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Case Series

Waardenburg syndrome: case series

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ABSTRACT

Waardenburg syndrome is a rare genetic disorder of neural crest cell development with incidence of 1:42000 to 1:50,000. The syndrome is not completely expressed and hence adds to its hetergenecity with symptoms varying from one type of syndrome to another and from one patient to another. Unilateral heterochromia that manifests in some people is associated with Waardenburg syndrome and Parry-Romberg syndrome. This is a case series of four cases with features of Waardenburg syndrome with variable presentations and familial inheritance.

Keywords: Autosomal dominant deafness, Heterochromia, Pigmentation anomalies, Waardenburg syndrome

INTRODUCTION

Waardenburg syndrome (WS) is a rare genetic disorder of neural crest development characterized by varying degrees of deafness and pigmentation anomalies. Dutch Ophthalmologist, D. J. Waardenburg, described the syndrome in 1951.[1] WS has the following features. Symptoms may vary from one type of syndrome to another and from one patient to another- heterochromia, eyes with iris having two different colours, poliosis, displacement of medial canthi combined with dystopia of lacrimal puncta and prominent broad nasal root. Moderate to profound hearing impairment.

CASE SERIES

Case 1

A 2-year-old girl brought by her mother to the ENT outpatient department (OPD) with the complaint of decreased hearing in both ears since childhood. She had a distinct white forelock of hair in the midline along with striking unilateral blue iris. Also, a white depigmented patch was present on the forehead and nasal bridge (Figure 1). Other Developmental milestones were however normal. Her mother also had similar hypertelorism with normal hearing (Figure 2). Also there is history suggestive of premature graying of hair in her grandmother since the age of 15 years. But none of their parent had a decreased hearing.

On investigating the girl, BERA was done which was: absent waveforms from both sides (profound sensorineural hearing loss) and pure tone audiometry of her mother showed right – moderate conductive hearing loss with left-hearing sensitivity within normal limits (Figure 3). Impedance of the patient showed bilateral A type graph. Examination of the eyes showed unilateral blue iris. Visual acuity was 6/6 in both eyes. On fundus examination, a bright red fundal reflex was seen in both eyes. Macula and optic disc was bilaterally normal. The girl was diagnosed as type II WS and her mother with type I WS and the girl was referred for cochlear implantation, under follow-up.

Case 2

A 5-year-old girl brought by her father to the ENT OPD with the complaint of pain in the nose since 5 days and was diagnosed with nasal vestibulitis. She had increased intercanthal distance with no neurological defect or any

skin abnormality. and when incidentally examined her father he had heterochromia iridis, hypertelorism with normal hearing. (Figure 4, 5). Other Developmental milestones were however normal.

Figure 1: Type II WS- heterochromia iridis, white forelock, leucoderma with hypertelorism with deaf mute (BERA showed absent waveforms from both sides).

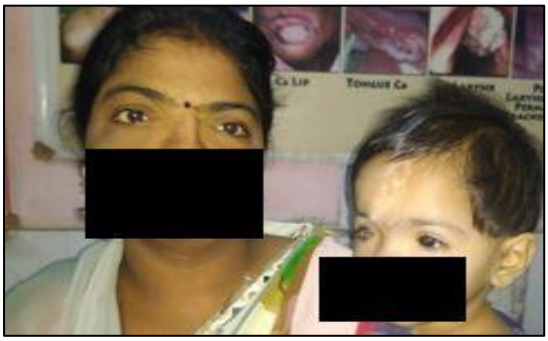

Figure 2: Patient with her mother.

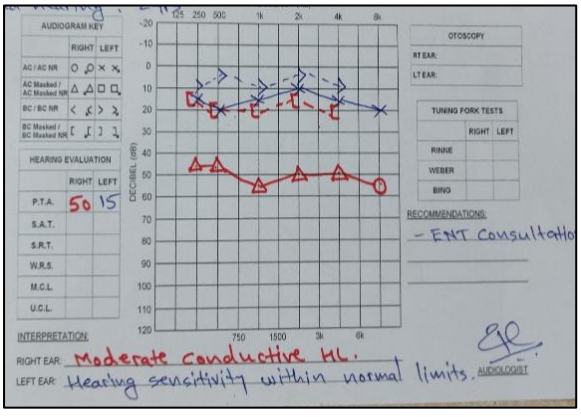

Figure 3: Pure tone audiometry of the patient's mother (type I WS), right- moderate conductive hearing loss and left: hearing within normal limits.

