Case Discussion in Medicine

Lady with A Lump in the Left Upper Abdomen

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The Case :

A nondiabetic non hypertensive 50 year old lady presented with a feeling of heaviness in the left upper abdomen for last few yearsand recent onset exertional dyspnoea. On examination, she had average build, moderate pallor, mild bipedal edema and massive splenomegaly. Her other clinical parameters were normal.

What are the differential diagnoses ?

Massive splenomegaly should be approached keeping in mind the following aetiology:

Infections – Kalaazar, hyperreactive splenomegaly syndrome

Haematological disorders – Thalassemia major, hairy cell leukaemia, Non Hodgkin Leukemia, Chronic Lymphoid Leukemia, Chronic Myeloid Leukemia, PolycythemiaVera, Myelofibrosis with myeloid metaplasia.

Portal Hypertension - Cirrhosis of liver, Non Cirrhotic Portal Hypertension (NCPH).

Inherited disorders – Gaucher's Disease

Our patient had no history of fever, recurrent blood transfusion, jaundice, encephalopathy, ascites or hematemesis.

On examination also there was no short stature, jaundice, lymphadenopathy, hepatomegaly, tortuous venous prominence over abdomen.

What directed investigations are to be ordered ?

Complete hemogram with peripheral blood smear – it showed moderate microcytic hypochromic anemia, leucopenia without any atypia or morphological abnormality in other cell lines.

Liver function test including P Time was normal ,RK 39 ,Malarial antigen, Hepatites B,C and HIV werenegative.HPLC was also normal.

USG Abdomen with doppler study revealed massive splenomegaly, mild hepatomegaly with normal echotexture, dilated portal vein (18mm) with portalcavernoma.Patent splenoportal axis and hepatic veinwere seen.

Upper GI endoscopy revealed small esophageal varices.

Liver biopsy showed phlebosclerosis in medium sized portal vessels and periportal fibrosis. There was no parenchymal necrosis or regenerative nodule.

A diagnosis of idiopathic noncirrhotic portal fibrosis was made.

What is non cirrhotic portal Fibrosis ?

It is an disease of small to medium branches of portal vein leading to portal hypertension in the absence of cirrhosis of liver. The liver function is primarily normal with a normal or mildly raised wedged Hepatic Venous Pressure Gradient (HVPG)[1].

Noncirrhotic Portal hypertension may be of two types namely, Extra Hepatic Portal Venous Obstruction (EHPVO) and Noncirrhotic Portal Fibrosis (NCPF/IPF).

NCPF/IPH is a disorder of young adults or middle aged women, whereas EHPVO is a disorder of childhood. Both disorders present with clinically significant PHT with preserved liver functions.While EHPVO results from an acute infection in neonatal period and affects the main portal vein, NCPF/IPF involves the smaller branches of portal vein.

Editor's Comment :

- **The approach to massive splenomegaly should encompass hematological, infectious,vascular and gastrointestinal etiologies.**
- **Patients of cirrhosis of liver will develop portal hypertension but all cases of portal hypertension do not have cirrhosis of liver.**
- **10-30% of variceal bleeding due to Non cirrhotic Portal Hypertension.**

Early age acute or recurrent infections in an individual with thrombotic predisposition constitute the likely pathogenesis. Similar illness is said to be associated with connective tissue disorders HIV infection, schistosomiasis and arsenicosis, drug intake like azathioprine, vinyl chloride or didanosine. Although Idiopathic Noncirrhotic Portal Hypertension (INCPH) has a worldwide distribution, it is particularly prevalent in Asia. It is more frequent in socioeconomically disadvantaged individuals[2,3,4].

Over 95% of patients have splenomegaly and it can cause left upper quadrantabdominal pain or fullness. Commonest presentation is variceal bleeding. Ascites is reported in up to 50 % of cases, and it usually develops in the context of precipitating factors such as variceal bleeding or infections. Generally, it is easily controlled with low dose of diuretics and resolution of the trigger. Features of hypersplenism may be present. Hepatic encephalopathy is a rare complication and it is also related to precipitating factors. There are anecdotic reports of hepatopulmonary syndrome, portopulmonary hypertension and hepatocellular carcinoma.

There is a lack of a specific positive test that leads to an INCPH diagnosis. The diagnosis of INCPH is a diagnosis of exclusion, based on the following previously reported criteria]: (1) presence of unequivocal signs of portal hypertension (eg, gastroesophageal varices, ascites, and/or splenomegaly); (2) absence of cirrhosis, advanced fibrosis or other causes of chronic liver diseases that can cause PH by appropriate serological, biochemical tests and liver biopsy and; (3) absence of thrombosis of the hepatic veins or of the portal vein at imaging studies performed at diagnosis. Histopathology reveals an obliterative portal venopathy, phlebosclerosis and periportal fibrosis[5].

