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RESEARCH ARTICLE

WAARDENBURG SYNDROME: ABOUT 7 CASES.

Souhaib Aboutoufayl, Jihane Hakam, Sarah Belghmidi,Ibtissam Hajji and Abdeljalil EL Moutaouakil.
Ophtalmology department, Mohamed VI University hospital, Marrakech, Morocco.

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Abstract

Introduction:-

Waardenburg syndrome (WS), was originally described as a syndrome with six characteristic features: lateral displacement of the medial canthi, broad and high nasal root, hypertrichosis of medial part of eyebrows, partial or total heterochromia iridis, white forelock and congenital deaf-mutism. WSI is 1.5–2 times more common than WSII; type III and IV are far rarer forms of WS. It is an autosomical disorder with genetic heterogeneity and not all of its forms are dominantly inherited [1]. Sensorineural hearing loss is quite a frequent feature in Waardenburg syndrome, reported in 60% and 90% of patients with type I and type II, respectively. Bilateral forms of hearing loss are more frequent than unilateral, but not necessarily symmetrical.

The aim of our study is to describe the ophtalmological and otorhinolaryngological aspects of this syndrome, to demonstrate the importance of routine screening for hearing impairment in children with this syndrome so as to improve the conditions and the period of care in patients with such a syndrome.

Materials and Methods:-

We conducted a retrospective study of including 7 children over a period of two years from January 2013 to January 2015. A multidisciplinary ophthalmological and otorhinolaryngological consultation was performed. Each child received a complete eye and otorhinolaryngological examination and a general review. The informations were collected on a standardized form including both the hearing impairment , eye and detailing the following criteria : Age , sex , heredity, ophthalmological examination with uncorrected and corrected visual acuity , the eye position , color vision, visual field test, index Waardenburg(W index), images of the anterior and posterior segment and the otorhinolaryngological examination.

Results:-

The average age of patients was 7 years with extremes ranging from 5 to 10 years; a male predominance was found (5 boys and 2 girls). The clinical symptomatology was dominated by hearing loss and discoloration of the eyes (Image 1, 2, 3).

Ophthalmological examination found a Heterochromia with a total blue iris hypoplastic in 6 cases, a partial in one case, unilateral in 3 cases and bilateral in 4 cases. The broad nasal root was found in 3 cases. All children had an

Corresponding Author:-Souhaib Aboutoufayl.
Address:- Ophtalmology department, Mohamed VI University hospital, Marrakech, Morocco.

internal canthal dystopia with a significant index W in all cases. The White forelock was found in two cases. The shapes of their eyelids, ear auricles and lacrimal puncta were normal. The fundus examination found an albinoide retina in all children including 3 cases where it was bilateral (Image 4, 5). The rest of the examination of the anterior segment was normal. In all of the 7 cases, the macula had a normal configuration, and all had good vision except for one young girl who had hyperopic amblyopia, in whom an optical treatment was introduced by corrective lenses associated with orthoptical management of amblyopia. No exotropia or visual field defect was found in any of the students. There were no abnormalities in the tests of eye position, stereoacuity, and color vision. All children underwent otorhinolaryngological examination and audiogram that confirmed sensorineural hearing loss. The otorhinolaryngological management consisted on hearing aids in 5 cases, and cochlear implants in two cases (Image 6). The rest of systemic examination was normal.

