**Waardenburg syndrome type II,associatedwith atrial septal defect and rocker bottom foot in a new born – a rare case presentation**


**Abstract**

***Background;*** There are a number of syndromes with a combination of pigmentary abnormalities,hearing abnormalities and other defects. One of the most common among these pigmentary syndromes is waardenburg syndrome, which is further classified into four types. All these forms show marked variability even within families with these syndromes.

***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 paediatricians coming across a child with white forelock of hair or heterochromia irisshould get the child's hearing tested and further systemic evaluation, at the first instance, because an early intervention for hearing impairment and otherdefects can improve the outcome of child.Family counselling is at-most important for these children with syndromes.

We report a uniquecase of Waardenburg syndrome type 2 with an unusual presentation ofatrial septal defect androcker bottom foot.


**INTRODUCTION**

Waardenburg syndrome is an auditory-pigmentory syndrome, caused by physical absence of melanocytes from the skin,hair,eyes or the stria vascularis of cochlea.

Although a wide variety of normal hair pigmentation exists,a number of specific findings may warrant further investigation.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", defined as a localized patch of white hair in a group of hair follicles, can involve any hairy area on the body including the 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]The classic white forelock observed in approximately 43% to 48% of individuals is 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.[9]WS1 and WS2 are equally common.

**CASE REPORT**

A male baby born at 38 weeks of gestation to a 22 year old primigravida motherwas admitted in NICU at Rajkiya Mahila Chikitsalaya, Ajmer Rajasthanwith a presentation of white forelock of hair associated with atrial septal defect and left rocker bottomfoot that were unusual presentation.The pregnancy was uncomplicated and mother received appropriate prenatal care.Baby was born at our hospital at full term with meconium stained liquor andan emergency LSCS was done due to inutero 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 airand 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, leftrocker 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 anorthopaedic opinion on follow up.

Fig. 1:- white forelock on forehead.

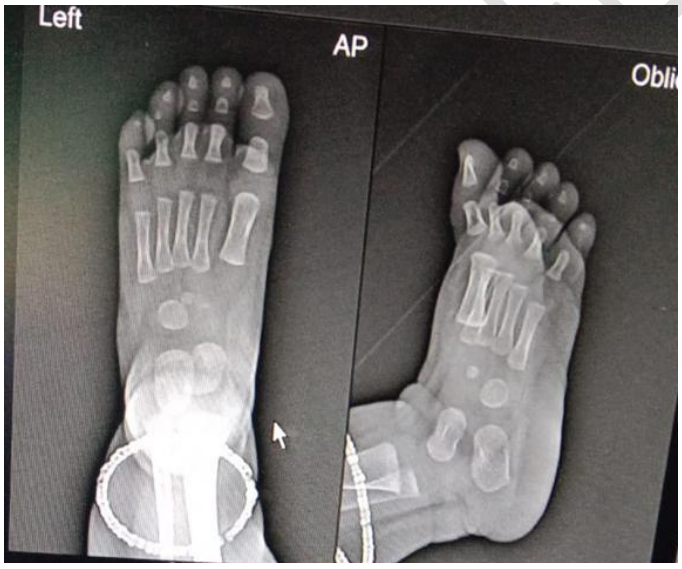


Fig 2:- Xray left rocker bottom foot.

**DISCUSSION**

Based onthe presence of white forelock,bilateral sensorineural hearing loss, bilateral gray blue eyes,atrial septal defect, leftrocker bottom foot andan absent startle reflex.Baby was evaluated for followingdifferential diagnosis:

