual facial shapes, premature grey hair, different coloured iris and congenital deafness. People of all races and either sex are at risk of WS. WS is an autosomal dominant trait that is only one parent has to pass on the faulty gene for a child to be affected. As it is a congenital disorder, it is present from birth. There is no cure for the condition but it can be managed.

It may be diagnosed at birth or early childhood on view of clinical presentation, physical findings, a complete patient and family history and from other specialized studies.² There are many other typically dermatological disorders that are similar to WS such disorders may include partial albinism and deafness, vitiligo and congenital sensorineural deafness or a condition called Vogt-Koyanagitarada syndrome. Different types of WS are present and which are differentiated with its typical sign and symptoms and gene involvement. WS will not affect the life expectancy and no other further disease will accompany for a person having WS other than deafness or Hirschsprungs disease.

This was the case report of a pregnant woman who came to our tertiary care hospital after completing her pregnancy period and gave birth to a child having WS.

CASE REPORT

A 24 year old woman visited our clinic for parturition after her 6 year of sterility. During the pregnancy period she was diagnosed with hypertension and hyperglycemia. She was prescribed with tablet labetalol (100 mg) half OD and metformin 500 OD along with iron, folic acid and calcium supplements from her 3rd month of pregnancy. After the successful completion of three trimesters the woman gave birth to a baby girl with white forelock. Self-assurance was given to the family and then investigations were started to rule out the syndrome. To identify the disease, we consulted different specialists including ophthalmologist, dermatologist and audiologist. On ophthalmology consultation the colour change in the eye of the baby was noticed and on further examination the brilliant blue color of iris was confirmed as a major symptom of WS (Figure 5). Various hearing testes including otoacoustic emissions (OAE) were done and hearing loss of right ear was confirmed by the audiologist. Dermatologist confirmed that there were no distinguishable changes in baby except the white color hair on the forehead and confirmed it as white forelock (Figure 2).

After performing various diagnostic tests, the baby was diagnosed with type II WS due to the absence of dystopia cantharum and three major symptoms of WS such as white forelock, brilliant blue iris and congenital hearing impairment. Also there is history suggestive of premature grey hair in her father at the age of 20 and also have patches on the skin. The pediatrician confirmed that the baby is having WS.

During the hospitalization baby was treated with ciplox eye drops and moxclav drops (amoxicillin 80 mg+clavulanic acid 11.4 mg). Patient was discharged after under observation for four days with discharge medications for 5 days.

Discharge medications

The discharge medications were V total drop: 10 drops OD (orally); wikory drop: 5 drops TDS (orally); mucolite drops: 5 drops TDS (orally).

After few months of observation, patients white coloured hairs get changed to grey colour which implies that in future the color can be changed to normal black colour. But other impairments were still present. Till now the patient is not taking any kind of medicines and leading a normal life.

Family tree of the patient

The family tree of the patient is depicted below. Colored square box is the affected father, uncolored circle is the unaffected mother and colored circle is the affected baby girl.

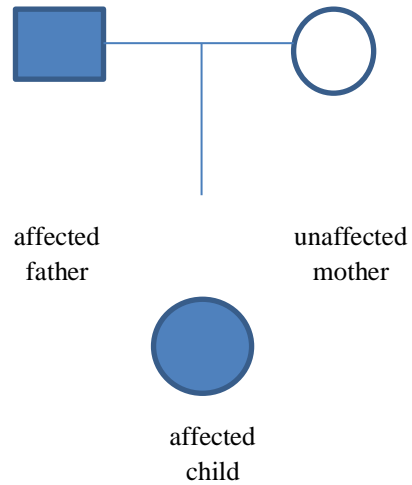


Figure 1: Family tree of the patient.

In this case study, the new born baby had three major symptoms of WS such as white forelock, iris pigmentary abnormality (brilliant blue iris) and sensory neural hearing loss for the right ear and there is no dystopia canthorum (W index <1.95) (Figure 2 and 5). By all these investigation WS type II is confirmed for this baby. On follow-up, the white colour of the hair is changing to grey colour and then to almost black, this will be a positive sign to the patient that sometimes the colour can change back to its normal colour (Figure 3 and 4). The patient can change their physical appearance by hair colouring, keeping contact lens of normal eye colour, this will make them to feel comfortable to face the society. This case report showed the crucial role of consanguineous parents on this syndrome because the children affecting this rare syndrome is increasing.



Figure 2: White forelock present on the baby at the time of birth.



Figure 3: White coloured hairs get changed to grey colour.



Figure 4: Grey coloured hairs changed to almost black colour.



Figure 5: Baby with brilliant blue coloured iris.

DISCUSSION

WS is a rare congenital genetical disorder and it was first described by Dutch ophthalmologist and geneticist Peter Johannes Waardenburg in 1951. Based on the gene involved and the clinical features WS can be classified into 4 types such as type 1 (WS1), type II (WS2), type III (WS3) and type IV (WS4). The most common type of WS is 1 and 2. The main genes involved in WS are PAX3, MITF, SOX10, EDNRB and EDN3.³

WS type I is related with sideways dislocation of the inner angles of the eyes (dystopia canthorum), type II does not show this feature. Type I and type II are caused by mutations of different genes. Type III, has facial, eye (ocular) and hearing (auditory) abnormalities associated with distinctive malformations of the upper limbs. Type 4 or Waardenburg-Hirschsprung disease, characterized by primary features of WS in association with Hirschsprung disease.⁴

Causes

Type 1 is due to mutation in the gene PAX3 resulting in the lack of development of some face cartilage and bones, also immature inner ear structures and a lack of melanocytes in the iris stroma.⁷

Type 2 is caused by a mutation in gene MITF, when it is type 2A. This MITF activates transcription of tyrosinase, the enzyme that performs the first step in the production of melanin.¹⁰

Type 2B is caused by mutation in an unknown gene on chromosome 1 in the locus range of 1p21-1p13.3 The gene is termed as WS2B.

