

CASE REPORT:

Turner Syndrome with Intra-Hepatic Periportal Cuffing And Non-Cirrhotic Portal Hypertension (NCPH) - A Rare Association

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ABSTRACT: Turner syndrome is a comparatively commonly encountered chromosomal disease with well known congenital malformations involving the cardiovascular and renal system in addition to its typical phenotypic characteristics. Liver involvement in Turners syndrome is seldom reported. We describe a case of a 9-year old girl with Turner syndrome, presenting with massive upper gastrointestinal bleed from Grade-III esophageal varices and portal hypertension due to a rare vascular anomaly involving the hepatic vasculature.

KEY WORDS: *Turner syndrome, Non cirrhotic portal hypertension, Non-cirrhotic portal fibrosis, Esophageal varices, hematemesis, Intra-hepatic periportal cuffing*

INTRODUCTION: Approximately 1 in 2,500 live female births is affected by Turner syndrome which is one of the common genetic conditions encountered

in pediatric practice [1]. Cardiovascular and renal malformations are among the well known associations and are usually screened for[2]. In this report we describe a 9 year old child presenting with massive hematemesis and portal hypertension. Although different body systems can be affected to varying degrees in Turner syndrome, gastrointestinal bleeding due to portal hypertension is rare. The main causes of liver involvement in Turner syndrome are vascular disorders of congenital origin, and non-alcoholic fatty liver disease. In the instant case however, liver function tests and hepatic echotexture on sonography were fairly normal, making the evaluation of cause of portal hypertension a diagnostic challenge.

CASE REPORT: A 9 year old girl born in our hospital, a known case of Turner syndrome (confirmed by Karyotyping) presented with 3 episodes of vomiting containing 50-100 ml of blood and black colored stools for past few days. She had no other bleeding manifestations or petechiae. There was no history of fever, chronic cough, epigastric pain, drug intake, jaundice or abdominal distention. Patient had a history of an episode of hematemesis two years back for which she was hospitalized and managed with oral iron supplements in view of iron deficiency anemia. She had splenomegaly and doppler studies were normal at that time. Patient was however lost to follow up and thereafter presented with current symptoms.

On examination (Figure 1) child had typical features of turner syndrome with short stature, low hair line, webbed neck, shield chest, widely spaced nipples and wide carrying angle. Tachycardia and pallor were present. No jaundice or signs of liver failure were seen. Abdomen was soft and not distended. Spleen was soft to firm, 6 cm below costal margin. Liver was not enlarged. Examination of other systems was unremarkable. 3rd episode of hematemesis in hospital amounted to about 200 ml frank blood, rendering her hypertensive and pale. CBC showed severe anemia (Hb 4.6 gm/dL) with a progressive fall in all three cell lines on subsequent tests indicating hypersplenism. Peripheral smear for RBC morphology showed a microcytic hypochromic picture. No parasites were seen. Liver function tests were normal. Stool for occult blood was positive. She was managed with four packed cell transfusions, octeotride and ethamsylate.

Upon hemodynamic stabilization of the patient, further evaluation of suspected variceal origin of hematemesis was done. Upper gastrointestinal endoscopy (Figure 2) confirmed grade III esophageal varices & grade IV

gastric varices which were actively bleeding. Endoscopic band ligation of esophageal varices was done and 3 monthly endoscopies for repeat ligation were advised. Portal venous doppler (Figure 3,4,5) showed normal hepatopedal flow with monophasic flow in main portal vein and loss of respiratory phasicity. Periportal cuffing was noted around main portal vein and in the distal branches of portal vein, indicative of fibrosis. Enlarged spleen measuring 12.8cm was seen in contrast enhanced CT abdomen (Figure 6,7,8), with a normal liver in shape and size. Multiple dilated varices were seen in wall of esophagus. Splenic vein appeared prominent, measuring 10mm and multiple dilated tortuous vessels were seen at the splenic hilum suggestive of perisplenic collaterals. Portal vein and superior mesenteric vein measured 10 mm & 8mm respectively.

Liver biopsy (Figure 9,10,11,12) was performed which showed normal liver architecture with minimal fibrosis, mild steatosis and mild dilatation of sinusoids. PAS positive and diastase negative material was seen within hepatocytes. There was no evidence of cholestasis, bile duct proliferation or infiltration of chronic inflammatory cells. A diagnosis of Turner Syndrome with Grade III Esophageal Varices, Intra-Hepatic Periportal Cuffing and Non Cirrhotic Portal Hypertension was hence made.