In cirrhosis of liver, on the other hand, there is parenchymal necrosis with fibrosis and regenerative nodules. It is a sinusoidal

APASL criteria for NCPF/IPH :

1. **Presence of moderate to massive splenomegaly**
2. **Evidence of portal hypertension, varices, and/or collaterals**
3. **Patent spleno-portal axis and hepatic veins on ultrasound Doppler**
4. **Test results indicating normal or near normal liver functions**
5. **Liver histology - no evidence of cirrhosis or parenchymal injury**

type of portal hypertension with a raised HVPG. There is deranged liver function with progressive decompensation[6].

Management rests on control and prophylaxis of variceal bleeding. Prophylactic beta blocker therapy and endoscopic variceal ligation are the principal modalities of therapy. Surgical shunts are indicated in patients with failure of endotherapy, bleeding from sites not amenable to endotherapy, symptomatic hypersplenism or symptomatic biliopathy. In EHPVO, there are additional concerns of growth faltering, portal biliopathy, minimal hepatic encephalopathy and parenchymal dysfunction.Persistent growth failure, symptomatic and recurrent hepatic encephalopathy, impaired quality of life or massive splenomegaly that interferes with daily activities are other surgical indications[7,8].

Overall, prognosis is generally better than in patients with cirrhosis and a similar degree of portal hypertension. This may be due to the fact that most INCPH patients have well preserved liver function. However, a small subgroup of patients will develop liver failure and will require liver transplantation.

References

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Causes of Non cirrhotic Portal Hypertension :

Pre Hepatic:
- **i) Extrahepatic portal vein obstruction**
- **ii) Portal Vein thrombosis**
- **iii) Splenic Vein thrombosis**
- **iv) Infiltrative Disorders**

Hepatic:
- **i) Pre-sinusoidal**
  - **a) Congenital Hepatic Fibrosis**
  - **b) Primary biliary cirrhosis**
  - **c) Sclerosing Cholangitis**
  - **d) Neoplastic occlusion of portal vein**
  - **e) Granulomatous lesion – schistosomiasis, sarcoidosis**
- **ii) Sinusoidal**
  - **a) Drugs (methotrexate, amiodarone)**
  - **b) Toxins (Vinyl Chloride, copper)**
  - **c) Metabolic (NASH, Gaucher's)**
  - **d) Inflammatory (viral hepatits, Q fever)**
- **iii) Post sinusoidal**
  - **a) Veno-occlusive disorders**

Post hepatic :
- **i) Inferior Vena cava obstruction**
- **ii) Tricuspid Regurgitation**
- **iii) Severe Right sided heart failure**
- **iv) Constrictive Pericarditis**

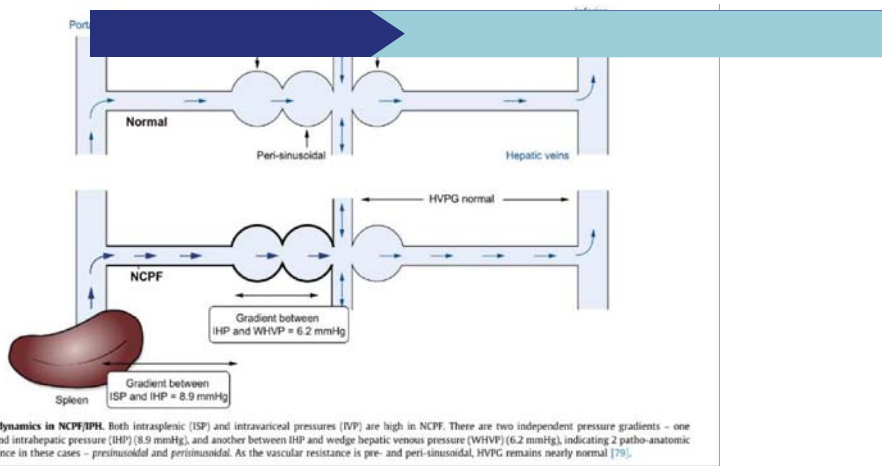

Fig. 3. Hemodynamics in NCPF/IPH. Both intrasplenic (ISP) and intravariceal pressures (IVP) are high in NCPF. There are two independent pressure gradients – one between ISP and intrahepatic pressure (IHP) (8.9 mmHg), and another between IHP and wedge hepatic venous pressure (WHVP) (6.2 mmHg), indicating 2 patho-anatomic sites of resistance in these cases – *presinusoidal* and *perisinusoidal*. As the vascular resistance is pre- and peri-sinusoidal, HVPG remains nearly normal [79].

Learning Points :

- **NCPF is an obscure disease of small to medium branches of portal vein**
- **There is presinusoidal portal hypertension in the absence of cirrhosis of liver.**
- **The liver function is more or less preserved.**
- **The HVPG is normal or mildly raised.**
- **NCPF may idiopathic or secondary to connective tissue disorder, infection, drugs or toxins.**
- **Common presentation is upper G I bleed and splenomegaly.**
- **Diagnosis is by exclusion and confirmed by histopathology.**
- **Control and prophylaxis of variceal bleeding is the mainstay of therapy.**
- **Decompensation is transient and easily managed.**