Cholangiocarcinoma Presenting with Recurrent Venous Thrombosis

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Abstract
A 38 years female presented with three episodes of venous thrombosis over one year - first in left femoral vein, next in splenic vein causing haematemesis and melena and lastly in inferior vena cava causing Budd-Chiari syndrome. During third episode, endoscopic cholangiopancreatography and guided biopsy established a diagnosis of cholangiocarcinoma at the mid portion of common bile duct. The disease was far advanced with cervical lymph node metastasis.

Recurrence venous thrombosis though common with adenocarcinoma, reported rarely with cholangiocarcinoma in literature. We report a case of cholangiocarcinoma of common bile duct presented with multiple venous thrombosis at unusual sites.

Case Report
A 38 years female went to her doctor in December 2000 with complaints of pain and swelling of left lower limb. On examination, she had posterior calf tenderness, swelling of left lower limb with increased tissue turgor. She was diagnosed to be having deep vein thrombosis of left femoral vein, and put on subcutaneous heparin followed by oral warfarin which she continued for next one month. Routine investigations and abdominal ultrasound were normal. She remained asymptomatic for next three months. In April 2001; she came to our hospital and history of two episodes of haematemesis over last one week along with continuous passage of black tarry offensive stool. Examination did not reveal any abnormality except mild pallor and splenomegaly. Routine investigations were normal except stool examination showed presence of occult blood. Upper gastrointestinal endoscopy showed presence of gastric varix without any esophageal varix. Abdominal ultrasound revealed splenic vein thrombosis. Hepatic echotexture, portal-biliary system, portal veins, hepatic veins were normal. Liver function tests and chest radiography were normal. Serology for hepatitis B, hepatitis C, anti-nuclear factor was negative. Abdominal ultrasound showed hepatomegaly with homogenous echotexture and non-dilated intra-hepatic biliary radicals. Gall bladder was distended without any mass of calculus within it. Extrahepatic bile ducts were marginally dilated with abrupt termination at the lower half of common bile duct. Multiple thrombi were visualized inside the portal vein, splenic vein and intrahepatic portion of inferior vena cava. Doppler confirmed presence of thrombotic occlusion. Endoscopy revealed gastric varix. ERCP demonstrated a growth in the common bile duct, partially occluding the lumen, midway between its formation and termination. Pancreatic duct was cannulated and was normal. Punch biopsy revealed cholangiocarcinoma with excessive stromal desmplasia. Cervical lymph node biopsy showed mucus secreting adenocarcinoma metastatic to lymph node. Coagulation profile and stool examination was normal. Patient refused any form of therapy.

Discussion
Cholangiocarcinoma represents approximately 25% of
hepatobiliary cancers affecting individuals between 50-70 years of age with a male preponderance.\textsuperscript{1} There is strong association with certain risk factors like Caroli’s disease, choledochal cyst, clonorchiasis, hepatolithiasis, sclerosing cholangitis, thorotrust, etc. Patients present with jaundice (90%), pruritus, weight loss, abdominal pain (vague, non-specific), cholangitis (rare) and usually have jaundice, hepatomegaly, palpable gall bladder in varying combination. Fever, ascites and extrahepatic metastasis are less common.\textsuperscript{2}

Hematological changes in disseminated malignancy include increase in production of blood cells and enhanced thrombotic tendencies. The last one may be due to host response to malignancy (causing increased production of tumour necrosis factor and interleukin-1, downregulation of activated protein C or decreased activity of tissue factor pathway inhibitor) or due to cancer itself (by increased liberation of tissue factor or release of cancer procoagulant stimulating the activity of activated factor Xa). Cancers of the gastrointestinal tract, liver, pancreas, lung, breast and kidney are implicated in causation of venous thrombosis in different or atypical sites. Adenocarcinomas are particularly notorious. Episodes of venous thrombosis may predate the malignancy by several years.\textsuperscript{3}

The illness in our patient evolved through three phases. Initially she had deep vein thrombosis in left lower limb which was treated and patient responded. In second phase she presented with bleeding from gastric varices which developed as a result of splenic vein thrombosis. Routine investigations could not reveal the cause for such thrombosis. Ultimately, patient presented with features of Budd-Chiari syndrome due to inferior vena cava thrombosis and by this time malignancy was evident by both local symptoms and metastatic manifestation. Thus the entire profile of the patient was unusual for a cholangiocarcinoma which usually presents with local symptoms, but here presented with recurrent venous thrombosis at different sites. There is a single case report of Budd-Chiari syndrome in cholangiocarcinoma.\textsuperscript{4} In addition, this patient had three atypical features - developed this malignancy at the age of 38 years without any predisposing risk factor, had peripheral blood eosinophilia and had metastasis to the cervical lymph nodes without any detectable local or regional nodal enlargement.

**References**


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**Erratum**

Obituary published in J Assoc Physicians India, 2003; 51 : 654. The date written below the photograph is wrongly printed.

It should be read as (3.10.1913 - 5.6.2003) instead of (3.10.1013 - 5.6.2003).

Sd/-

Hon. Editor