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Case Note

Waardenburg syndrome Type II

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Abstract
Two rare cases of Waardenburg type II are reported. First case had three main features of WS-profound SN hearing loss, hetrochromia iris and white forelock of hair. Second case had moderate SNHL and depigmentation of hair.

Key words: Hetrochromia iris, white forelock hair

In 1951 PJ Waardenburg, a Dutch ophthalmologist described a autosomal dominant syndrome that has almost complete penetrance and variable expressivity [1]. The various clinical features of Waardenburg syndrome (WS) are dystopia canthorum, flat nasal root, confluent eyebrows , heterochromic irides or unusually brilliant blue irises, white forelock, pigmentary abnormalities, diminished vestibular function, cleft lip and palate and sensorineural hearing loss[2]. Minor diagnostic criteria include medial flaring of the eyebrows with synophrys, a broad high nasal root, hypoplasia of the nasal alae and areas of depigmented skin[3]. Due to presence of white forelock of hair; it has been named as white forelock syndrome as well. The commonest and most important feature is sensory neural hearing loss, with eye lid deformity and hetrochromia or deep blue eyes[4]. We are reporting two interesting cases of WS type II seen by us with review of literature.

Case I
A six year old female child was presented to ENT OPD for decreased hearing and unable to speak since birth. General physical examination was normal except a white forelock of hair at forehead since birth. Both the eyes showed hetrochromia of iris. There was no other depigmentation patch seen any where on the body. The medial canthi were slightly laterally displaced. Clinical examination of ear nose & throat was normal. Pure tone audiometry revealed a bilateral severe to profound hearing loss, more so in higher frequency. There was no history of consanguinity and no other member of the family had similar findings (Fig 1). A diagnosis of WS type II was made.

Case II
A 38 year old female presented to ENT services for unable to hearing properly and unable to speak clearly since childhood. Clinical examination showed a white forelock of hair on forehead since birth. The colour of iris was black, without widening of the medial canthi. No other depigmentation patch was seen. ENT examination was with in normal limits. Audiometry test showed a moderate hearing loss on both sides. Other members of the family were healthy. A diagnosis of WS type II was made (Fig 2).

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Fig 1: six year old female child showing white forelock of hairs and hetrochromia iris

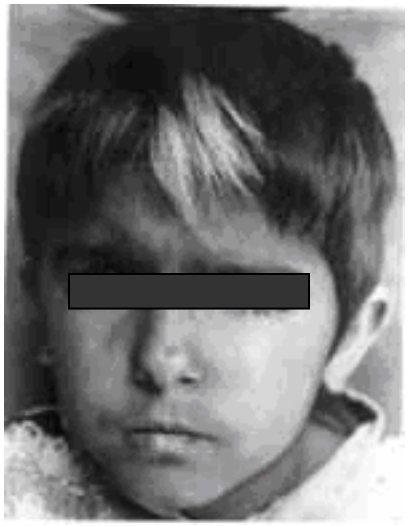
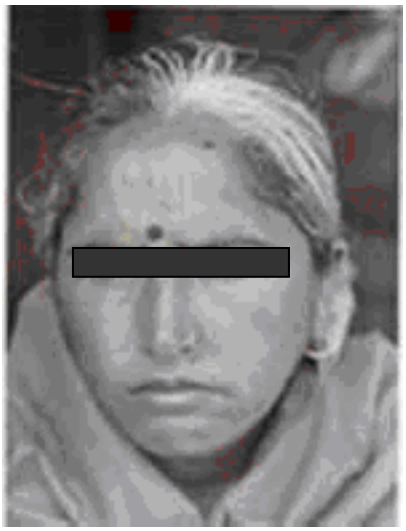


Fig 2: 38 year old female showing forelock of white hairs.



Discussion

WS is also known as auditory- pigmentary syndrome. Incidence of WS is 1 in 4000 live birth[5]. Estimates of prevalence suggest that WS may affect 2% to 5% of all infants with congenital deafness [6, 7]. WS has been divided in two types, on the basis of presence of dystopia canthorum (lateral displacement of the medial canthi) as type I or absence of dystopia canthorum as in type II[8]. Later on two types of WS have been added[9].

