MEDICAL CHANNEL

Original Article

INTESTINAL AGANGLIONOSIS IN SHAH -WAARDENBURG SYNDROME; ANALYSIS OF 12 CASES

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ABSTRACT

Background: Shah Waardenburg Syndrome (SWS) is a rare variant of Waardenburg Syndrome (WS), which is characterized by aganglionosis, deafness, pigmentary anomalies of irides, skin and hairs. The purpose of this article was to analysis the extent of aganglionosis and its outcome in Shah Waardenburg syndrome.
Methodology: Twelve consecutive patients of Shah -Waardenburg syndrome reviewed retrospectively with respect to age, sex, clinical presentations, family history and surgical outcome, selected from Liaquat University of Health Sciences and King Edward Hospital Lahore..
Results: This study comprised of twelve patients (8 males and 4 females). White forelock was seen in all patients. Nine patients had blue irides , three had blue and brown irides. None of them had white skin patches and facial deformity. Deafness could not be assessed in 8 new born patients while remaining four had no deafness. Clinical presentation in all patients was intestinal obstruction in 1st few days of life. Laparotomy revealed total colonic aganglionosis in eight new born patients while four patients had no proper diagnosis of leveling of lesion and had multiple surgeries and finally they fit in the diagnosis of total colonic aganglionosis. Histopathology showed total colonic aganglionosis in all patients. Eight expired due to severe sepsis/ enterocolitis, while two had endorectal pull through surgery and two patients are waiting for definitive surgery.
Conclusion: Shah-Waardenburg Syndrome is a rare anomaly and highly associated with total colonic aganglionosis which leads to high morbidity and mortality in neonatal age group.

Key words: Aganglionosis, Shah-Waardenburg syndrome, Mortality, Clinical presentations

INTRODUCTION:

Shah-Waardenburg syndrome (SWS), also called as type IV Waardenburg syndrome (WS) or Hirschsprung associated WS is an unusual variant of Waardenburg syndrome.[1, 2] Clinical manifestations of syndrome are megacolon, deafness, pigmentary anomalies of irides, skin and hairs. Many reports describe long segment aganglionosis as a common variety, while there have been occasional reports of total colonic (TCA) and extensive aganglionosis (EA) in SWS .[3, 4]Defective migration or function of neural crest cells is supposed to be the main reason for clinicopathological presentation. Mutation in endothelin-B receptor, endothelin-3 genes and sox10 genes may lead to autosomal recessive or dominant trait.[5]
Very limited cases have been reported in literature so far. We are sharing our experience in managing total colonic aganglionosis with SWS.

METHODOLOGY:

The data has been retrieved from the medical record of patients who have been operated for Shah Waardenburg syndrome in the department of Pediatric surgery at Liaquat University hospital Jamshoro and King Edward University Lahore during the period

from June 2005 to June 2010.
Total No of patients was 12, selected 8 from Liaquat University of Health Sciences and 4 from King Edward Hospital Lahore.
Basic parameters noted were age, sex, family history, presentation, surgical outcome and follow up. All patients had complete blood count, serum electrolytes, urea, x-ray plain abdomen and ultrasound abdomen. Gastrograffin enema was made in seven patients, while four were operated elsewhere and one was very sick.
Surgical option opted were laparotomy with multiple seromuscular biopsies (due to non availability of frozen section) from collapsed intestinal segments and ileostomy proximal to narrowed segment in all patients

RESULTS:

Data of all patients were 12 with selected 8 from Liaquat University of Health Sciences and 4 from King Edward Hospital Lahore. retrospectively reviewed during a period of five years extending from June 2005 to June 2010. Out of twelve patients eight were males and four females. Intestinal obstruction and white forelock (Figure I) were prominent features in all babies. Nine had blue irides and three had blue and brown irides. Deafness could not be assessed in eight neonates, while remaining four had no deafness. Facial deformity and skin depigmentation were not detected in any one of them.
Laboratory investigations were within normal limits. X-ray abdomen was suggestive of intestinal obstruction and ultrasound abdomen revealed dilated bowel loops. Gastrograffin enema was performed in 7 patients that showed unused colon in all, while four were referral and one was very sick
On laparotomy entire colon along with 30-50 cm of distal ileum was found collapsed suggestive of total colonic aganglionosis in 8 patients (Figure II). After multiple seromuscular biopsies from collapsed segment, ileostomy was performed proximal to collapsed segment in these patients. Four referral patients had colostomy after having multiple surgeries. On exploration by our team it has been proved that they had total colonic aganglionosis. Histopathological report confirmed the total colonic aganglionosis along with nerve hypertrophy Figure III).
Eight patients expired during the first few months of life, while parents of three babies were offered definitive surgery but they refused because their same types of previous babies expired and they believe that this disease has bad prognosis. Two patients had definitive surgery having on and off gastrointestinal problems while remaining two are waiting for definitive surgery.
In this series eight patients had strong family history of this lesion. Two of the patients were brothers, and had a family history of three neonatal and infantile deaths with features consistent of SWS. Two babies were sister and brother with no history of this condition in family. While four had same lesion in family and none is alive.

