Case Report

Type III Waardenberg Syndrome : a case report

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Abstract:

Waardenberg syndrome is an autosomal dominant genetic disease which frequently manifests as sensorineural hearing loss, heterochromic iris, premature greying of hair. This is a case report of rare Type III waardenberg syndrome of a patient who presented to plastic surgery department of Rajindra Hospital, Patiala

Key Words:

Genetic Disease, Autosomal Dominant, Sensorineural Hearing Loss, Hypoplastic Blue Eyes, Mental Disabilities.

Introduction

Waardenburg syndrome (WS) was first described by P.J.Waardenburg, ophthalmologist and Dutch geneticist in 1951. It is a genetic disease with autosomal dominant heritage pattern, with incomplete penetrance and variable phenotypes. The same author estimates the incidence of this syndrome to be approximately 1.43% of patients with congenital deafness and 1: 42,000 in the general population[1]. It accounts for 2 to 5 percent of all cases of congenital hearing loss. Types I and II are the most common forms of Waardenburg syndrome, while types III and IV are rare[2].

Its most frequent clinical signs are sensorineural hearing loss, affecting about 60% of the patients; heterochromia of the iris; hypoplastic blue eyes; white streak; premature gray hair; leucoderma; high nasal root and hyperplasia of the medial portion of the eyebrows (synophrys)[3]. WS has four clinical presentations. Type I patients have skin fold extending from the base of the nose to the end of medial eyebrow region (epicanthus), increasing the distance of the internal medial corners of the eyes (canthorum dystopia), iris isochromia with bright blue color or heterochromia of iris, white hair streak (poliosis) that can appear at any age, confluent eyebrows (synophrys) and changes in skin pigmentation. Type II differs from type I by not showing canthorum dystopia. Type III, also known as Klein Waardenburg Syndrome, has in addition to type I characteristics, microcephaly, malformation of the upper limbs and mental disabilities. Type IV, also known as Waardenburg-Shah Syndrome presents Hirschsprung's disease in addition to Type II manifestations, characterized by the absence of ganglion cells of Auerbach plexus and Meissner plexus[4]

Diagnostic criteria for WS were established by Farrer et al. in 1992. Major criteria are: congenital sensorineural hearing loss, hair hypopigmentation, abnormal pigmentation of the iris (complete or partial heterochromia), telecanthus, first-degree relatives affected. Minor criteria are: gray hair before the of age 30, synophrys, skin hypopigmentation, high nasal root or large, hypoplastic nose wing. The diagnosis is given by the presence of two major criteria or one major and two minor.

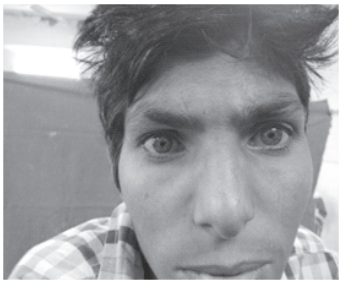
In current medical literature six genes are associated with WS: PAX3 (encoding the paired box 3 transcription factor), MITF (microphthalmia-associated transcription factor), EDN3 (endothelin 3), EDNRB (endothelin receptor type B), SOX10 (encoding the Sry bOX10 transcription factor) and SNAI2 (snail homolog 2). PAX3 alterations can be found in malignant tumors (such as melanomas and neuroblastomas) and in WS. It is involved in the development of the central nervous system, skeletal muscle, cardiac tissue, melanocytes and enteric ganglia. Around 70 different mutation points have been identified with very few recurrences reported. The MITF gene is known as the key to melanocyte development. Mutations in this gene occur in about 15% of WS Type II patients. The endothelins, represented by EDN3 and EDNRB, have an important role in the development of neural crest cells. Over fifteen endothelin mutations have been described in WS patients. SOX10 is involved in the early development of the neural crest; it expresses proteins linked to cell fate determination and cell linage. It also has shown the capacity to regulate PAX3 and MITF genes. These functions are crucial for cell differentiation in glial cells and oligodendrocytes. It is the main gene involved in type IV WS. SNAI2 has an essential role in germinative cells, melanocytic and hematopoietic stem cells. This gene has minor involvement in type II WS[5].

Case Presentation

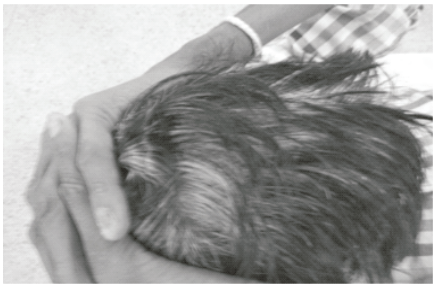
A young male patient reported to plastic surgery out-patient department after road side accident associated skin loss and split thickness skin grafting was done. He was unable to communicate verbally and

complaints were documented from his relatives. They gave history of patient being deaf and dumb since birth except for making some irrelevant noises. There is no family history of hearing loss or affected individual.

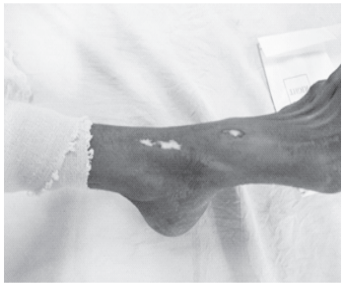
On examination, the patient is moderately built. Dermatological examination revealed grey hairs, and patchy depigmentation over right leg. Ophthalmological examination showed heterochromic iris (grey), dystopia canthorum. The patient had sensorineural hearing loss established by tuning fork tests, tympanic membrane being intact. On an attempt to assess the intelligence quotient (IQ), The patient was able to understand sign language and follows commands, could ask for his needs, good in calculation and money handling, which puts him under the category of mild mental retardation. His left lower limb revealed deformed arch of foot.



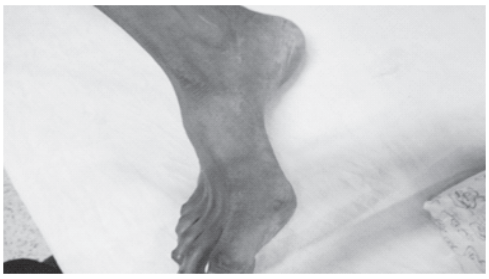
Heterochromic iris



Premature grey hairs



Depigmented skin lesions



Deformed foot arch

25 year old patient

Discussion

Type III Waardenberg syndrome, otherwise called Klein-Waardenberg syndrome is generally inherited in autosomal dominant pattern and has mental changes and deformities in the upper limb.

The patient in our case would have probably manifested the syndrome by new genetic mutations as there is no relevant family history. He has the following signs and symptoms of Waardenberg syndrome : white forelock of hair, heterochromia iridis, dystopia canthorum, sensorineural deafness, mental abnormalities, skin pigmentation and deformed lower limb. He fits into three of the major criteria for diagnosis.

The treatment involves multidisciplinary approach such as mental and auditory rehabilitation and genetic counseling. Early diagnosis of the syndrome helps in providing a better quality of life for patients.

Conflict of Interest: None

References

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