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# A case of waardenburg syndrome type 2 in an Indian individual presenting with an unusual pattern of fundus pigmentation and its correlation with choroidal thickness

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**Abstract**
**Background:** Waardenburg syndrome is a rare genetic disorder due to abnormalities of neural crest derivatives.
**The Case:** We describe a male patient showing constellation of hearing loss, hypoplastic blue iridis, dystopia can thorum and broad nasal root and ocular fundus pigmentary disturbances associated with changes in choroidal thickness. Patient has also has a positive family history.
**Conclusion:** It's important to be aware of genetic inheritance and phenotype variants of Waardenburg syndrome.

**Keywords:** waardenburg syndrome; swept source OCT; Fundus pigmentation; Neural crest derivatives

## Introduction

Waardenburg syndrome (WS) is an auditory pigmentary syndrome presenting with sensorineural hearing loss, segmental abnormal pigmentation of the eyes, hair and skin, and various defects of neural crest derivatives [1, 2].

The syndrome is classified into four clinical types based on genetic typing [3]. WS 1, 2&3 are autosomal dominant inherited, WS 3 may be sporadic and WS4 is inherited as autosomal recessive trait.

Waardenburg syndrome type 1&3 are associated with mutations in PAX3 gene on chromosome 2q37 and type 4 associated with endothelial-3 gene [3, 4].

And MITF mapped on 3p12-p 14.1 are mutated in type 2 WS [5].

The diagnostic criteria for WS type 2 proposed by Liu *et al.* [1] include, congenital sensorineural hearing loss and pigmentary disturbances of the hair, pigmentary disturbances of the iris but not of the fundus.

In the present report the patient from Indian descent the pattern of fundus pigmentation was one of the most striking clinical features, with dense hyper pigmented areas next to hypo pigmented areas. Here we want to implicate the importance of pattern of fundus pigmentation as a unique clinical phenotype and the usage of swept source OCT to relate the choroidal thickness in areas with pigmentary changes in the fundus

## Case Report

A 16year old male with clinical features of Waardenburg syndrome. The child was born to a second degree consanguineous marriage visited ophthalmology department for a routine check-up.

The best corrected visual acuity was 20/20 in both the eyes. Gross examination revealed telecanthus, flare of the medial eyebrows, and hypoplastic nasal alae (Figure 1).

**Fig 1:** showing hypoplastic ala nasi, eye lid notching, dystopia canthorum and heterochromia

He also had right sided microtia and had a profound and decreased hearing. The hearing loss was documented at the age of 3 and has not changed over the past years (Figure 2).

**Fig 2:** showing right sided microtia

Ocular examination revealed bilateral upper lid notching representing incomplete coloboma of the lids. He had brilliant blue iris in the right eye (Figure 3) with relatively poor pupillary dilatation and dark brown iris in the left. There was a congenital nevus at 3'0clock position in the right eye. IOP was noted to be normal and the gonioscopy in the right eye showed grade II closure and vessels seen at the angles.

**Fig 3:** showing right eye brilliant blue iris

On fundus examination right eye disc appeared pale, severe fundus pigmentary disturbances were found in the right eye, with extensive albinoid areas nasally and on the posterior pole, whereas the temporal region showed a homogeneous area of dense hyperpigmentation (Figure 4). Left disc and macula were normal with no choroidal hypopigmentation.

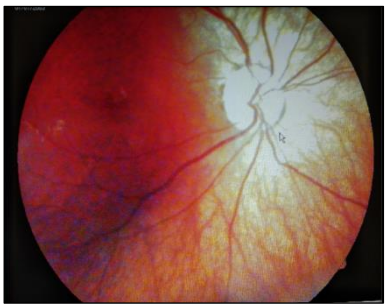

**Fig 4:** showing fundus image of right eye showing pigmentary disturbances in the fundus

Conventional audiological examination showed bilateral sensorineural hearing loss.

However no pigmentary changes in hair/skin were noted.

There was no evidence of vitiligo, scleral pigmentation, or any sign of chronic uveitis in both eyes. Based on the clinical findings, she was diagnosed of Waardenburg syndrome.

The choroidal thickness was measured using swept-source optical coherence tomography and compared between the two eyes and between the pigmented and the vitiliginous areas in the right eye. The subfoveal choroidal thickness was 458 µ and 572 µ in the right and left eye, respective.In the right eye, a comparison of two equidistant points from the foveola along a radial scan passing through the superotemporal vitiliginous area revealed a thinner choroid (452 µ) compared to the corresponding point in the pigmented inferonasal quadrant (581 µ).

## Discussion

Waardenburg syndrome presents with variable expression. Fundus pigmentary abnormalities seen in isolation could confound an ophthalmologist. Various disorders can present with disturbances in choroidal pigmentation. Conditions presenting with choroidal hypopigmentation such as ocular albinism, choroidal vitiligo, Vogt-Koyanagi-Harada syndrome, high myopia, and Waardenburg syndrome. Disorders with increased choroidal pigmentation are isolated ocular melanocytosis, oculo (dermal) melanocytosis, giant choroidal nevus, diffuse choroidal melanoma, and bilateral diffuse uveal melanocytic proliferation (BDUMP). The ocular melanocytosis simulates the Waardenburg syndrome the most. It is critical to distinguish between these two distinct clinical entities as oculo (dermal) melanocytosis, even if sectoral, is associated with the risk of development of choroidal melanoma in the area of increased choroidal pigmentation and necessitates life-long follow-up [6]. Although waardenburg syndrome is not associated with risk of malignancy.

Goldberg in the year 1966 described iris and fundus pigment abnormalities tend to parallel each other and are an integral part of this syndrome [7]. In our patient, the striking facial features, iris heterochromia, 'brilliant blue' iris, and choroidal hypopigmentation were suggestive of Waardenburg syndrome.

The choroidal thickness was less in the hypopigmentated area of the right fundus compared to the pigmented area. Subfoveal choroidal thickness was greater than that reported in the general population, again probably because of pigmentation [8]. The normal subfoveal choroidal thickness in Indian eyes on SS-OCT has been reported to be 307±79 µm [9]. Shields *et al*. have reported a slightly lesser choroidal thickness (mean 197 µ) on OCT imaging of the hypopigmented area compared to normal choroid in the fellow eye (mean 243 µ), but the choroidal thickness within the same eye at different areas were not compared [10]. Unlike the observations in our case where the subfoveal choroidal thickness was much higher than normal values, choroidal thickness in their series was much closer to the normative data. Choudhry *et al*. have reported a thicker hypopigmented foveal choroid (430 µ and 435 µ) in their case report [11]. Histological examination of the hypopigmented iris has shown a significant decrease in melanosome size. Defects in melanosome migration and melanin synthesis have been implicated [12]. Dense hyperpigmentation next to a hypopigmented area may be attributed to defective migration of melanocytes leading to their increased concentration in localized area of the choroid and their relative absence in other areas leading to hypopigmentation. This is in contrast to a more uniform pigmentation of the choroid if the melanosomes were to have migrated normally and distributed evenly [8].

Thus the knowledge of Waardenburg is vital among clinicians to aid diagnosis of simukating conditions.

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