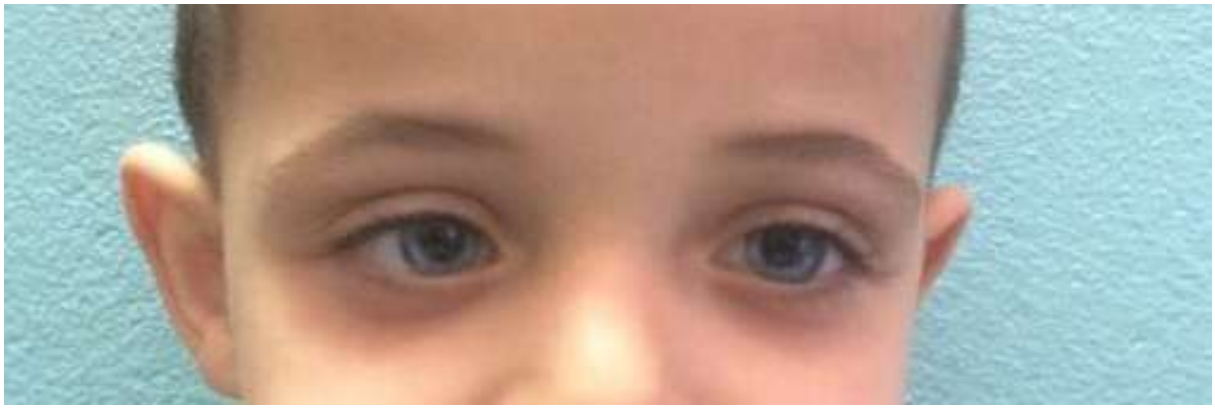

Image 1

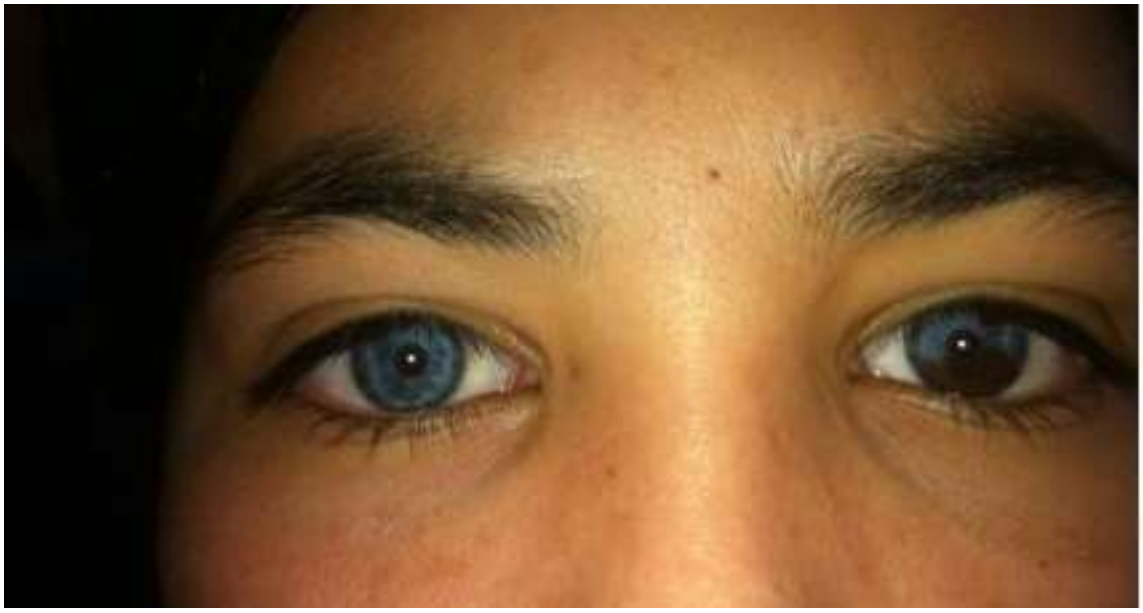

Image 2

Image 3

