Case Report

Waardenburg Syndrome; A Case-report

Abstract

Waardenburg syndrome is an uncommon autosomal disorder, distinguished by hypopigmentation of either skin or hairs or both, segmental, partial or complete heterochromia iridis or isohypochromia, hypertrichosis of eyebrow, synophyrys, dystopia canthorum, broad and high nasal root and congenital deafness. The diagnostic criteria consisit of major and minor criteria, major includes congenital sensorineural hearing loss, pigmentary abnormality in iris, segmental, partial or complete heterochromia iridis, isohypochromia, fore hair's achromia, dystopia canthorum, affected first degree relative and minor criteria includes congenital leukoderma, synophyrys, broad and high nasal root, hypoplasia of nasal alae, premature graying of hair.

Herein we report a case of two days old baby boy having uncommon pigmentation of hair and iris beside dystopia canthorum. He was diagnosed as a case of WS1.

Keywords:

Waardenburg syndrome, Heterochromia iridis, Dystopia canthorum

Introduction:

Waardenburg syndrome is an uncommon autosomal either dominant or recessive genetic disorder. It is characterized by achromia (absence of normal pigmentation) of either skin or hair or both, segmental, partial or complete heterochromia iridis (difference in color of iris) or isohypochromia (pale blue eyes), hypertrichosis (excessive hair growth) of eyebrow, synophyrys (flare of medial side of eyebrow), dystopia canthorum (lateral displacement of inner canthi), broad and high nasal root and congenital deafness (1).

Four different types of Waardenburg syndrome are there on basis of clinical characteristics, including WS1, WS2, WS3 and WS4 (2-4). Waardenburg syndrome was 1st diagnosed by Waardenburg Consortium in 1951. He gave a diagnostic criteria including major and minor criteria, major includes congenital sensorineural hearing loss, pigmentary abnormality in iris, segmental, partial or complete heterochromia iridis, isohypochromia, fore hair's achromia, dystopia canthorum, affected first degree relative and minor includes congenital leukoderma, synophyrys, broad and high nasal root, hypoplasia of nasal alae, premature graying of hair (5). Diagnosis of WS1 need either two characteristics from major criteria or one major-characteristics with two minor characteristics. In WS2 dystopia canthorum is absent while WS3 is having the

same features as that of WS1 but only the difference is involvement of upper limb. WS4 is easy to diagnose as it is always linked with hisrschsprung disease (6, 7).

Herein we report a case of two days old baby boy having unusual pigmentation of hair and iris beside dystopia canthorum. He was diagnosed as a case of WS1.

Case Presentation:

A three-days-old baby girl presented to the emergency room with complain of reluctant to feed, high grade fever, respiratory difficulty and abdominal distension for 1 day. Her weight was 2kg with fronto-occipital circumference (FOC) of 30cm. She had a triangular patch of achromia of skin of frontal scalp and fore hairs since birth. On enquiring she was born pre-term with spontaneous normal vaginal delivery. Family history was non-significant but her parents were having first degree consanguineous marriage. On clinical examination, a triangular patch of achromia with irregular borders was on the forehead along with hypopigmented fore hairs.

Her vitals were respiratory rate 60 br/min, pulse rate 200 b/min while having temperature of 101°F. Her sub-vitals including anemia, jaundice, clubbing, cyanosis, edema and dehydration were negative. Her moro reflex was complete, while sucking and grasp reflex were fair enough. On CVS examination, S_1, S_2 were audible with no added sound. Her chest was clear while abdomen was distended. Ophthalmological examination showed partial heterochromia iridis, dystopia canthorum, synophyrys and broad nasal root while neurological examination was insignificant. To rule out sensorineural hearing loss, the Bera-test was done which was normal. The patient was identified as a victim of Waardenburg syndrome with early onset sepsis and low birth weight. On the basis of major and minor Waardenburg diagnostic criteria the patient was labelled as a case of WS1. For further clearing the differential diagnosis of WS1 fromWS2, the W-index was calculated and was 2.12mm.

O_2 inhalation was given on immediate basis. She was kept NPO (nothing per oral) and N/G (nasogastric) tube was passed. For the treatement of sepsis, Inj: Cefotaxime 100mg BD, Inj: Amikacin 15mg BD and Inj: Flagyl 3cc 8-hourly were given. Beside this she was given 100ml IV fluid, containing 0.18% D/S 76cc, KCl 2cc, Ca-gluconate 2cc and 20cc of 25% D/W. At the 5^{th} day of given treatment, she was discharged from the hospital as the fever was subsided and baby started to take breast milk.

