International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2016): 79.57 | Impact Factor (2015): 6.391

Waardenburg Syndrome: A Case Study of 2 Patients

Dr Shruti Muddebihal[1], Dr Ravindra Banakar[2]

[1]Post Graduate in Ophthalmology
[2]Professor and HOD department of Ophthalmology JJM Medical College Davangere

Abstract: ***Waardenburg syndrome is an autosomal dominant disease with incidence of 1 in 40000 that manifest with pigmentation defects of skin, hair and iris, sensory neural hearing loss and various defects of neural crest derived tissues. Mutations in EDN3, EDNRB, MITF, PAX3, SNAI2 and SOX10 genes. We report two isolated cases of newborn who presented with complaints of vomiting since day one of birth and other symptoms of intestinal obstruction and all clinical features were consistent with Waardeburg syndrome in the form of white forelock in the midline along with heterochromia iridium, bright red fundal reflex with choroidal depigmentation. Exploratory laparotomy in both cases confirmed Hirschprung disease with histopathological examination report. No family history was noted in both cases.***

Keywords: Waardenburg syndrome, White forelock, Heterochromia iridium, Hirschprung disease.

1. Introduction

Waardenburg syndrome described by Dutch ophthalmologist Petrus Johannes Waardenburg[1]. Autosomal dominant disease with incidence of 1 in 40000 that manifest with pigmentation defects of skin, hair and iris, sensory neural hearing loss and various defects of neural crest derived tissues[2]. Mutation in EDN3,EDNRB,MITF,PAX3,SNAI2 and SOX10 genes involved in formation and development of cells such as melanocytes. Melanocytes are required for melanin pigmentation of skin, hair, iris.

Based on clinical features and genes involved WS is classified into 4 clinical types. Type I and Type II are most common whereas Type III (Klein-WS) and WS IV (Waardenburg-Shah) are rare[3]. Type I and III shows mutation in PAX3 gene. Mutations in MITF and SNAI2 in Type II and mutations in SOX10, EDN3, EDNRB responsible for Type IV WS[4].

We report two isolated cases of type IV WS. A 4 day old and 5 day old male babies presented with signs and symptoms of intestinal obstruction and clinical features consistent with WS.

2. Case Report

Case 1:
A 4 day old full term male baby born to parents' second degree consanguineous marriage presented to paediatric casualty with vomiting which was bilious, 4-5 episodes, non projectile and after every feeds with birth weight of 3.3kg and anthropometry was appropriate for his age.

On examination white forelock, abdominal distension with abdominal circumference of 31cm, heterochromia iridium (BE), bright fundal reflex with choroidal depigmentation were present.

Radiological findings: **X-ray erect abdomen**: multiple air fluid levels

Barium enema: dilation of whole bowel

USG abdomen:

- Gall bladder sludge
- Bilateral echogenic kidneys
- Dilated and fluid filled small bowel loops
- Collapsed colon and minimal ascites
- Exploratory laparotomy with jejunostomy and loop ileostomy for suspected Hirschsprung's disease with Waardenburg syndrome was done.
- Biopsies for frozen section from distal jejunum, distal ileum, caecum, transverse colon & sigmoid colon showed AGANGLIONOSIS WITH HYPERTROPHIED NERVES on Histopathological examination.
- Baby died on post-operative day 10.

Case 2

- In the second case it was 5 day old male infant born to parents of second degree consanguineous marriage presented with similar complaints of vomiting since day one of birth, bilious, non projectile after every feed with birth weight of 3kg and anthropometry was appropriate for age.
- On examination
- White forelock, jaundice, heterochromia iridium, bright red fundal reflex, abdominal distension with abdominal circumference of 32cm were present.