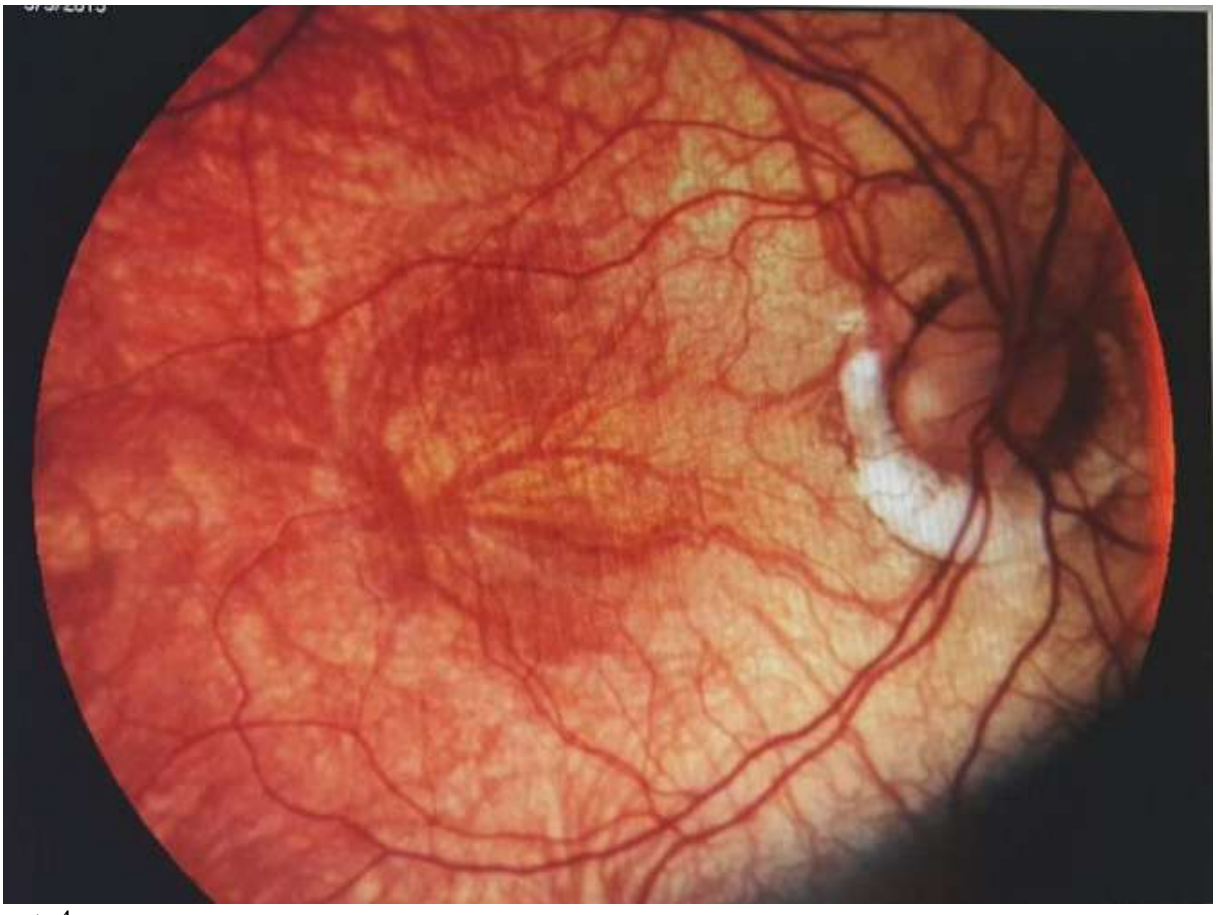

Image 4

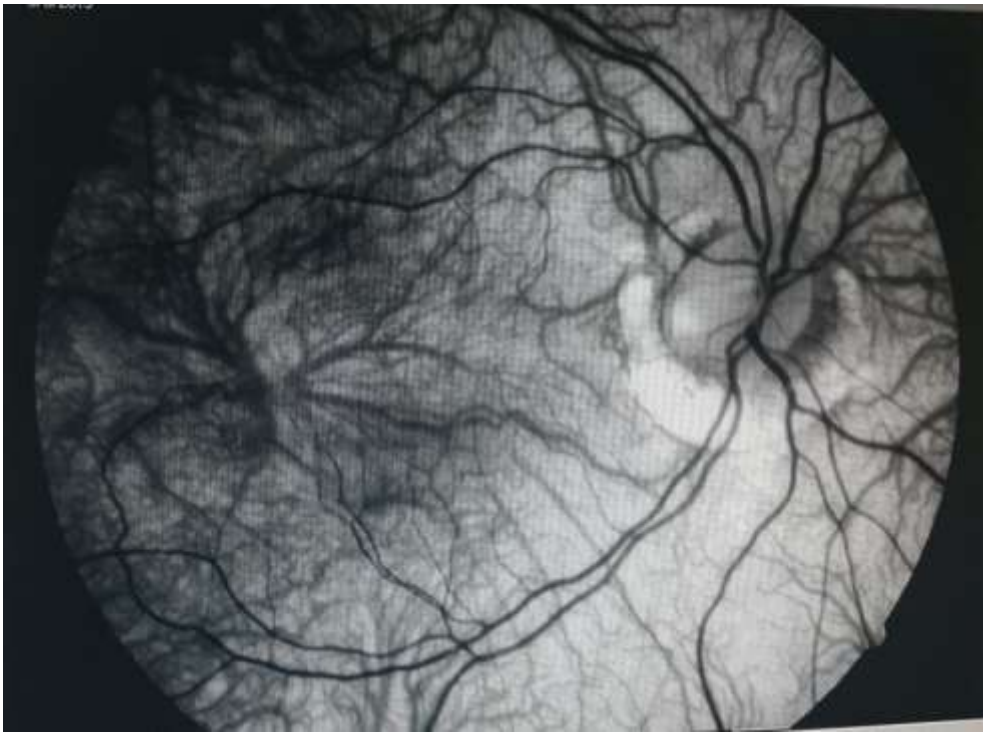

Image 5

