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SCHIZOPHRENIA WITH WAARDENBURG SYNDROME – A CASE REPORT FROM A TERTIARY CARE HOSPITAL IN PUDUCHERRY

Psychiatry

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ABSTRACT

Waardenburg syndrome is a rare autosomal dominant disorder, with an incidence of 1 in 42,000, manifests with sensorineural deafness, pigmentation defect of skin, hair, iris and various defects of neural crest-derived tissues. There are few mutations in EDN-3, EDNRB, MIT-F,PAX-3,SNAI-2 and SOX-10 genes were identified. Here we report a case of a 32-year-old unmarried male with treatment-resistant schizophrenia with white forelock hair in the midline with a hypopigmented patch in left infra-axillary region and dystopia canthorum. On investigation, he had bilateral sensory neural hearing loss. All primary care physicians who come across a person with a white forelock, hypopigmented patch, dystopia Canthorum and premature graying of hair are advised to get them tested for hearing loss and genetic testing .SOX 10 gene mutation is also found to be a gene defect in schizopheria,so patient are at higher risk of developing psychiatric illness.

KEYWORDS

Schizophrenia, Waardenburg syndrome, autosomal dominant, white forelock.

INTRODUCTION:

Waardenburg syndrome (WS) is a rare genetic condition characterized by at least some degree of congenital hearing loss and pigmentation deficiencies which can include white forelock, premature graying of hair, lateral displacement of medial canthus, prominent broad nasal root, moderate to profound hearing impairment very pale or brilliantly blue eye, eyes of two different colors (heterochromia). It is an autosomal dominant disorder caused by a mutation in several genes affecting the division and migration of neural crest cells including melanocytes, various bones, cartilages of the face, inner ear, and peripheral nerves of the intestine.[1]

Waardenburg syndrome is associated with sox -10 mutation which is also found to be affected in early-onset schizophrenia frequencies were found to be associated with earlier age of onset in male schizophrenia. sox -10 is related to developing schizophrenia in a gene-specific manner.

Table 1. Different characteristics and types of WS [2]

Type	Characteristics
Type 1 (more common)	Persons usually have wide space between inner canthus. Hearing impairment occurs in 20% of cases.
Type 2 (More common)	Persons who do not have a wide space between the inner canthus of their eye but have many other characteristics of WS are described in type II. However, 50% have a hearing impairment or are deaf
Type 3 (Less common)	WS type III is also known as Klein–WS (Patients have limb abnormality).
Type 4 (Less common)	WS type IV is known as Shah–WS (these patients have (Hirschsprung disease).

Table 2. Diagnostic criteria [3]

Major criteria:	Minor criteria:
1. Sensorineural hearing loss	1. Skin hypopigmentation
2. Iris pigmentation	2. Medial eye brow flare
3. Hair hypopigmentation	3. Broad nasal alae
4. Dystopia canthorum	4. Premature graying of hair
5.1st degree relative affected	

Case Presentation

A 32-year-old male with schizophrenia on treatment for 10 years came with hearing of voices from sun (auditory hallucination), delusion of control, thought withdrawal, thought echo. Patient is on antipsychotics combination of olanzapine and haloperidol for past 5 years. He has white forelock of hair in the midline. Patient's academic performance was normal. He studied up to ITI, normal IQ, normal developmental milestone.

Figure1. Patient with White Forelock and dystopia canthorun present

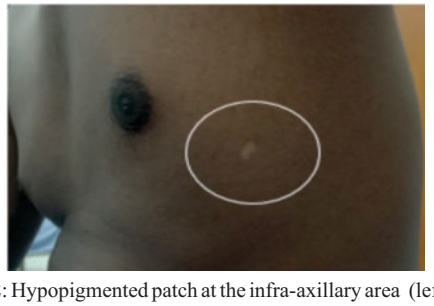

Figure 2: Hypopigmented patch at the infra-axillary area (left side)

Figure 3: Patients father with White Forelock

On Investigation pure tone audiometry (PTA) was found to have bilateral sensorineural hearing loss (right and left). On ophthalmic examination dystophia canthorun present, with no heterochromia iridum or brilliant blue iris. Family history reveals his father has white forelock, but his father has no hearing loss. With the presentation and investigation available reveals the presence of 3 major criteria. He is diagnosed to have Waardenburg syndrome.

DISCUSSION:

Waardenburg syndrome (WS) is autosomal dominant and inherited in most of the cases, WS-4 also presents as an autosomal recessive disorder. WS is usually diagnosed by clinical findings that include sensorineural hearing loss, pigmentary change in hair and eye and dystopia Canthorum, prominent broad nasal root with increased intercanthal distance. Our case was diagnosed as WS with 3 major and 2 minor criteria, with presence of white forelock, dystopia Canthorum and hearing loss. sensorineural hearing loss in bilateral ears, hypopigmented patch present at the infra-axillary area in left side.

Heterochromia iridis is one of the major criteria of WS consortium was not present in our patient. Heterochromia iridis the clinical finding is not a universal feature of WS, but penetrance of 21-28% present. Hearing loss is the major criterion of WS present in patient. WS has penetrance of 69%-87% sensorineural hearing loss.

Multiple genes have been implicated in WS syndrome. Abnormalities paired box gene 3 (pax3) accounts for most WS-1 and WS-3. Micropthalmia-associated transcription factor (MITF) gene abnormality is responsible for WS-2. Whereas WS-4 is heterogenous with reported mutation endothelin 3 (EDN3) in receptor endothelin receptor type B (EDNRB) or Sry -sex determining region Y box (SOX 10). **[4]**

SOX 10 mutation is also found to be affected in early-onset schizophrenia. Frequencies were found to be associated with earlier age of onset in male schizophrenia. SOX 10 related to the development of schizophrenia in a gender-specific manner. The majority of the proband have affected parents. We could not perform gene sequence and deletion and duplication analysis in our patient, but it seems to be a de novo mutation because the patient has healthy family members.

CONCLUSION:

This case is a rare presentation of Waardenburg syndrome with schizophrenia. To our knowledge, this is the first case report with this combination. With the presentation of early-onset Schizophrenia in a male patient with a white forelock and bilateral sensorineural hearing loss probably, the gene mutation would be SOX-10. On the basis of clinical criteria, the case is diagnosed to be WS Syndrome with Schizophrenia. It would be a genetic inherited Schizophrenia requiring a long duration of treatment and it may also be treatment-resistant. Genetic and familial counseling is a good tool for these syndromed patients.

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