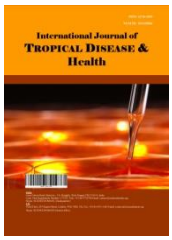

International Journal of TROPICAL DISEASE & Health

42(19): 1-5, 2021; Article no.IJTDH.76717
ISSN: 2278–1005, NLM ID: 101632866

Waardenburg Syndrome Type II, Associated with Atrial Septal Defect and Rocker Bottom Foot in a New Born – A Rare Case Presentation

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/ijtdh/2021/v42i1930537

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/76717

Case Study

Received 05 October 2021
Accepted 11 December 2021
Published 14 December 2021

ABSTRACT

Background: There are a number of syndromes with a combination of pigmentary abnormalities, hearing abnormalities and other defects. One among these pigmentary syndromes is waardenburg syndrome, which is further classified into four types. All these types show marked variability even within pedigrees.
Case-Report: We are reporting a case of Waardenburg syndrome type 2, with an unusual presentation of atrial septal defect and rocker bottom foot.
Conclusion: All clinicians on noticing, any child with white forelock of hair or heterochromia iris should get the child's hearing tested and further systemic evaluation, at the first instance, because an early intervention for hearing impairment and other defects can improve the outcome of child. Family counselling is at-most important for these children with syndromes.
We describe a unique case of Waardenburg syndrome type 2 with an unusual presentation of atrial septal defect and rocker bottom foot.

Keywords: Waardenburg syndrome; pigmentary abnormalities; hearing abnormalities; pigmentation; Alar Hypoplasia.

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1. INTRODUCTION

A large array of normal hair pigmentation exists, but when aasociated with specific findings needs further evaluation. Localised patches of hypo pigmentation are usually insignificant; however, a white forelock may indicate waardenburg syndrome, piebaldism, chediak higashi syndrome and may be sometimes associated with other systemic disorders [1]. A “white forelock” or “poliosis circumscripta”, a localized patch of white hair, can be seen on scalp, eyebrows, and eyelashes. The majority of individuals with Waardenburg syndrome type1 (WS1), have either a white forelock or early greying of the scalp hair before age 30 years [2]. Approximately 43% to 48% of individuals have the classic white forelock,the most common hair pigmentation anomaly seen in WS1 [3]. Hageman and Delleman reported that bilateral sensorineural hearing loss is seen in 25% cases of Waardenburg syndrome type 1 and in 50% cases of Waardenburg syndrome type 2. [4]Reported prevalence of WS is 1 in 42000.[5] WS1 and WS2 are equally common. The pathology of waardenburg syndrome is absence of melanocytes from the skin,hair,eyes or the stria vascularis of cochlea and also helps in diagnosis, as auditory-pigmentory syndrome.

2. CASE REPORT

A male baby born at 38 weeks of gestation to a 22 year old primigravida mother was admitted in NICU at Rajkiya Mahila Chikitsalaya, Ajmer Rajasthan with a presentation of white forelock of hair associated with atrial septal defect and left rocker bottom foot that were unusual presentation. The pregnancy was uncomplicated and mother had received appropriate prenatal care.Baby was born at our hospital at full term with meconium stained liquor and an emergency LSCS was done due to in-utero fetal distress. At birth, APGAR scores were 7 and 8 at 1 and 5 minutes respectively and baby weighed 2600g with a head circumference of 35cm and length 48cm. Later baby developed difficulty in breathing within first hour of life with SpO2 88% on room air and was admitted in NICU. Baby received assisted ventilation (bubble CPAP) and supportive therapy. On physical examination we noticed bilateral grey blue iris, white forelock of hair on forehead, left rocker bottom foot and on neurological examination an absent startle reflex and startle acoustic reflex. Oxygen saturation was equal in all four limbs. Baby’s general condition improved after 2 days and was weaned off oxygen therapy. Mother feed was started from day 3.All base line investigations were normal. On 2D Echography ostium secondum atrial septal defect of size 1.5 mm with left to right shunt was diagnosed. Baby was discharged on live day 7 with weight of 2500g.The complete eye examination was unremarkable. BERA showed right ear moderately to severe hearing loss and left ear severe to profound hearing loss, was advised to get a repeat test after 3months. Parents were advised to get an orthopaedic opinion on follow up.