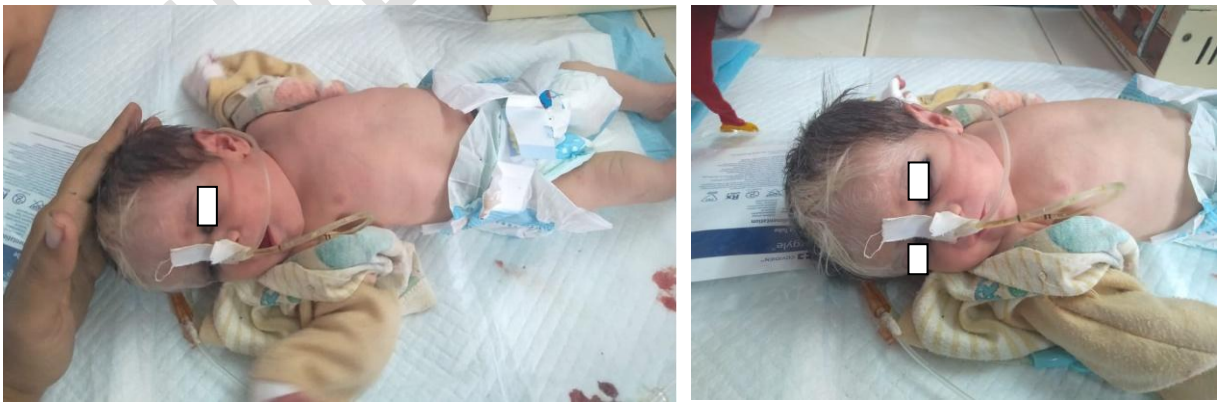

Fig 1 A triangular patch of achromia, partial heterochromia iridis, synophyrys, dystopia canthorum and broad nasal root

Discussion:

The variation in the clinical presentation of WS is because of expression of different genes, same in many other genetic syndromes. WS1 is identified if there is presence of either two major characteristic or one major with two minor characteristics of Waardenburg diagnostic criteria. Among all the features of WS, the dystopia canthorum is a differentiating point between WS1 and WS2 (8). Dystopia canthorum is an increase in intercanthal distance with broadness of nasal root. It is expressed in W-index, the formula for its calculation is given as:

$$W = X + Y + a/b$$

For calculating X:

$$X = (2a – (0.2119c + 3.909))/c$$

For calculating Y:

$$Y = (2a – (0.2479b + 3.909))/b$$

Where: a is inner canthal distance

b is interpupillary distance

c is outer canthal distance (9)

Previously for the diagnosis of WS1, the W-index must be greater than 2.07mm beside diagnostic criteria. But the molecular analysis of a diagnosed case of WS2 showed mutation in PAX3 gene so the diagnosis was changed as WS1 because of the gene expression (10). Therefore, the W-index diagnostic value is reduced from 2.07mm to 1.95mm (8).

Looking over the differential diagnosis of WS1 from WS2, the W-index must be greater than 1.95mm for WS1 while the most common differentiating clinical feature for WS1 are white forelock and leukoderma. On the other hand, sensorineural hearing loss and heterochromia iridis are the prominent characteristics of WS2 (11).

The current case was diagnosed as WS1 on the basis of three major criteria including partial heterochromia iridis, fore hair's achromia and dystopia canthorum with two minor criteria consisting of synophyrys and broad and high nasal root. W-index supported our diagnosis as its 2.12mm which was greater than 1.95mm. About 8.3-50% of the reported cases have cutaneous pigmentary defect (6, 9) but our patient had no such presentation. However, 21-28% of WS cases reported partial heterochromia iridis (6, 9) and the current case also favored this finding. Considering sensorineural hearing loss, about 67% of WS1 cases while 87% of WS2 cases had reported congenital deafness (6) but the current case was negative for this finding.

Multiple genes are involved in the WS like PAX3 gene (paired-box-gene-3) shows mutation in the patients of WS1 and WS3 while mutation of MITF (microphthalmia-associated-transcription factor) gene is involved in WS2. In WS4 cases, multiple gene mutations are involved including either EDN3 (endothelin-3) or EDNRB (endothelin-receptor type-B) or SOX10 (SRY-sex-determining region Y-box-10) gene (12). Looking specifically PAX3 gene in WS1, lie over the 2q35-chromosome, is involved in transcription during embryogenesis (13). WS1 is an autosomal dominant disorder which shows the presence of affected gene in parents but rarely in few of the cases there is *de novo* mutation as the parents are not affected (8). In the current case we couldn't

perform the PAX3 gene sequencing but it looks like *de novo* mutation as the parents were not affected and this highlight its rarity.

Conclusion:

Waardenburg syndrome is very rare in our population so it is important to report this case. Though the baby was normal but there is a need of parent's education regarding this genetic disorder.

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