Radiological examination

X-ray erect abdomen: multiple air fluid levels

Barium enema : dilation of whole bowel

USG abdomen:

- Dilated and fluid filled small bowel loops
- Collapsed colon and minimal ascites
- Exploratory laparotomy with jejunostomy and loop ileostomy for suspected Hirschsprung's disease with Waardenburg syndrome was done.
- Biopsies for frozen section from distal jejunum, distal ileum, caecum, transverse colon & sigmoid colon showed AGANGLIONOSIS WITH HYPERTROPHIED NERVES on Histopathological examination.
- Baby died on post-operative day 13.

3. Discussion

Waardenburg syndrome is an autosomal dominant disorder that manifests with sensorineural deafness, pigmentation defects of the skin, hair and iris and various defects of neural crest-derived tissues. These syndromes are caused by physical absence of melanocytes from the skin, hair, eyes, or the stria vascularis of the cochlea. Usually the melanocyte deficiency is patchy, but alternatively a general dilution of pigmentation may be seen. Absence of melanocytes could be because of a failure of differentiation in the neural crest, a failure of melanoblasts to migrate, or a failure to terminally differentiate and survive in their final location. WS2 may be melanocyte specific, whereas WS 1 and the rare variants WS3 and WS4 are neurocristopathies, involving the frontal bone, limb muscles, and enteric ganglia, respectively. All these extra tissues are neural crest derivatives[5].

Mutations in the EDN3, EDNRB, MITF, PAX3, SNAI2, and SOX10 genes can cause Waardenburg syndrome. These genes are involved in the formation and development of melanocytes and Mutations in any of these genes can disrupt the normal development of melanocytes, leading to abnormal pigmentation of the skin, hair, and eyes and problems with hearing[4].

Diagnostic criteria[13]

Major	Minor
Sensorineural deficit(threshold > 25dB)	Congenital leukoderma
Iris pigmentary abnormality	Synophrys or medical eyebrow flare
Hair hypopigmentation	Broad high nasal root
Dystopia canthorum	Hypoplasia of alae nasi
First-degree relative diagnosed with WS	Premature graying of the hair
RARE	
HIRSCHSPRUNG DISEASE	
Spina bifida	
Cleft lip and/or palate	
Limb defects	
Congenital heart abnormalities	
Abnormalties of vestibular function	
Low anterior hair line	

Waardenburg syndrome is a group of rare genetic conditions[1]. Features vary among affected individuals, even among people in the same family. It has been classified into four types, of which type IV is also known as Shah-Waardenburg syndrome or Waardenburg syndrome associated with long-segment Hirschsprung disease[6]. Shah-Waardenburg syndrome is very rare. Defective migration of the neural crest derived cell lines, melanocytes and the neuroblasts (contributing the enteric ganglion cells) during the embryonic phase, has been postulated as a cause of this disorder[7]. Thus characterizing it as a type of neurocristopathy[8]. Bowel involvement in Shah-Waardenburg syndrome is characteristic in the form of aganglionosis in the myenteric (Auerbach) plexus and the submucous (Meissner) plexus, with long-segment Hirschsprung disease[9]. The unusual finding in our case was the extension of the aganglionosis in the entire colon (total colonic aganglionosis) and familial incidence of Shah-Waardenburg syndrome.

Shah-Waardenburg syndrome have three variants described on the basis of genetics. Type IVA and type IVB are inherited as an autosomal recessive trait, while type IVC as an autosomal dominant trait[10,11]. Folic acid supplementation in pregnancy has been recommended for women at increased risk of having a child with Waardenburg syndrome[8].

Initial surgical approach in Shah-Waardenburg syndrome is histopathological confirmation of diagnosis by routine seromuscular colonic biopsy and stoma formation depending upon the involvement of the colon. Frozen section examination if available remains a useful diagnostic modality for this purpose with its inherent advantages of prompt intraoperative diagnosis. The definitive treatment of Hirschsprung's disease is performed at a later date[12]. Genetic counseling must be provided for families with this disorder.