Fig. 1. Both eyes with blue color iris

Fig. 2. White forelock on forehead

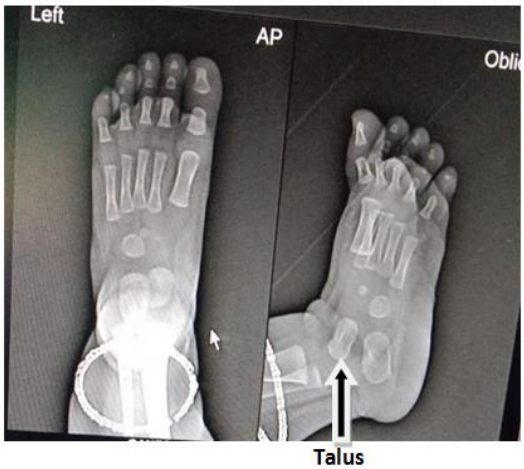

Fig 3. Xray anteroposterior and oblique views of left rocker bottom foot

Major criteria	Minor criteria
Congenital sensorineural hearing loss With loss of >25 db for at least 2 frequencies, between 250 and 4000 Hz.	Congenital Leucoderma with several hypopigmented areas of skin (penetrance 30–36%)
Pigmentary disturbances of iris, complete heterochromia iris or segmental heterochromia iris, Hypoplastic blue iris (pentetrance 15–31%)	Medial eyebrow flare (synophrys)
White forelock of hair (penetrance 43–48%)	Broad nasal route (Penetrance 52–100%)
Dystopia Canthorum (penetrance 98%) *W > 1.95 is abnormal*	Alar Hypoplasia
Affected first degree relative	Premature graying of hair (penetrance 23–38%)

3. DISCUSSION

Based on the presence of white forelock, bilateral sensorineural hearing loss, bilateral blue eyes, atrial septal defect, left rocker bottom foot and an absent startle reflex. Baby was evaluated for following differential diagnosis:

3.1 Waardenburg Syndrome

[4] Waardenburg syndrome was first described by Waardenburg in 1951, consisting of lateral displacement of the inner canthi of the eye and of the inferior lacrimal puncta (dystopia canthi medialis and punctorum lacrimalium lateroversa), high, broad nasal root, confluence of the eyebrows, with hypertrichosis of the medial parts (hyperplasia supercilii medialis and radicis nasi), partial or total heterochromia iridium, white forelock (albinismus circumscriptus pilorum) and unilateral or bilateral congenital deafness. Waardenburg syndrome type 1 is caused by loss of function mutations in the PAX3 gene. [6]In 1971 that Arias' drew attention to the existence of a separate division of the syndrome, which he named Waardenburg syndrome type II(WS2), which is about 15% of Waardenburg syndrome.WS2 is similar to WS1 but lacks dystopia canthorum. This group shows heterozygous mutations in MITF gene. [7] Klein described Waardenburg syndrome type 3(WS3) with usual features of WS1 and presence of hypoplasia of limb muscles; contractures of elbows, fingers.[8] Waardenburg syndrome type 4(WS4) is the association of Waardenburg syndrome with Hirschsprung disease and with mutations in gene for endothelin-3 or one of its receptors, EDNRB. [9] The Waardenburg Syndrome Consortium proposed diagnostic criteria for Waardenburg syndrome in 1992, with five major and five minor diagnostic criteria for Waardenburg syndrome. Two major or one major and two minor criteria are must to diagnose WS1.