On investigating the girl and her father with pure tone audiometry showed hearing sensitivity within normal limits. Visual acuity was 6/6 in both eyes. On fundus examination, a bright red fundal reflex was seen in both eyes (Figure 6). On indirect ophthalmoscopy, there was bilateral choroidal depigmentation perhaps due to visibility of larger choroidal vessels especially near the equator. Macula and optic disc was bilaterally normal. The girl and her father was diagnosed incidentally as type I WS, are under follow-up.

Case 3

A 1.5-year-old boy brought by his parent with history of decreased hearing bilaterally as his parent complaining about him not turning when called and not speaking. On examination patient had bilateral blue sapphire iris (Figure 7) and was sent for Audiological examination as no other deformities were seen. BERA was suggestive of absent wave forms from both sides and hence HRCT Bilateral temporal bone was done which was normal. Patient was diagnosed with Type II WS and was counselled about the disease and referred for cochlear implantation, under follow-up.

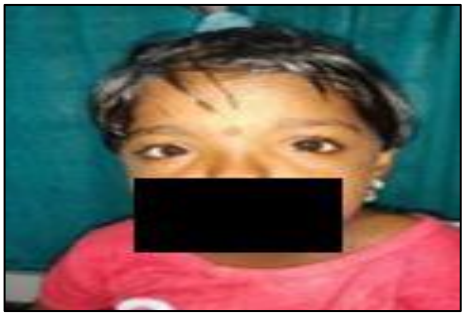

Figure 4: Type I WS- hypertelorism with Normal hearing.

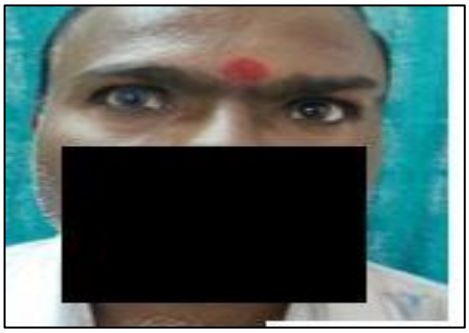

Figure 5: Patient's father type I WS with heterochromia iridis.

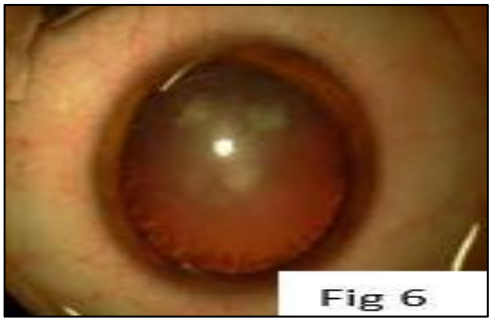

Figure 6: Girl had bright red reflex on fundoscopy.

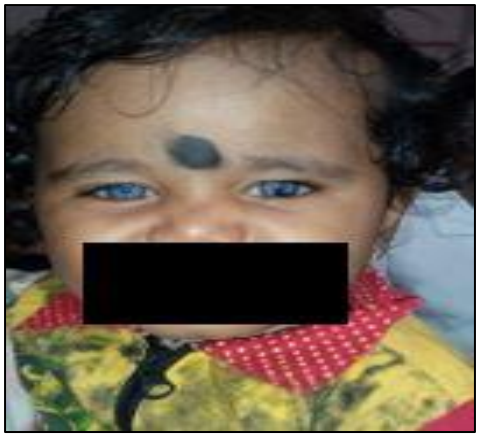

Figure 7: Type II WS- isochromic sapphire blue eyes with bilateral profound hearing loss

Figure 8: BERA of the patient- absent waveforms from both sides.

Case 4

A 5-year-old boy brought by his father with history of decreased hearing bilaterally. The patient was a deaf-mute child and none of their family members had similar history but there was history of consanguineous marriage of his parent. Examination of the eyes showed right blue iris. (Figure 8) Hearing assessment with BERA was done which showed Absent Wave Forms from both sides (Figure 9), With HRCT bilateral temporal bone showing absent ossicles on right side. Visual acuity was 6/6 in both eyes. This patient was diagnosed as Type II WS and referred for cochlear implantation.