Mutational analysis was not possible due to resource constraints. In conclusion, a high index of suspicion for Shah-Waardenburg syndrome should be present, in a child, particularly neonate with Waardenburg syndrome presenting with constipation since birth or with features suggestive of intestinal obstruction, white forelock, heterochromia iridium.

Case 1

Figure 1

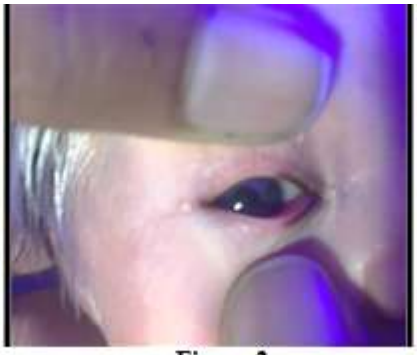

Figure 2

Figure 3

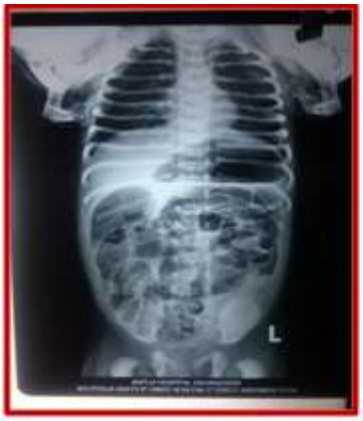

Figure 4

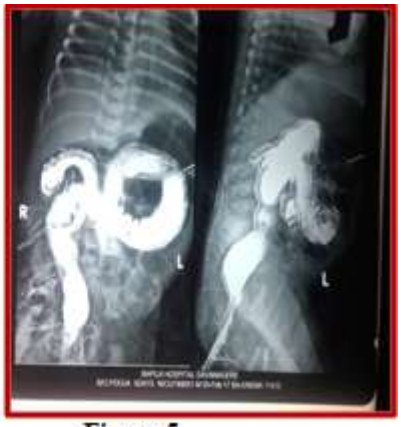

Figure 5

Fig 1: Baby with white forelock
Fig 2&3: Heterochromia iridium (both eyes)
Fig 4: X-ray erect abdomen: multiple air fluid levels
Fig 5: Barium enema : dilation of whole bowel

Case 2

Figure 6

Figure 7

Figure 8

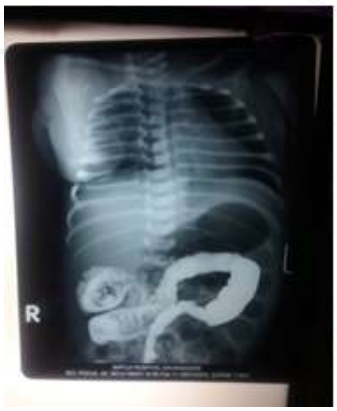

Figure 9

Figure 10

Case 2
Fig 6&7: Baby with white forelock
Fig 8: Heterochromia iridium
Fig 9: Barium enema: dilation of whole bowel
Fig 10: Intra-operative