Liu et al, [2] criteria for WS2 were suggested. Two major features should be present to make the diagnosis of WS2.The major features are as in the list above, except for the exclusion of dystopia canthorum and inclusion of premature greying

When family members were probed about any white forelock in family they recalled baby's father also had white forelock of hair persisting since childhood [10]. The W index of both baby and father were <1.95 which rules out dystopia canthorum. The following measurements are needed to calculate the W index (in mm): inner canthal distance (a), inter-pupillary distance (b), and outer canthal distance (c).

Calculate X = (2a – (0.2119c + 3.909))/c
Calculate Y = (2a – (0.2479b + 3.909))/b
Calculate W = X + Y + a/b

2. Deaf blind hypopigmentation syndrome, Yemenite type[11]
   An uncommon genetic disorder first described in 1990, in a brother and sister of Yemenite family , having cutaneous patchy hypo and hyperpigmentation on the trunk and extremities, gray hair, white brows and lashes. Also microcornea, coloboma, abnormalities of the anterior chamber of the eye, severe hearing loss and dental abnormalities with normal intelligence. The inheritance pattern appears to be autosomal recessive.
3. *Piebaldism*[12]is a rare autosomal dominant trait with congenital absence of melanocytes in affected areas of the skin and hair. A white forelock of hair, commonly triangular in shape, or both the hair and the underlying forehead may be involved. The eyebrows and eyelashes may be affected.Usually symmetrical distributed, irregularly shaped white patches may be observed on the face, trunk, and extremities. Classically Islands of hyperpigmentation are present within and at the border of depigmented areas .
4. Chédiak-Higashi syndrome (CHS) – It was first described by Beguzz (1943), Steinberk

(1948), Chédiak (1952) and Higashi (1954) [13] as childhood autosomal recessive immunodeficiency disorder. Since its first description, fewer than 500 cases published worldwide over the last 20 years [14]. Occulocutaneous albinism, photophobia, silver grey hypo pigmented hair and recurrent pyogenic infections particularly of skin, respiratory tract and gastrointestinal tract due to defective neutrophils are seen in patients. Characteristic giant cytoplasmic granules in all the granule-containing cells of the body, particularly in white blood cells (WBC) of the blood and the bone marrow confirms diagnosis of CHS[15].

5. *Griscelli syndrome* (GS)-is an infrequent autosomal recessive disorder with pigmentary dilution of the skin and the hair (silver hair), the presence of large clumps of pigment in hair shafts, and an accumulation of melanosomes in melanocytes. Three variants of Griscelli syndrome have been identified: Griscelli syndrome types 1-3. Most common type is Griscelli syndrome type 2 and has the most severe presentation. In 1978 [16]Griscelli and [17] Siccardi initially described Griscelli syndrome, or partial albinism with immunodeficiency.

Based on our baby's clincal features like white forelock, bilateral sensorineural hearing-loss and bilateral grey blue eyes without dystopia cantorum favours a diagnosis of waardenburg syndrome type 2. The unusual presentation is an ostium secundum atrial septal defect and left rocker bottom foot. [18]In 1986 A K Banarjee first described a case of waardenburg syndrome associated with secondum ostium atrial septal defect and described the association as defect in[19,20] differentiation of mesodermal derivatives at the end of sixth week of fetal life. However he did not mention about absence or presence of dystopia canthorum in his patient.We could not find any other case of waardenburg syndrome associated with atrial septal defect in literature. A rocker bottom feet is characterised by a prominent calcaneus and a convex round bottom to the foot.

CONCLUSION

All clinicians on noticing, any child with white forelock of hair or heterochromia iris should get the child's hearing tested and further systemic evaluation, at the first instance because an early intervention for hearing impairment and other defects can improve the outcome of child. Family counselling is at-most important for these families with children syndromes .It is extremely rarely reported a case of Waardenburg syndrome type 2 associated with atrial septal defect and rocker bottom foot.

CONSENT

The authors confirm that caregivers of their patients were fully informed and they agree to report his case.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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