CASE 3

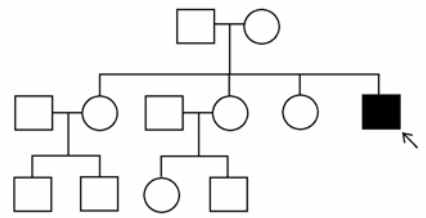
Patient: A 26-year-old Thai male from Prajuabkirikhan

Chief Complaint: Hirschsprung's disease with unilateral blue iris

Present Illness: The patient presented with chronic dull abdominal pain and constipation. One week before admission, he had bloating and abdominal distention which got worsen after meals. He also had nausea and vomiting. The symptoms quickly progressed. He was admitted at surgery unit and was diagnosed as gut obstruction. After investigations, the final diagnosis was Hirschsprung's disease. Total colectomy with ileo-rectal anastomosis was done. During admission, he developed aspirated pneumonia and was transferred to intensive care unit. The in charged physician noticed that the patient had left blue eye and consulted for proper evaluation and management.

Past History: He had delayed in passing meconium at the age of 2 months

Family History:



The patient's mother informed that the patient had left blue eye since birth and the hair at frontal area changed from black to white when he was 18 (the patient use hair dye to cover his white hair). Other family members were normal.

Dermatological Examination (Figure 3.1)**:** A young Thai male, on ET tube, has heterochromia with blue iris on the left side and black iris on the right, white forelock, synophrys and increase the distance between the inner canthi.

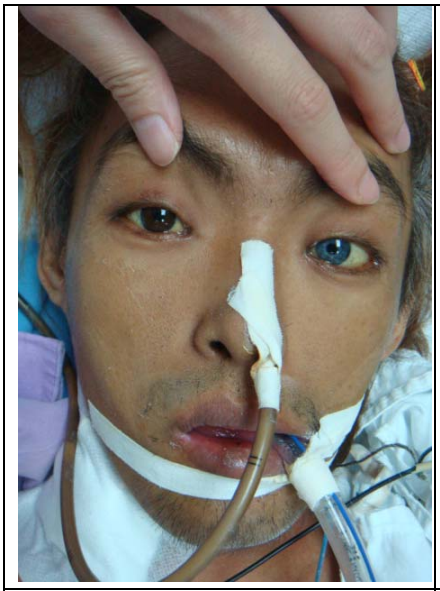


Figure 3.1

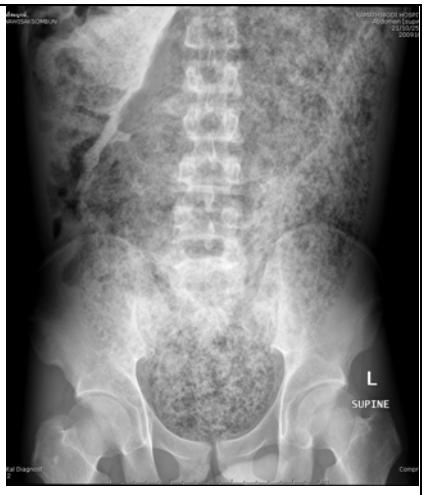


Figure 3.2

Investigations:

Abdominal x-ray (Figure 3.2) and MDCT whole abdomen: Marked dilatation from sigmoid colon to cecum

Colon biopsy: absence of ganglion cell in sigmoid colon

Diagnosis: Waardenburg syndrome type IV

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Discussion

Waardenburg syndrome (WS) was defined by a German ophthalmologist Utrecht Waardenburg [1] in 1951. It is an autosomal dominant disease derived from the neural crest that presents with sensorineural hearing loss and pigmentation disorders of the hair, eyes, and skin.[2] Waardenburg syndrome is divided into 4 types according to the symptoms.

Diagnostic criteria of WS [3]

Major criteria	***Minor criteria***
Congenital sensorineural hearing loss (unilateral or bilateral)	Congenital hypopigmentation
Iris heterochromia, partial or total	Synophrys or medial eyebrow flare
White forelock	Broad and high nasal root
Lateral displacement of the inner canthi of the eyes in the presence of normal interpupillary distance (dystopia canthorum)	Hypoplasia of alar nasi
Affected first degree relative	Premature graying of hair before age 30

** The clinical diagnosis of WS requires at least 2 major or one major and one minor criteria*

Clinical and genetic criteria of various type of WS

WS type	**Inheritance**	**Clinical manifestations**	**Gene**
Type I (Waardenburg)	AD	Heterochromia irides, Dystopia canthorum, Congenital deafness	PAX3
Type II (Waardenburg)	AD	No dystopia canthorum	MITF, SOX10
Type III (Klein-Waardenburg)	AD	Hypoplasia of limb muscles elbows, fingers	PAX3
Type IV (Shah-Waardenburg)	Mostly AR	Hirschsprung's disease	EDNRB, EDN3, SOX10

Type-IV is the association of WS with Hirschsprung's disease (HD) described by Krishnakumar N.

Shah In 1981.[4] This type is called Shah-Waardenburg syndrome (SWS) which is declared as a rare condition, inherited either as an autosomal recessive trait from mutations of endothelin-B receptor (EDNRB) or endothelin-3 (EDN3) genes, or as an autosomal dominant trait when related to SOX10 gene mutations.[5-6] The incidence of WS is estimated as 1:40,000, but the incidence of SWS is not known. Defective migration of the neural crest cells (i.e., the melanocytes and the neuroblasts contributing the enteric ganglion cells) has been postulated as a cause of this disorder.[7]

The classic presentations of SWD include HD which characteristic absence of the myenteric (Auerbach) plexus and the submucous (Meissner) plexus with hyperganglionosis and ectopic ganglia in the lamina propria of the long segment.[8] Total colonic (ileocecal) aganglionosis and long segment (up to the splenic flexure) aganglionosis have been observed in 60.4% and 14%, respectively; whereas rectosigmoid aganglionosis has been reported at a rate of 23.2% and ultrashort aganglionosis at 2.3%. The clinical findings of the patient and the age at presentation can vary according to the length of the involved segment. Patients with short segment involvement mostly present at a more advanced age with chronic constipation, malabsorption, and enterocolitis, whereas those with long segment involvement present with intestinal obstruction findings such as bilious vomiting, abdominal distension, and inability to feed orally from the first few days of life.[9] Depigmentation with a white forelock are common skin manifestations which presented in almost all patients, blue iris and sensorineural deafness are present in nearly half of the patients.

The clinical picture of this syndrome is very typical. Treatment requires surgical intervention for the Hirschsprung disease. Proper audiological assessment at birth

and at periodic intervals can detect hearing impairment. Only a few patients, described to specific SOX10 mutations, have additional neurological impairment. The white forelock can regress or persist throughout life. Genetic counseling must be provided for families with this disorder, and the occurrence rate depends on the specific molecular etiology.

References

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