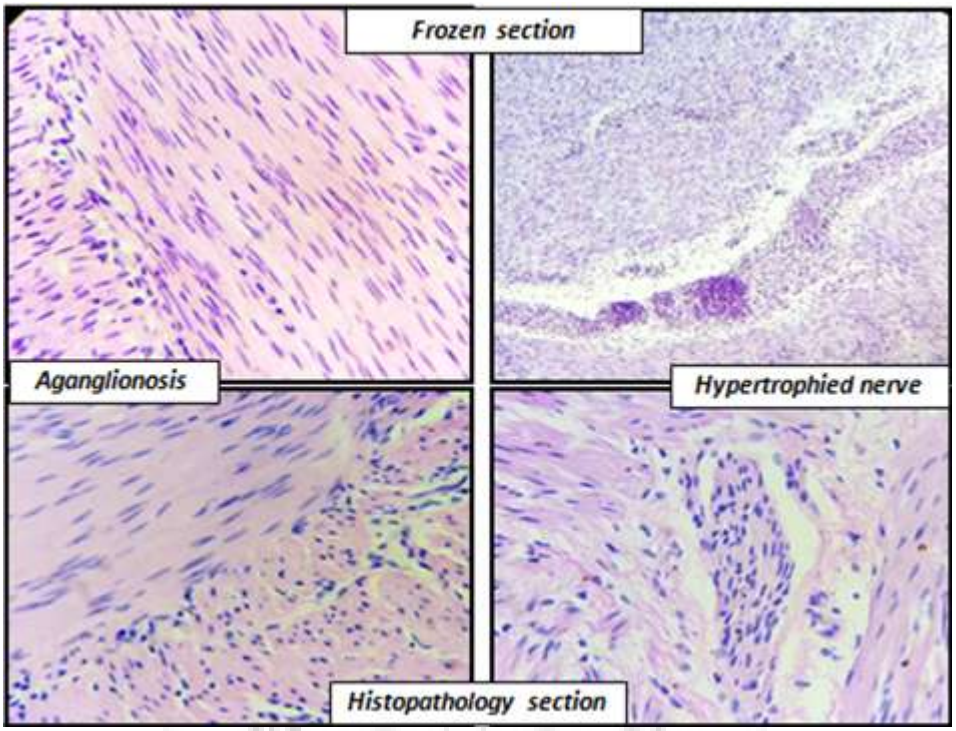

Figure 11: Frozen section and histopatholgy of dissected bowel segment

References

[1] Waardenburg PJ (1951) A new syndrome combining developmental anomalies of eye lids, eye brows and nasal root with pigmentary defects of iris and head hair with congential deafness. Am J Hum Genet 3:195–253.
[2] Bondurand N, Pingault V (2006) Interaction among SOX10, PAX3 and MITF, three genes altered in Waardenburg syndrome. Hum Mol Genet 9(13):1907–1917.
[3] Wadhwani M, Gupta Y K. Waardenburg shah syndrome: A rare case from India. Oman J Ophthalmology.2015;8:74-75.
[4] Waardenburg syndrome. http://ghr.nlm.nih.gov/condition/waarden burg-syndrome. Accessed March 23 2015.
[5] Read AP, Newton VE (1997) Waardenburg syndrome. J Med Genet 34:656–665.
[6] Shah KN, Dalal SJ, Desai MP, Sheth PN, Joshi NC,Ambani LM. White forelock, pigmentary disorder of irides, and long segment Hirschsprung disease: possible variant of Waardenburg syndrome. J Pediatr. 1981;99:432-5.
[7] Ambi US, Adarsh ES, Hatti R, Samalad V. Anesthetic management of Shah-Waardenburg syndrome: Experience of two cases and review of literature. Saudi J Anaesth. 2012;6:172-4.
[8] Sankar R. Shah-Waardenburg syndrome. Dermatol Online J. 2008;14:19.
[9] Shim WK, Derieg M, Powell BR, Hsia YE. Near-totalintestinal aganglionosis in the Waardenburg-Shah syndrome. J Pediatr Surg. 1999;34:1853-5.
[10] Egbalian F. Waardenburg-Shah syndrome; A case report and review of the literature. Iran J Ped. 2008;18:71-4.
[11] Syrris P, Carter ND, Patton MA. Novel nonsense mutation of the endothelin-B receptor gene in a family with Waardenburg-Hirschsprung disease. Am J Med Genet. 1999;87:69-71.
[12] Sharma SB, Gupta R. Total colonic aganglionosis: A rare entity in children. CIBTech J Surg. 2013;2:58-61.
[13] Farrer A, Kenneth M, Amos GJ (1992) Waardenburg syndrome(WS) Type I is caused by defects at multiple loci, one of which is near ALPP on chromosome 2: first report of the WS consortium Lindsay. Am J Hum Genet 50:902–913.