Case Reports

Waardenburg's Syndrome (Type 1) in A Newborn of Consanguineous Parents: A Case Report

SHARIFUN NAHER[1], ANIMESH CHANDRA DAS[2]

Introduction:

Waardenburg syndrome (WS) is a rare genetically heterogeneous inherited disorder characterized by sensorineural hearing loss, pigmentary disturbances of the skin, hair and iris and dystopia canthorum (lateral displacement of both medial canthai and lacrimal puncta)[1].

The syndrome is caused by the physical absence of melanocytes from the skin, hair, eyes or stria vascularis of the cochlea. Based on the presence of variable clinical characteristics and additional signs, Waardenburg syndrome is classified into four clinical types as WS 1, WS 2, WS 3 and WS 4[2-4]. WS 1 is associated with dystopia canthorum; WS 2 lacks dystopia canthorum; WS3 is quite similar to WS1 with additional Hirschsprung disease [5,6]. We report here a case of WS1 from Bangladesh for its rarity and relative paucity of reports in the pediatric literature.

Case report:

A 2 hour old female baby hailing from Ekuria, Dhaka was admitted to neonatal care unit of Mitford Hospital on 9th June, 2012 with the complaints of delayed cry after birth and repeated convulsion. Mother, 22 years of age had irregular antenatal check up. She was immunized with 2 doses of Tetanus toxoid. Her pregnancy was uneventful up to 37 weeks of pregnancy then she developed labour pain and delivered at a CNG auto-rickshaw on the way to hospital. Baby cried 30 minutes after birth. On the place of delivery baby was managed with tactile stimulation but umbilical cord was cut in the hospital after her arrival. Baby developed convulsion 3 times which was generalized tonic clonic in nature. On query, there was leaking membrane for 3 days and this was the 2nd issue of consanguineous parents. There was no history of maternal hypertension, fever or any other complication during the pregnancy. On examination, her birth weight was 2.6 kg. Occipitofrontal circumference (OFC) was 34.5 cm and length was 49.5 cm. Anterior fontanel was normal. Pallor and jaundice, cyanosis was absent. Temperature was 98.4 degree F. There was hypopigmented area over the forehead and in the middle portion of the head (White forelock). (Fig I)

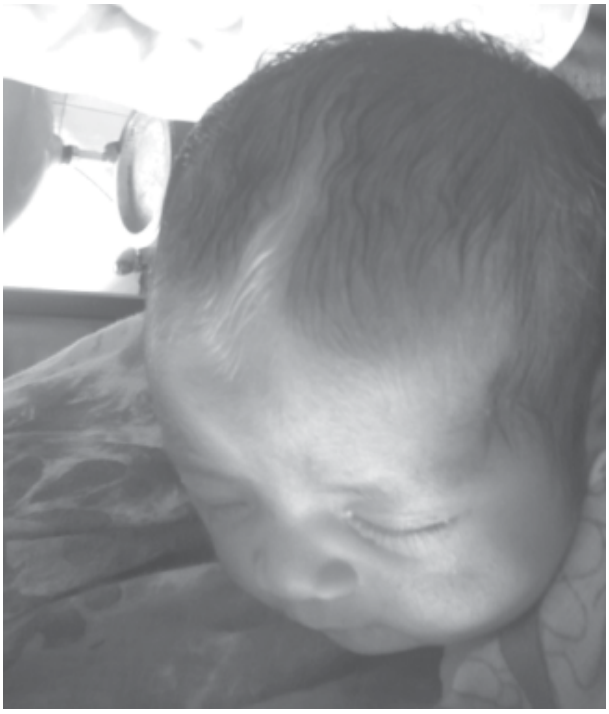

Fig. 1: *Photograph shows white forelock.*

Skin colour was pink but hypopigmented area was found over the front of the abdomen (Fig.2) and on the posterior aspect of both forearm below the elbow joints. (Fig.3).

1. Associate Professor, Neonatology, SSMC Mitford, Dhaka
2. HMO, Department of Paediatrics, SSMC Mitford, Dhaka
Correspondence to: Dr. Begum Sharifun Naher, Associate Professor, Neonatology, SSMC Mitford, Dhaka, Cell: 01819-263555, E-mail: dr.sharifun_nahar@yahoo.com