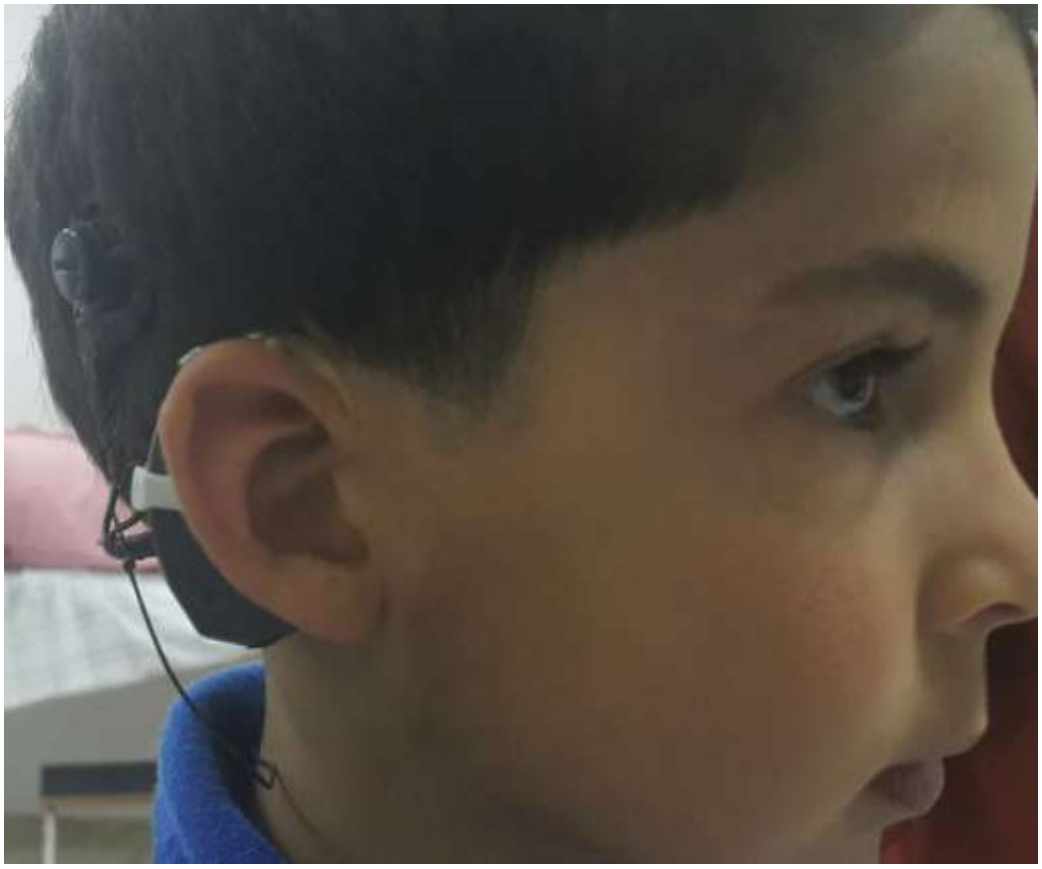

Image 6

Table 1
Summary of distinguishing characteristics of WS subtypes.