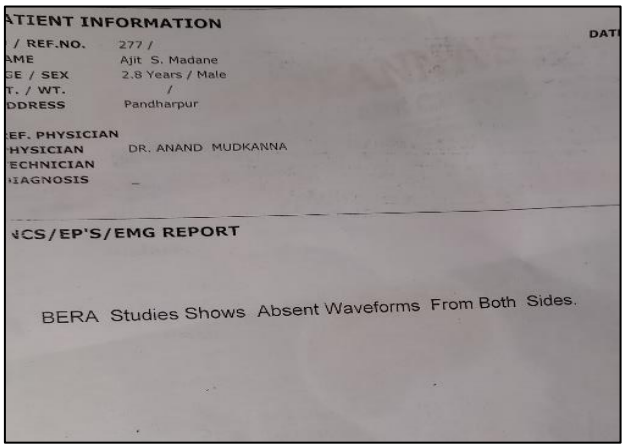

Figure 9: BERA (Brainstem evoked response audiometry) report of the patient- absent wave forms depicting profound hearing loss.

DISCUSSION

Scientists have identified four different genes for WS PAX3, MITF, EDNRB and EDN3.[2]

The PAX3 gene is located on chromosome 2 and controls some aspects of development of face and inner ear. The MITF gene is located on chromosome 2. It also controls development of ear and hearing.[1,5] Overall, the syndrome affects 1 in 42,000 people. The highly variable presentation of the syndrome makes it difficult to arrive at a precise figure of prevalence.

Table 1: Types of Waardenburg syndrome.

Type	Clinical features	Gene mutated (chromosome)
I (WSI)	Dystopia canthorum, broad nasal root (hearing impariement-20%)	PAX3(2q35)
II (WS2)	No dystopia canthorum (hearing impariement -50%)[3]	MITF (3p14.2-p14.1). SNAI2 (SLUG)(8q11)
III(WS3) (Klein-Waardenburg)	Hypoplasia of limb muscles,contractures of elbows, fingers (hearing impariement -50%)	PAX3(2q35)
IV (WS4) (Shah-Waardenburg)	Hirschsprung disease [4] (There is currently no cure for the syndrome).	EDN3(20q13.2-q13-3) EDNRB (13q22), SOX10(22q13.1)

This syndrome is autosomal dominant for most persons with type I, II, and III. WS type IV is autosomal recessive with variable penetrance. A small percentage of cases result from new mutations in gene; these occur in people with no history of disorder in their family. Early diagnosis and improvement of hearing defects are most important for psychological development of children with this disease. Genetic counseling is a good idea for patient with this syndrome.

Waardenburg syndrome: A case series Saqib et al showed None of the patients had musculoskeletal abnormalities, gastrointestinal manifestations or mental deficiency or

retardation as comparable with our study.[6] As per study of Sharma et al of a case study of two cases of Waardenburg syndrome showed Type III and Type IV are rare compared to Type I and Type II which had two cases of Type II Waardenburg syndrome which corelates with our study of four cases showing two of each Type I and II cases.[7]

Table 2: Diagnostic Criteria of Waardenburg syndrome Type I and II.

Major criteria	Minor criteria
Congenital sensorineural hearing loss	Skin pigmentation
Pigmentary disturbances of iris	Medial eyebrow flare (synophrys)
Hair pigmentation (white forelock)	Broad and high nasal root
Dystopia canthorum	Hypoplasia of nasi alae

As per the case report of Pattebahadur et al of a rare case in an Indian child of Type IV Waardenburg syndrome depicting that type IV is rare and correlating our study with only type I and II.[8,9]

CONCLUSION

All the primary care physicians coming across a child with blue eyes and white forelock of hair should get the child's hearing tested at the first instance, if not already done. An early diagnosis and improvement of hearing impairment with timely intervention are the most important for psychological and intellectual development of children with Waardenburg syndrome. Genetic and familial counselling is also a good tool for these syndromed patients. Our case report showed cases with Type I and II WS, and their parent were given counselling about the genetic inheritance and also about hearing aids\cochlear implantation and kept under follow-up.

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Ethical approval: Not required

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