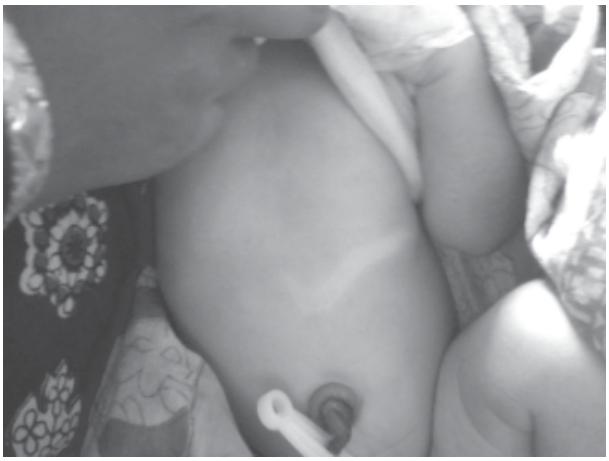

Fig.-2: *Photograph shows hypopigmented area over the abdomen*

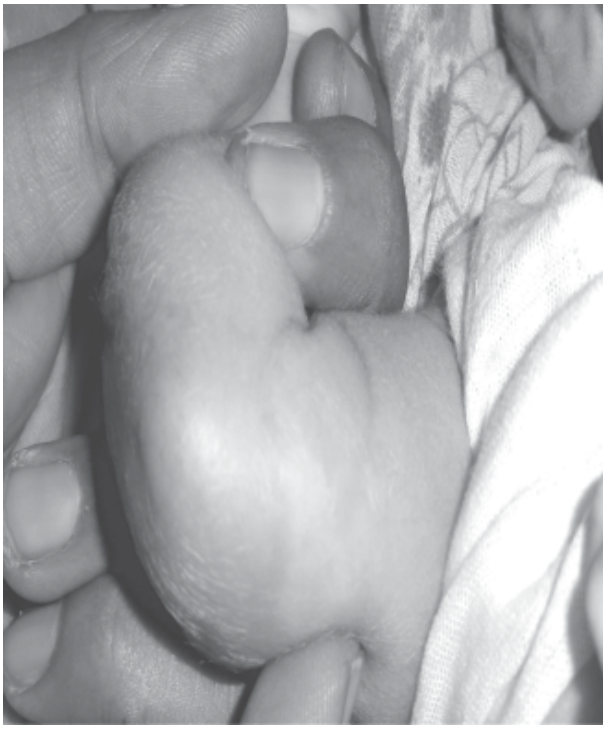

Fig.-3: *Hypopigmentation in forearm*

In addition, lateral displacement of medial canthus, broad nasal bridge and hypochromia of iris was also there. His vital signs were normal. All primitive reflexes were poor. So she was diagnosed as a case of severe perinatal asphyxia with Hypoxic ischaemic encephalopathy (HIE) stage 2 with early onset neonatal sepsis with Waardenburg syndrome on the basis of clinical criteria as the diagnosis of WS is essentially clinical. On investigation TC of WBC was 15000/cmm, Hb – 17.6 gm/dl, DC of WBC was neutrophil- 70%, Lymphocyte was 25%, Monocyte-3% and Eosinophil was 2%. Platelet count was 160,000/cmm. Serum Calcium- 8.2mg/dl, Serum electrolytes was normal.C reactive protein (CRP) was positive. She was diagnosed as a case of Waardenburg syndrome with HIE stage 2 and early onset neonatal sepsis. She was managed with O_2 supplementation, IV fluid, antibiotics, Injection Phenobarbitone and Inj Konakion.

Discussion:

Waardenburg syndrome(WS) was named after the Dutch ophthalmologist Petrus Johannes Waardenburg who first described this syndrome in 1951.Since then four subtypes (WS1-WS4) based on variable clinical presentations have been described[1]. The clinical variability of WS is attributed to the different penetrance and expression of the responsible genes. WS1 and WS2 are autosomal dominant in inheritance in most cases. WS3 may be sporadic or autosomal dominant and WS4 is autosomal recessive in inheritance.[7] WS 1 is associated with dystopia canthorum;Waardenburg syndrome type 2 (WS2) was defined by Arias in 1971[8]. Patients with WS2 have all the features of type 1 except dystopia canthorum. Waardenburg syndrome type 3 (WS3) also known as Klein- Waardenburg syndrome has a similar phenotype to WS1 but with additional musculoskeletal characteristics, including Sprengel shoulder, limb muscle hypoplasia, contractures, aplasia of the ribs and bilateral cutaneous syndactyly.[9] Waardenburg syndrome type 4 (WS4) has features of type 2 combined with Hirschprung disease.

Diagnosis of WS is essentially clinical. Unfortunately not every case expresses all clinical manifestations of complete WS and the incomplete form is commonly described. The Waardenburg consortium proposed the diagnostic criteria of WS1 in 1992[10]. Two major or one major plus two minor criteria are necessary for diagnosis of WS1.

Diagnostic criteria for WS proposed by the Waardenburg consortium.

Major criteria

- Congenital sensorineural hearing loss
- Pigmentary disturbances of Iris: Complete heterochromia iridium, partial or segmental heterochromia, hypoplastic blue eyes
- Hair hypo- pigmentation: White forelock
- Dystopia canthorum
- Affected first degree relative

Minor criteria

- Congenital leukoderma: Several areas of hypo-pigmented skin
- Medical eyebrow flare (synophrys)
- Broad and high nasal root
- Hypoplasia of alae nasi
- Premature graying of hair.