DISCUSSION:

Shah-Waardenburg syndrome is a neurocristopathy and an unusual variant of WS characterized by Hirschsprung disease, deafness and pigmentary anomalies of skin, irides and hairs.[6]
Petrus Johannes Waardenburg described a constellation of features in 1947 and klein in 1950. This condition was labeled as Waardenburg syndrome in1951 with following characteristic feature; lateral displacement of medial canthi and lacrimal puncti, broad and high nasal root, hypertrichosis of medial part of eye brows, partial or



Figure I: showing white forelock



Figure II: Showing collapsed distal small intestine.

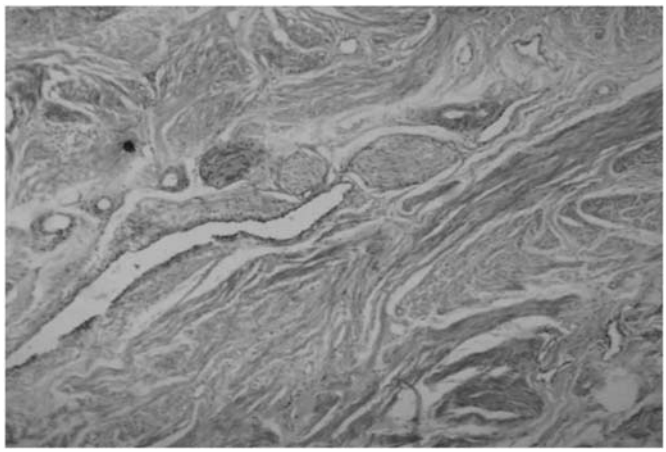


Figure III; Histological view of ileum showing aganglionosis

total heterochromia of irides, white forelock and congenital deafness.[7] Krishnakumar N-Shah in 1981 described the association of Hirschsprung disease with WS, later on this condition was known as Shah-WS.[3]

Incidence of WS was estimated to be 1 in 20000-42000, [7,8] while SWS is rare and only fifty cases have been reported in literature.[9] This disease is inherited either as autosomal recessive trait from mutation of endothelial B receptor (EDNRB) or endothelin 3 (EDN3) genes mutation[10] or autosomal dominant when related to SOX10 gene mutation .[11,12] Other variants of WS are autosomal dominant in inheritance.

Defective migration or differentiation of neural crest cells is solely assumed to be the reason of this condition.[13] Pigmentary anomalies affecting the hairs, irides and skin are the hallmark of this syndrome.[14]White forelock or poliosis is variable in size and mostly present at birth, but cases of late presentation of poliosis have also been reported. White forelock may persist throughout the life or may disappear at later age. In our study white forelock was prominent feature in all patients at birth.

Cutaneous pigmentary lesions: achromic patches and hyperpigmented macules occur in 8.3-50% of patients. [15,16] In our cases no cutaneous lesions were found.

Pigmentary eye anomalies includes; heterochromic irides (21-28%), bilateral hypochromic irides (14-42%) and pigmentary anomalies in fundus .[14, 17]Other eye anomalies are; dystopia canthrum, synophrys or medial eye brow flare with a broad nasal root. In our cases nine patients had blue irides and threee had blue and brown irides while none had other facial anomalies.

Hearing loss is not a universal feature of SWS, it is estimated that 1-2% patients of WS are congenitally deaf, but their percentage may be raised at later life. [18,19] In our patients we have no assessment of deafness because of tiny age group, while other had no deafness

Bowel involvement in SWS is a pertinent feature, which is presented by delay passage of meconeum, chronic constipation, failure to thrive or intestinal obstruction [1]. Our patients presented with intestinal obstruction in 1st few days of life. Most of the cases of aganglionosis in association with SWS are long segment[20], while rectosigmoid, total colonic and extensive aganglionosis have also been reported. [21] Total colonic aganglionosis TCA) is defined as aganglionosis limited to the total colon and distal 30-50 cm of terminal ileum, whereas extensive aganglionosis (EA) is defined as aganglionosis of total colon with involvement of more proximal small intestine .[21,22] Our all patients fall within category of TCA. According to a survey, frequency of TCA is 4.5% and EA is 2-5.2% .[23] Histopathological features in aganglionosis associated with SWS are controversial. Shim et al [24] described the absence of myenteric (Auerbach) plexus and submucosal (Meissenrs) plexus with hyper ganglionosis and ectopic ganglia of lamina proparia, while Sham et al[25] described the absence of ganglion cells and hypertrophy of nerves bundles. Histopathological findings in our patients were consistent with what Sham has described.

Treatment modality for aganglionosis in SWS is surgical intervention and regular follow-up, because these patients are more prone to enterocollitis, fluid electrolytes imbalance and short bowel syndrome. In our patients laparotomy findings were suggestive of TCA and ileostomy performed. We observed 66.6% mortality.

Genetic counseling to parents is an important task, because affected family on subsequent pregnancies has a chance of 50% risk of having an affected offspring.

CONCLUSION:

Shah-Waardenburg Syndrome is a rare anomaly and highly associated with total colonic aganglionosis which leads to high mortality in neonatal age group. Clinical features may be variable in individual patient.

Contribution of Authors#

Author No 1: Designing, Drafting, References Setting
Author No 2: Final revision and rewriting
Author No 3: Designing and Final revision
Author No 4: References collection and checking
Author No 5: Data Collection and primary review

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