Type 2C is caused by an autosomal dominant mutation in an unknown gene on chromosome 8 in the locus of 8p23. The gene is termed as WS2C.

Type 2D is caused by an autosomal recessive mutation in both copies of the gene SNAI2 leads to cause patches of hair depigmentation without any other symptoms.

Type 2E is caused by an autosomal dominant mutation in the gene SOX10.⁵

Type 3 is caused by a mutation in the gene PAX3. If both the parents having WS type 1 to have a child with type 3 WS a missense mutation has been documented to have this effect.

Type 4 has subtypes. Type 4A is caused by an autosomal dominant or autosomal recessive mutation in the gene EDNRB. Type 4B is caused by an autosomal dominant or autosomal recessive mutation in the gene EDN3. Type 4C is caused by an autosomal dominant or autosomal recessive mutation in the gene SOX10 (Table 1).

Diagnosis

WS can be diagnosed at the time of birth or at later age by physical and clinical evaluation. Waardenburg consortium develops major and minor criteria in 1992. WS need two major criteria or one major and two minor criteria for diagnosis. By the absence of dystopia canthorum type 2 can be easily distinguished from type 1. In type 3, the upper limb abnormalities and joint contractures are the additional features from type 1. Type 4 is similar to that of WS2 but the distinguishing characteristic feature is the presence of Hirschsprung disease (Table 2).^{6,9}

Treatment

Early diagnosis will play a major role in the treatment of WS as symptomatic management is only possible since there is no cure for WS. The symptomatic management can be done with the supervision of a team of medical professionals such as dermatologist, hearing specialist,

orthopedists, gastroenterologist, speech language pathologist and physical therapist.

Individuals with pigmentary abnormality is in risk of sunburn and skin cancer so they are advised to avoid direct sunlight and also use sunscreen with a high sun protection factor, hats and full sleeve dresses. White forelock can be managed by hair color and skin patches can be managed by getting inked. One of the most complicated symptoms is deafness which can be managed by appropriate supportive measures and cochlear implants, special instructions are also recommended for the communication such as sign language and lip reading.⁸

In individuals with upper limb abnormalities management can be done by physical therapy and surgical measures.¹¹ In case of WS4, Hirschsprung's disease removal of affected intestine and rejoining the healthy intestine is recommended or temporary colostomy (creation of an artificial outlet for colon) can be done for some extent. Genetic counselling will also be of beneficial for affected individuals and their families.¹²

Rare diseases are many in number but their treatments are less, as most of these rare diseases are genetical and there is no complete cure for a genetic disorder.¹³ WS is one among that type of rare genetic disorder thus the treatment is limited but the number of cases are increasing.¹⁴ In this case study, the newborn baby born with three major symptoms of WS such as white forelock, iris pigmentary abnormality (brilliant blue iris) and sensory neural hearing loss for the right ear and there is no dystopia canthorum (W index <1.95) by all these investigation WS type II is confirmed for this baby. Resolving the sign and symptoms in a genetic disorder is not possible but the only thing to do is to control. Here, the patient showed a positive sign that without any treatment the white colored hair got changed to grey color, thus there is a hope of getting the normal hair color to this patient after a certain period of life. Further studies are required to check how the colour of the hair is changing in WS patients and what is happening to the gene involved in the production of melanin. Also studies are required the find why WS typically affecting the major sensory organs such as eyes, ears, nose and skin.

Table 1: Types of WS with gene involved and major characteristic features.

Types of WS	Genes involved	Characteristic features
Type 1	PAX 3	Iris pigmentary abnormality; congenital sensorineural hearing loss; telecanthus; dystopia canthorum; poliosis; high nasal bridge; flat nose tip
Type 2	MITF and SNA12	Sensorineural hearing loss is most common; there is no dystopia canthorum; hole in the iris (coloboma); small eyes; albinism
Type 3	PAX 3	Upper limb abnormalities; joint contractures of the figure (camptodactyly); fused digits (syndactyly); developmental delay
Type 4	EDN3/EDNRB, SOX10	Hearing loss; pigmentation of skin eye and hair; Hirschsprung's disease

Table 2: Major and minor diagnostic criteria in WS.

Major criterias	Minor criterias
White forelock	Congenital leukoderma
Dystopia canthorum	Synophrys or medical eyebrow flare
Iris pigmentary abnormality	Broad nasal bridge
Congenital sensorineural hearing impairment	Hypoplasia of alae nasi
First degree relative with WS	Premature grey hair (<30 years of age)

Diagnostic test for detecting the presence of dystopia canthorum.

It is used to determine whether dystopia canthorum is present or not.

If W index >1.95 it indicates dystopia canthorum.

$$W = \frac{X+Y+a}{b}$$

Where, a=inner canthal distance, b=interpupillary distance, c=outer canthal distance, X=(2a-(0.2119c+3.909))/c, Y=(2a-(0.2479b+3.909))/b.

CONCLUSION

This report shows that further studies are required to check how the colour of the hair is changing in WS patients and what is happening to the gene involved in the production of melanin. Also studies are required the find why WS typically affecting the major sensory organs such as eyes, ears, nose and skin.

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