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BRIEF LETTERS

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Iris coloboma: A Rare Case Of Waardenburg Syndromes?

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ABSTRACT

Waardenburg syndromes (WS) are characterized by deafness, in addition to pigmentation anomalies. WS can be distinguished by clinical findings such as dystopia canthorum within the phenotypic series. WS type 2 (WS2) is characterized by congenital deafness and pigmentation anomalies but is different from WS1 due to absence of dystopia canthorum. In this paper, we present a rare case of WS2 case featuring bilateral iris coloboma.

Keywords: *Waardenburg Syndrome, WS2, Iris heterochromia, Iris coloboma*

INTRODUCTION

Waardenburg Syndromes (WS) are auditory-pigmentary disorders consisting of four types (WS1-4) and eight subtypes (Table 1). WS1 is the most common type [1] and is well defined with its clinical and molecular findings. WS1 is characterized by congenital sensorineural hearing loss and pigmentary disturbances of the iris, hair, and skin, with lateral displacement of the inner canthi (dystopia canthorum). *PAX3* mutations are suggested to be responsible for WS1 [2]. WS1 can be diagnosed according to diagnostic criteria [3], however other types and subtypes are poorly characterized clinically, till this date. WS2 is distinguished from WS1 with an absence of dystopia canthorum. Deafness is a common and the most frequent feature of WS2 and seems to be more severe than WS1 [3].

Ocular pigmentation anomalies were defined in WS. Pigmentation anomaly of the iris including complete, partial/segmental heterochromia of iris, hypoplastic blue irides, or brilliant blue irides is a common feature of WS2, seen in approximately 47% of the cases [4]. Other pigmentation anomalies defined in WS2 cases are white forelock, hair hypopigmentation, premature graying of the hair (before 30 years) and leukoderma (irregular skin depigmentation), among others [3]. We would like to discuss another ocular finding in the present case, coloboma, whether it is a common association or an unnoticed finding of WS.

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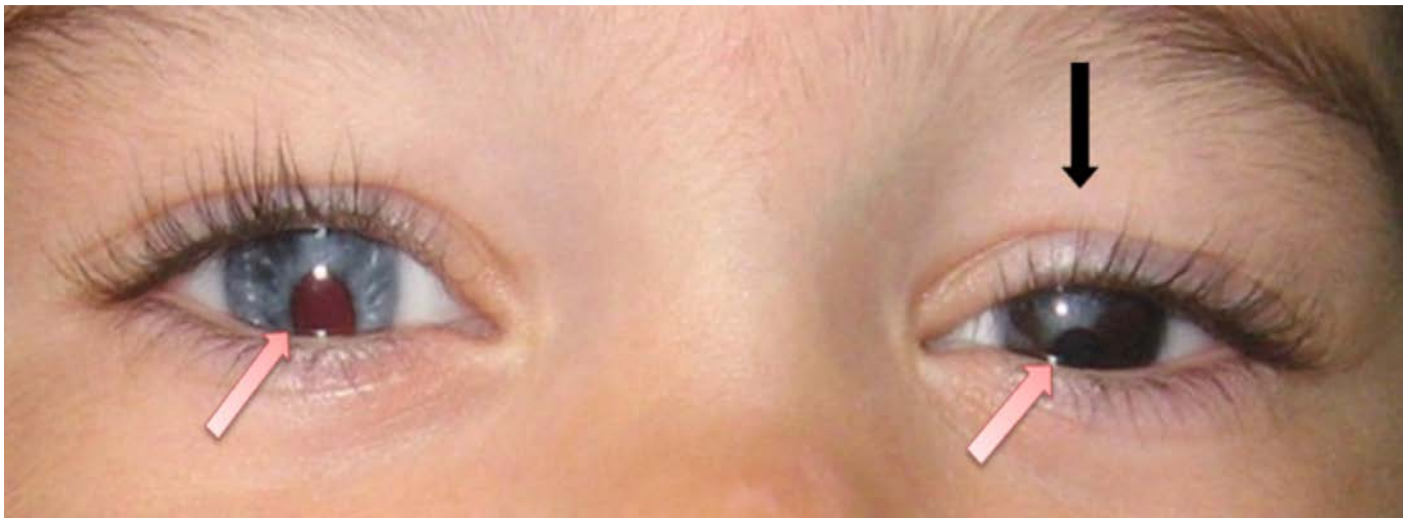
CASE STUDY

We diagnosed a 2-year-old boy as WS2 as characterized by congenital hearing loss, iris heterochromia and absence of dystopia canthorum. Additionally he had coloboma of iris, choroid and optic disc. His right eye was blue and left eye was brown and microphthalmic (Fig 1). Heterochromia and coloboma of iris seems to be associated and in one study the frequency was found as 17.3% [4].

DISCUSSION

Waardenburg syndrome was first described as a group of anomalies including eyelids, eyebrows, with congenital deafness [5]. According to the genetic heterogeneity WS2 has five subgroups (WS2A-E) (Table 1). It is important to recognize subtypes clinically in order to perform the appropriate molecular tests. WS2A is caused by *MITF* (microphthalmia-associated transcription factor) mutations [6]. WS2B and WS2C were mapped to chromosome 1p21-p13.3 and 8p23, respectively. WS2D is caused by *SNAI2* mutations [7]. WS2E is caused by *SOX10* mutations. *MITF* transactivates the gene for an enzyme taking role in melanogenesis particularly melanocyte

Figure 1: Bilateral iris coloboma with heterochromia (indicated with pink arrows). Left brown eye with microphthalmos (indicated with black arrow)



differentiation. Therefore a *MITF* mutation affects pigmentation with the absence of melanocytes in the eyes and cochlea that leads to hypopigmentation and hearing loss in WS2A [9]. *SNAI2* plays an important role by triggering epithelial-mesenchymal transitions. [10]. *SNAI2* heterozygous deletions were found in sporadic and affected cases of piebaldism (congenital white forelock) [11].

In the present case parents were nonconsanguineous, father and paternal aunt had piebaldism. Therefore *SNAI2* might be the responsible gene in this case, as discussed above. In addition, microphthalmic left eye may be due to mutations in *MITF* gene. It is possible that this may be a mere co-incidence of an association for coloboma and heterochromia of irides *or* a rare finding of WS2 depicting the characteristic molecular basis, as reported in previous literature. This hypothesis is just a speculation at this point and can only be confirmed through molecular analysis. We are in a process to molecularly characterize the phenotypic basis of different types and subtypes of Waardenburg Syndromes.

Table 1: Types and subtypes of Waardenburg Syndromes

Types	Subtypes
1	
2	A, B, C, D, E
3	
4	A, B, C

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