1. *Waardenburg syndrome-*

[4]IN 1951 Waardenburg first described the syndrome 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.[5]In 1971 that Arias' drew attentiontotheexistenceofaseparatedivision of the syndrome, which he namedWaardenburg syndrome type II(WS2)is a heterogeneous group, about 15% of Waardenburg syndrome.WS2 has identicalauditoryandpigmentaryfeaturestoWS1 but lacks dystopia canthorum.These group shows heterozygous mutations in MITF gene.[6]Klein described Waardenburg syndrome type 3(WS3) with usual features of WS1 and included hypoplasiaoflimbmuscles;contracturesofelbows,fingers.[7] Waardenburg syndrome type 4(WS4) is the association of Waardenburg syndrome with Hirschsprung disease. This can be caused by mutations in gene for endothelin-3 or one of its receptors,EDNRB. [8]In 1992, the Waardenburg Syndrome Consortium proposed diagnostic criteria for Waardenburg syndrome, that included five major and five minor diagnostic criteria for Waardenburg syndrome (Farrer et al., 1992).For a diagnosis of WS1, must have two major or one major and two minor criteria.

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

[2] CriteriaforWS2weresuggestedbyLuietal.These authors recommendedthattwo majorfeaturesshouldbepresent to makethediagnosisofWS2.The majorfeaturesare as inthe listabove,except fortheexclusionofdystopiacanthorum andinclusionofpremature greying

When family members were probed about any white forelock in family they recalled baby's father also had idiosyncratic 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 measurements necessary to calculate the W index (in mm) are as follows: inner canthal distance (a), interpupillary 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 exceedinglyrare genetic disorder with characteristics of cutaneous pigmentation anomalies, ocular disorders and hearing loss. The syndrome was described in 1990 in two patients from the same Yemenite family. A brother and sister were described as having cutaneous patchy hypo and hyperpigmentation on the trunk and extremities, gray hair, white brows and lashes. Ocular manifestations were microcornea, coloboma and abnormalities of the anterior chamber of the eye. Both patients had severe hearing loss and dental abnormalities. Intelligence was reported to be normal. Their parents were unaffected and possibly consanguineous. The cause of this syndrome has not been determined. The inheritance pattern appears to be autosomal recessive
3. *Piebaldism*[12]is a rare autosomal dominant trait characterized by the congenital absence of melanocytes in affected areas of the skin and hair. A white forelock of hair, often triangular in shape, may be the only manifestation, or both the hair and the underlying forehead may be involved. The eyebrows and eyelashes may be affected. Irregularly shaped white patches may be observed on the face, trunk, and extremities, usually in a symmetrical distribution. Typically, islands of hyperpigmentation are present within and at the border of depigmented areas (summary by Thomas et al., 2004).
4. Chédiak-Higashi syndrome (CHS) - is a rare childhood autosomal recessive immunodeficiency disorder described by Beguzz (1943), Steinberk (1948), Chédiak (1952) and Higashi (1954)[13]. Since its first description, fewer than 500 cases published worldwide over the last 20 years [14]. Clinically it is characterized by occulocutaneous albinism, photophobia, silver grey hypo pigmented hair and recurrent pyogenic infections particularly of skin, respiratory tract and gastrointestinal tract due to functional abnormality of neutrophils. Diagnosis of CHS can be done by finding 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 [15].
5. *Griscelli syndrome* (GS)-is a rare autosomal recessive disorder that results in 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. Griscelli syndrome type 2 is the most common type and has the most severe presentation, if left untreated.[15]Griscelli and [17] Siccardi initially described Griscelli syndrome, or partial albinism with immunodeficiency, in 1978.

Basedon our baby's clincal features like white forelock,bilateral sensorineuralhearing-loss and bilateral grey blue eyes without dystopia cantorum favours a diagnosis of waardenburg syndrome type 2. The unusal presentation is an ostium secundum atrial septal defect and left rocker bottom foot. [17]In 1986 A K Banarjee first described a case of waardenburg syndromeassociated with secondum ostium atrial septaldefect and described the association as defect in[19,20] differentiation ofmesodermal 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 paediatricians coming across a 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 withatrial septal defect and rockerbottom foot.

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

**Disclosure Statement** – The authors have no conflicts of interest to disclose.

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