ORIGINAL RESEARCH PAPER

ENT

KEY WORDS: Waardenburg, Syndrome, Rare

WAARDENBURG SYNDROME: A RARE GENETIC DISORDER

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ABSTRACT

Waardenburg syndrome is a rare genetic disorder with either autosomal recessive or autosomal dominant inheritance. It is believed to account for 2-5%of patients with congenital hearing loss, has an estimated prevalence of 1 in 42000persons (or 0.24 per 10000persons).It is a disorder of neural crest cell development with distinct cutaneous manifestations. It is a group of genetic conditions that can cause hearing loss and changes in pigmentation of the hair, skin and eyes (heterochromia).The hearing loss is present from birth (congenital).

Here we present 2 case reports who presented to our outpatient department with the hearing loss since birth. Audiological evaluation revealed bilateral severe –profound sensorineural hearing loss. Both case reports have positive family histories of congenital deafness.

In these clinical scenarios an early diagnosis and timely intervention has an important role in psychological and intellectual development of affected patients.

INTRODUCTION

WaardenburgSyndrome(WS)isararegeneticdisorder (1in42000) mostoftencharacteriz edbyvarying degreesofd eafness,minordefectsinstructuresarisingfromneuralcrestand pigmentationanomalies.Thesyndromegotitsnamefromada Dutc hophthalmologist,D.J.Waardenburg,whodescribedthesyndr omeindetailin1951.[1]

Symptomsmayvaryfromonetypeofsyndrometoanotherandfro monepatient toanother, buttheyinclude:

1. Very pale or brilliantly blue eyes, eyes of two different colors (heterochromia).
2. Aforelockofwhitehair (poliosis)orprematureg rayingo fhairs.
3. Lateraldisplacemento fmedialc anthic ombin edwithdystopiaoflacrimalpunctaand blephar ophimosis. Prominentb roadnasalroot.
4. Moderateto profoundhearingimpairment (Higherfreq uencyassociatedwithtypeII).

TherearefourtypesofWS.MostcommonaretypeIandII.

TypeI:Personsusuallyhavewidespacebetweeninnercanthus. Hearingimpairmentoccursin 20%ofcases.

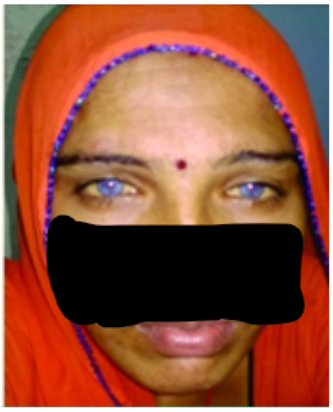
TypeII:Personswhodonothaveawidespacebetweeninnercathu softheireyebuthavemanyothercharacteristicsofWSdescribedi ntypeII.However,50%haveahearingimpairmentoraredeaf.[2]

TypeIIIandIVarelesscommon.WStypeIIIisalsokno wnasKlein-WS(Patientshavelimbabnormality).WStypeIVisknownasSha h-WS(thesepatientshaveHirshsprungdisease).[3]

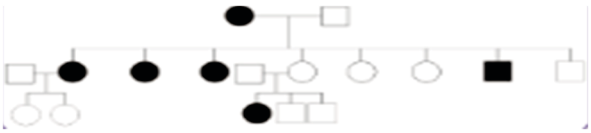
Overall,thesyndromeaffects1in42,000people.Thehighlyvari ablepresentationofthesyndromemakesitdifficulttoarriveata precisefigureofprevalence.

Case 1

A 24 yr old female presented with the complaint of decreased hearing bilaterally. Audiometry showed bilateral severe to profound sensorineural hearing loss. She also had bluish discolouration of iris with increased medial canthus distance. Detailed family history revealed that many of the family memvers had heterochromiairidis, white forelock of hairs and sensorineural deafness in various combinations (Figure 1 and 2). Her counselling was done.



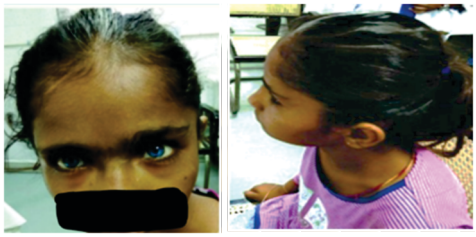
(Figure 1- Bluish discolouration of iris with broad nasal root and increased intercanthal distance)



(Figure 2: Pedigree chart showing familial inheritance of the disease)

Case 2

A 5 yr old female child presented in our outpatient department. The patient was deaf and mute. She was having characteristic brilliant blue iris with medial eyebrow flare with increased medial canthus distance. She was having premature graying of hairs (Figure 3). All these features go in favor of type 1 WS. Her father also had similar complaints. Counselling was done.



(Figure 3 : Bluish discolouration of iris with premature graying of hairs, increased intercanthal distance and medial eyebrow flaying)

DISCUSSION

Scientists have identified four different genes for WS: PAX 3, MITF, EDNRB and EDN3.[4] WS I and III – PAX 3, WS type II- MITF, WS type IV- EDNRB, EDN3.

The PAX 3 gene is located on chromosome 2 and controls some aspects of development of face and inner ear. The MTF gene is located on chromosome 2. It also controls the development of ear and hearing.[1,5]

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.

The presence of different manifestations of WS in different combinations in the other family members of the first patient represented the well-known variable expressivity of the disease.

Both cases fulfilled the diagnostic criteria of WS type I.

The diagnosis of WS is essentially clinical. Not every case expresses all clinical manifestations of the complete WS, and formfruste conditions are also relatively common.

At present there is currently no definitive treatment for WS. Severe sensorineural deafness, bony abnormalities and hirschsprung disease associated with WS are some of the potentially serious conditions and significantly deteriorates the quality of life.

Genetic counselling is a good idea for treatment of these patients.

CONCLUSION

Waardenburg syndrome is a rare genetic disorder with variable expressivity. Early diagnosis and improvement of hearing defects are most important for psychological development of children duffering from this disorder.

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