WS type III, is also known as Klein–Waardenburg syndrome. It is similar to WS type I but associated with musculoskeletal abnormalities of the upper limbs, microcephaly and mental retardation. WS type IV (Shah – Waardenburg syndrome) is the association of WS type I with congenital aganglionic megacolon (Hirschsprung disease)[10].

Genetic mutations

WS is the most common form of inherited congenital deafness and is autosomal dominant fashion. It has been demonstrated that mutation in the PAX 3 gene on chromosome 2 q 35 are associated with WS I and WS 3[11]. These mutations result in a change in the amino –acid sequence of the protein encoded by the PAX3 gene. This protein is normally a DNA binding protein that belongs to a family of proteins which regulate transcription of DNA during embryogenesis. It leads to a defect in neural crest cell migration development. Type II WS is a heterozygous group, about 15% of whom are heterozygous for mutations in microphthalmia associated transcription factor gene 3p 14.1- p12. WS type IV can be caused by mutation in the genes for endothelin – 3. WS has been linked with 2 other genes, EDN3 on 20 q 13.2 – 13.3 chromosome EDNRB, 13 q 22 chromosome SoX10 on 22 q 13 chromosome[12].

This rare audiotory – pigmentory syndrome is caused by a defect in neural crest cell migration and melanin synthesis. The physical absence of melanocytes from skin, hair, eyes or the stria- vascularis of cochlea is responsible for the typical clinical picture of the syndrome[13]. Histopathology of temporal bone in WS shows total absence of the organ of corti, atrophy of the stria vascularis and absence of the neuron of the spiral ganglion[13]. WS is the most common form of inherited congenital deafness[12]. Congenital deafness in both ears may occur in about 25% of the patients with WS type I and in about 50% with WS type II[14]. Patients with many WS component may have even normal hearing. However, only 17% of the patients with WS are deaf[12].

WS type II cases are more frequently seen as compared to type I and bilateral symmetrical sensorineural hearing loss is common type of hearing loss.

Four types of hearing loss in WS patients have been described[15].

Type I: Subtotal deafness on both sides
Type II: Serious lack of hearing on both sides
Type III: Subtotal deafness one side
Type IV: Moderate hearing deficiency on one side specially frequencies are affected. Our first case had profound hearing loss while second case had moderate hearing loss.

Vestibular examination of the patient showed that vestibular pathology does not occur more frequently in patients with deafness as a part of two WS than in patient with other from of congenital deafness[16].

In WS pigmentary disturbances of the hair are of two types

a. White forelock involving the forehead or posteriorly the vertex or other part of the scalp.
b. Premature graying of the scalp hair & eyebrows, cilia or body hair.[17] Both of our cases had white forelock involving the foreheads.

Ocular manifestation

Liv et al observed that there was no significant difference in the frequency of pigmentation disorders between type I and type II but hetrochromia irides was more common in type II than type I and other pigmentation abnormalities were more frequent in type I[14].

Ocular colour abnormalities in cases of WS are three types

1. Heterochromia iridis in 21-28% cases
2. Bilateral isohypochromia iridis(pale blue eyes)
3. Fundus pigmentary alteration[18].

Goldenburg reported 14 cases of WS in different races. He noted that the hypochromia iridium (light blue) is characteristically associated with hypochronic or albinoid funds. He also noted other congenital abnormalities like hare lip, cleft palate and high arched palate in cases of WS. In some cases one eye may be brown and other blue.[18] In our cases no such associated features were seen.

Criteria for diagnosis

Liv et al[14] also laid down the diagnostic criteria for WS type II and further stated that for a isolated case to be labelled as type II should have at least two of these criteria. For a family, at least one member should have two major criteria besides a family history. Other members of the family can be classified as affected if they show one criteria in addition to a family history. The criteria are: (1) congenital sensorineural hearing loss (2) pigmentary disturbances of iris (3) pigmentary disturbances of the hair and (4) a first or second degree relative with two or more of the above mentioned criteria (1-3). If Pendred's or WS are suspected, a temporal bone CT scan can help to visualize cochlear abnormalities such as Mondini deformarties[12]. Even the absence of semicircular canals on tomography are reported[19].

Though WS is a rare entity but patients may not have symptoms in few cases except depigmentation such individuals who manifest variations from normal anatomy but who are not seeking medical or surgical treatment or correction of the abnormalities do not like to be referred as patients . It is better to refer to them as an individual or family member rather than as patients[12].

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