DISCUSSION: Cardio-vascular and renal anomalies are known in Turners Syndrome. We present a rare association of portal hypertension due to vascular anomaly (periportal cuffing of portal vein and its distal branches) and NCPF with Turners syndrome in a 9-year old girl presenting with massive UGI bleed from Grade-III esophageal varices. Her splenic vein diameter on doppler was however found to be normal for age, as was the portal vein.

Muller, et al (2008) [1] had reported a 3 year old girl with Turners syndrome presenting with UGI bleed due to pre-hepatic PHT whose liver biopsy had shown anomalous intra-hepatic arteries and veins. Roulot et al (2004) [3] published a cohort of Turners Syndrome cases in the mean age group of 8 +/- 5.2 years showing vascular anomalies in liver. Out of 27 cases whose liver tissue samples were available, 10 showed marked liver architectural derangements, including nodular regenerative hyperplasia in 6, multiple focal nodular hyperplasia in 2 and cirrhosis in 2. These changes were often associated with obliterative portal venopathy and aortic malformation. Out of 17 others, there was mild to moderate portal fibrosis in 15, inflammatory

infiltrates in 9 and nonalcoholic fatty liver disease in 11. Bile duct alterations resembling small duct sclerosing cholangitis were observed in 21 with or without architectural changes. PHT was observed in 4 with marked architectural changes, including 3 in whom refractory ascites or recurrent variceal bleeding developed, needing transplantation. None of the patient without marked architectural changes experienced progressive or decompensated liver disease. There was no evidence of hepato-toxicity from estrogen replacement therapy.

The earlier terminology of NCPF (Non-cirrhotic Portal Fibrosis) has since been changed to NCPH (Non-Cirrhotic Portal Hypertension) to encompass the whole spectrum of vascular anomalies in portal system [4]. However the instant patient is likely to be a case of NCPF in view of periportal cuffing of terminal portal vein branches, minimal fibrosis seen within liver on biopsy and absence of any blocks (eg.thrombus) in the splenic vein or the portal vein branches.

CONCLUSION: Liver involvement in Turners syndrome is rare. High index of suspicion and selecting appropriate investigations and interventions in time is the corner stone to salvage such children. Main causes are vascular disorders, probably of congenital origin, requiring long-term follow-up with drug therapy, variceal ligation, and transfusion under close supervision and may be, liver transplantation in selective cases.

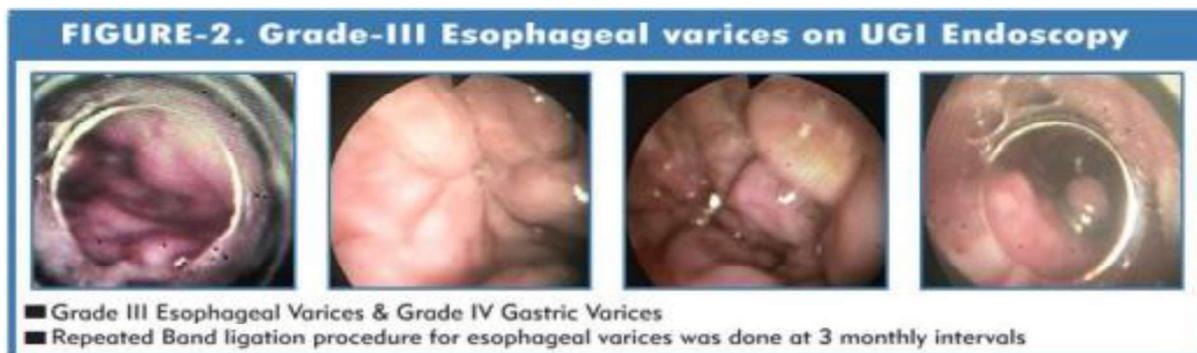
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PORTAL VENOUS DOPPLER



FIGURE-3

Main portal vein shows monophasic flow with loss of respiratory phasicity. Normal hepato-pedal flow seen.



FIGURE-4

Periportal cuffing noted in the distal branches of portal vein and around main portal vein, indicative of fibrosis.



FIGURE-5

- Spleen is enlarged in size measuring 12cm
- Splenic vein diameter 8.6mm →
- Multiple perisplenic collaterals seen →
- Portal Vein diameter 10mm, no thrombus

CONTRAST ENHANCED CT ABDOMEN

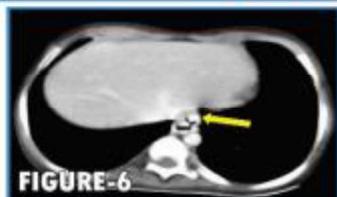


FIGURE-6

Multiple dilated enhancing structures are seen in wall of esophagus suggestive of esophageal varices.