Types	Main clinical features
WS1	Hearing loss + pigmentary abnormality + **dystopia canthorum (W > 1.95)**
WS2	Hearing loss + pigmentary abnormality, **without dystopia canthorum (W < 1.95)**
WS3	Hearing loss+ pigmentary abnormality + **musculoskeletal abnormalities**
WS4	Hearing loss + pigmentary abnormality + **aganglionic megacolon**

Table 1. Diagnostic Criteria for Waardenburg Syndrome Type 1[a]

Rank	Criteria
Major	Congenital sensorineural hearing loss; white forelock, hair hypopigmentation; iris pigmentation abnormality: complete heterochromia iridum, segmental heterochromia, or complete hypoplastic blue irides (brilliant blue irides); dystopia canthorum, W index >1.95; affected first-degree relative
Minor	Skin hypopigmentation (congenital leukoderma); synophrys/medial eyebrow flare; broad high nasal root, prominent columella; hypoplastic nasal alae; premature gray hair (age <30 years)

Abbreviations: W index, the measurements necessary to calculate the W index (in millimeters) are as follows: inner canthal distance (a), interpupillary distance (b), and outer canthal distance (c).

$X = [2a - (0.2119c + 3.909)]/c.$

$Y = [2a - (0.2479b + 3.909)]/b.$

$W = X + Y + a/b.$

[a] Criteria proposed by the Waardenburg Consortium.[8] An affected individual must have 2 major criteria or 1 major criterion plus 2 minor criteria.

Abbreviations:-

1. WS: Waardenberg syndrome.
2. W index: Index Waardenburg.
3. SOX10: Sex determining region Y boxes 10.
4. PAX3: Paired boxes 3.
5. MITF: Microphthalmia-associated transcription factor.
6. EDN3: Endothelin 3.
7. EDNRB: Endothelin receptor type B.
8. SNAI2: Snail family zinc finger 2.

Discussion:-

The vision and the hearing are two complementary essential meanings in the psychomotor development of a child. The eye-hearing damage is numerous because of the embryonic cell and similarity of these two bodies, including the retina and inner ear [2, 3].

More than 300 diseases and genetic syndromes involving hearing loss are being described [4].

Waardenburg syndrome (WS) is listed as rare diseases by the Office of Rare Diseases Research (USA) and Orphanet (Europe) [5].

Waardenburg syndrome (WS) is an autosomal disorder with genetic heterogeneity and not all of it forms are dominantly inherited. It is characterised by dystopia canthorum, hyperplasia of the eyebrows, heterochromia iridis, white forelock and congenital sensorineural hearing loss [6, 7]. The incidence of WS was estimated to be 1/ 40,000 at birth and both genders and all races are equally affected [8, 9]. The typical syndrome is classified into four subtypes (WS1–4) according to clinical characteristics [8] (Table1). Out of five major and five minor criteria of Waardenburg syndrome, either two major or one major plus two minor criteria must be present for the diagnosis of WS 1(Table2). WS type II patients do not show dystopia canthorum [10]. Type III WS (Klein–Waardenburg syndrome) is similar to type I but presents additional musculoskeletal abnormalities. Type IV WS (Shah–Waardenburg syndrome or Waardenburg–Hirschsprung disease) is characterized by the presence of Hirschsprung disease [1]. Six disease-causing genes have been identified so far for WS: SOX10, PAX3, MITF, EDN3, EDNRB, and SNAI2 [5, 11].

Dystopia canthorum is a crucial feature for diagnosing WS type 1 which differentiates it from WS2. Dystopia canthorum is confirmed by calculating W index (in mm) [10]. W index greater than 1.95 is considered abnormal.

Hearing loss which is a major criteria but this is not a universal feature of WS but penetrance study of sensorineural deafness showed 69% penetrance in WS1 and 87% in WS2 [1]. In our series two children among the seven received a cochlear implantatation. The other children are waiting because of socioeconomic problem causing a delay care in our context.

Patients with WS can have poor vision due to foveal hypoplasia, hypermetropic amblyopia and few cases have been reported of recurrent vitreous haemorrhage leading to poor vision associated with WS [12]. In our series, no family history of first degree did was noted. We could not perform PAX 3 sequence but an autosomal recessive transmission was considered to be inherited in the other sporadic cases.

The genetic evaluation of WS has not yet been able to predict the final outcome that can be expected in an individual showing a mutation of candidate gene thus complicating the issue of genetic counselling and limiting the scope for prenatal diagnosis [1].

Conclusion:-

Waardenburg syndrome is a syndrome involving ocular and otorhinolaryngological abnormalities requiring multidisciplinary collaboration to prevent neurosensory disability needing an early detection in order to improve the conditions and management of this syndrome.

Conflicts of interest:-

The authors do not claim to have any conflict of interest.

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