Dystopia canthorum is the most penetrating feature of WS and is found in 41-99% of the reported cases[5]. Dystopia canthorum is defined as a prominent broad nasal root with increased inter-canthal distance. It is not present in WS2. Arias and Mota[11] developed a Waardenburg index (WI) as a reliable measure of dystopia canthorum. Earlier WI>2.07 was considered dystrophic but now WI >1.95 is considered more practical[6]. Hearing loss is the most serious feature in WS. It is congenital, sensorineural and usually nonprogressive. It may be unilateral or bilateral. Penetrance of sensineurineural hearing loss has been observed to be 69% in WS1 and 87% in WS2[12] .

Cutaneous pigmentary defects include achromic spots and hyperpigmented macules and are observed in 8.3-50% of patients[13]. Pigmentary disturbances of hair may be in the form of white forelock or premature graying of scalp hair, eye brows, cilia as body hair. White forelock is observed in 17-58% of cases.

Ocular colour abnormalities of WS include three types of disturbances. Iris heterochromia, bilateral iris iso-hypochromia and fundus pigmentary alterations. Iris heterochromia was found in 21-28% of patients with WS. Table I shows distinguishing feature in different types of WS [14].

Table I

Distinguishing features in different types of Waardenburg syndrome (WS).

	WS1	WS2	WS3	WS4
Sensory neural hearing loss.	+/-	+/-	+/-	+/-
Dystopia canthorum	+	-	+	-
Hirschprung disease	-	-	-	+
Musculoskeletal abnormalities.	-	-	+	-

Three major like White forelock, hair hypopigmentation, pigmentation abnormality of the iris, dystopia canthorum index >1.95 and two minor like Skin hypopigmentation or congenital leukoderma and broad nasal root criteria were found in our case. According to these criteria the newborn was diagnosed as WS (Type 1). There was family history of such types of illness and history of consanguineous parents were found. So this syndrome may be the result of a new mutation with the gene as autosomal recessive in inheritance.

We tried for Evoked Otoacoustic emission (EOAE) test for detecting deafness but because of unavailability of this test in our institute we failed to do this but during discharge we advised them to do it from other institute as early as possible.

Conclusion:

Waardenburg syndrome can be diagnosed easily at birth because of prominent phenotypic features. Earlier diagnosis means a more successful rehabilitation of hearing though in our set up we could not arrange EOAE for detecting deafness which is the most serious feature of Waardenburg syndrome.

References:

1. Waardenburg PJ. A new syndrome combining developmental anomalies of the eyelids, eyebrows and nose root with pigmentary defects of the iris and head hair and with congenital deafness. Am J Hum Genet 1951; 3: 195-201.
2. Soni CR, Kumar G. Child neurology : A patient with dissimilar eye color and deafness. Neurology 2010; 74: 25-26.
3. Qin W, Shu A, Qian X, Gao J, Xing Q, Zhang J et al. A novel mutation of PAX 3 in a Chinese family with Waardenburg syndrome. Mol Vis 2006; 12: 1001-08.
4. Tomita Y, Suzuki T. Genetics of pigmentary disorders. Am J Med Genet C Semin Med Genet 2004; 15:75-81.
5. Dourmishev AL, Dourmishev LA, Schwartz RA, Janniger CK. Waardenburg syndrome. Int J Dermatol 1999; 38: 656-63.
6. Read AP, Newton VE. Waardenburg syndrome. J Med Genet 1997; 34: 656-65.
7. Tagra S, Talwar AK, Walia RL, Sidhu p. Waardenburg syndrome. Indian J Dermatol Venereol Leprol 2006; 72: 326.
8. Arias S. Genetic heterogeneity in the Waardenburg syndrome. Birth defects Original Article Series. 1971; 7: 87-101.
9. Klein D. Historical background and evidence for dominant inheritance of the Klein- Waardenburg

syndrome (type 111).American Journal of Medical Genetics 1983; 14: 231-39.

10. Farrer LA, Grundfast KM, Amos J, Arnos KS, Asher JH Jr, Beighton P et al. Waardenburg syndrome WS type 1 is caused by defects at multiple loci, one of which is near ALPP on chromosome 2: First report of the WS consortium. Am J Hum Genet 1992; 50: 902-13.
11. Arias S, Mota M. Apparent non-penetrance for dystopia in Waardenburg syndrome type 1, with some hints on the diagnosis of dystopia canthorum. J Genet Hum 1978;26:103-31.
12. Newton V. Hearing loss and Waardenburg syndrome; Implications for genetic counseling. J Laryngol Otol 1990; 104: 97-103.
13. Reed WB, Stone VM, Boder E, Ziprkowski L. Pigmentary disorders in association with congenital deafness. Arch Dermatol 1967; 95: 176-86.
14. Kiani R, Gangadharan SK, Miller H. Association of Waardenburg syndrome with intellectual disability, autistic spectrum disorder and unprovoked aggressive outbursts: A new behavioral phenotype? The British Journal of Disabilities. 2007; 104: 53-62.