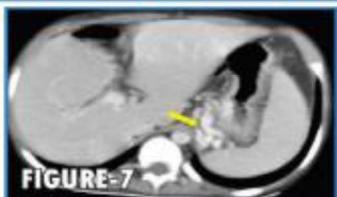


FIGURE-7

- Multiple dilated tortuous vessels at the splenic hilum suggestive of perisplenic collaterals.
- Liver appears normal in size and shape.

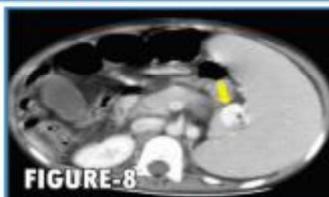


FIGURE-8

- Spleen is enlarged in size measuring 12.8cm
- Splenic vein appears prominent measuring 10mm

LIVER BIOPSY

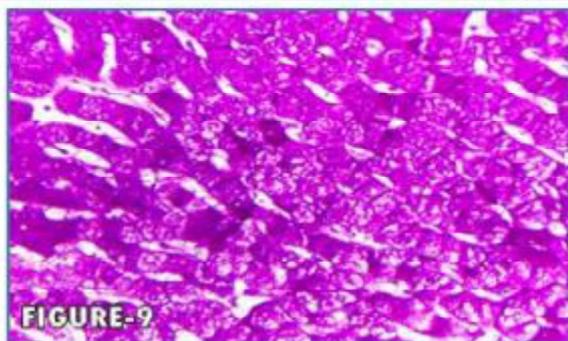


FIGURE-9

PAS Stain (40X)

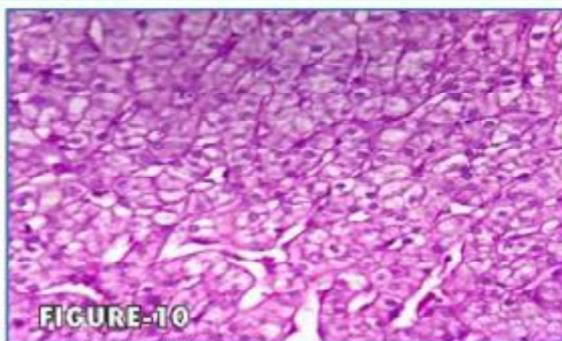


FIGURE-10

Diastase Stain (40X)

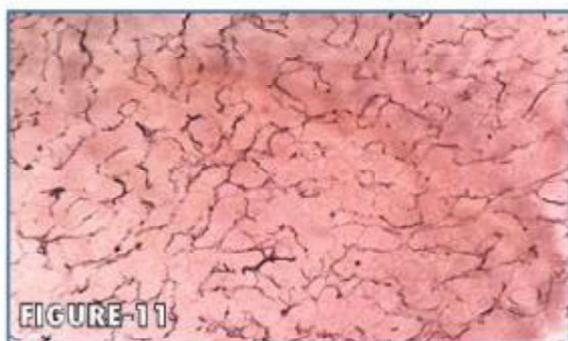


FIGURE-11

Reticulin Stain (40X)

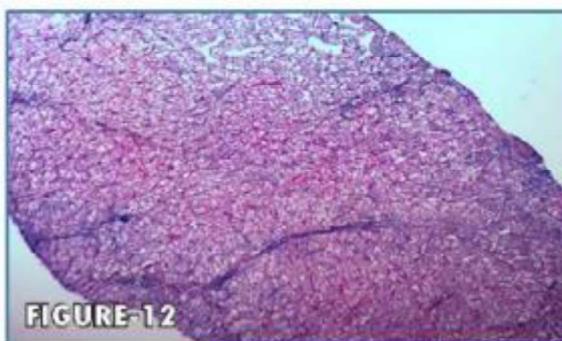


FIGURE-12

Masson Trichrome Stain (10X)

- Liver architecture normal. Mild steatosis and mild dilatation of sinusoids seen.
- Minimal fibrosis seen (Figure 11, 12).
- No evidence of cholestasis, bile duct proliferation or infiltration of chronic inflammatory cells.
- PAS+ve and Diastase -ve material within hepatocytes seen (Figure 9, 10).