Status of Vascular Involvement in Egyptian Patients with Budd-Chiari Syndrome: Relation to Etiology and Impact on Clinical Presentation

Thesis

Submitted for Partial Fulfillment of Master Degree
in Tropical Medicine

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List of abbreviations

Abbrev.	Meaning
ACAs	Anticardiolipin Antibodies
ACL IgG	Anticardiolipin IgG
ACL IgM	Anticardiolipin IgM
ANA	Anti nuclear antibody
APAs	Antiphospholipid antibodies
APC	Activated protein C
APCR	Activated protein C resistance
APS	Antiphospholipid syndrome
AT III	Antithrombin III
BCS	Budd-Chiari syndrome
BD	Behcet Disease
BM	Bone marrow
DVT	Deep venous thrombosis
FV	Facor V
FVa	Acivated factor V
FVLM	Factor V Leiden mutation
HCC	Hepatocellular carcinoma
Hetero	Heterozygous
Homo	Homozygous
HVO	Hepatic venous obstruction
HVOO	Hepatic venous outflow obstruction
HVs	Hepatic veins
IVC	Inferior vena cava

IVCO	inferior vena cava obstruction
IVCT	inferior vena cava thrombosis
JAK2	Janus tyrosine kinase-2
LAC	Lupus Anticoagulant
LCF	Liver cell failure
LHV	Left hepatic vein
LMWH	Low molecular weight heparin
MHV	Middle hepatic vein
MOVC	Membranous obstruction of IVC
MPDs	Myeloproliferative disorders
MTHFR	Methylene tetra hydro-folate reductase
OCPs	Oral Contraceptive Pills
PC	Protein C
PGM	Prothrombin gene mutation
PNH	Paroxysmal nocturnal hemoglobinuria
PS	Protein S
PV	Portal vein
PVT	Portal vein thrombosis
RHV	Right hepatic vein
SD	Standard deviation
SLE	Systemic lupus erythematosus
TIPS	Transjugular Intrahepatic Portosystemic Shunt
VOD	Veno-occlusive disease
VTE	Venous throboembolism
WHO	World Health Organization

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Introduction:

Budd-Chiari syndrome (BCS) is a rare but potentially life threatening hepatic disorder that results from obstruction of the hepatic venous outflow tract. Obstruction can occur at any level from the hepatic venules to the right atrium ***(Khan, 2005 and Valla, 2009).***

George Budd (1845), a British internist, described three cases of hepatic vein thrombosis due to abscess-induced phlebitis, and ***Hans Chiari (1899)*** an Austrian pathologist, added the first pathologic description in three additional cases of hepatic vein occlusion due to phlebitis. Inferior Vena Cava (IVC) involvement was present in one of the three cases ***(Musa et al., 2007).***

According to the etiology, BCS can be classified as primary (due to intrinsic intraluminal thrombosis or webs) or secondary (due to intraluminal invasion by a parasite or malignant tumor or extraluminal compression by an abscess, cyst or solid tumor) ***(Aydinti & Bayraktar, 2007).***

Hepatic venous outflow obstruction causes centrilobular congestion and hepatocyte necrosis, which if not treated can lead to hepatic lobulation and cirrhosis. The evolution and severity of these changes vary widely and depend upon the cause, degree and extent of obstruction. Thus, the clinical presentation of BCS has a wide spectrum

and ranges from asymptomatic cases to fulminant hepatic failure ***(Menon et al., 2004).*** The classic triad of abdominal pain, ascites, and hepatomegaly is nonspecific ***(Roy, 2006).***

According to duration of symptoms and signs of liver disease, BCS can be presented in acute, subacute or chronic form; the most common presentation is the chronic form. A high index of suspicion is necessary for diagnosis because clinical manifestations and laboratory results are non specific ***(Valla, 2002).***

Radiological imaging plays an important role in the evaluation of a patient suspected to have BCS. In fact, under current consensus recommendations, radiological imaging is sufficient to make a diagnosis of BCS. A liver biopsy is required only if radiological imaging is inconclusive. The relevant imaging modalities are Doppler ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI) and hepatic venography ***(Kamath, 2006).***

Classification of BCS according to site of obstruction *(Ludwig et al., 1990).*

Designation	Definition
Small hepatic veins	Veins that cannot be shown clearly on hepatic venograms or by ultrasound studies; they include intercalated veins and interlobular veins.
Large hepatic veins	Veins that are regularly demonstrable on hepatic venograms and ultrasound studies; segmental branches of hepatic veins are generally included
Inferior vena cava (IVC)	A segment of the IVC which extends from the entry level of the right, middle and left hepatic veins to the junction between the IVC and the right atrium
Combined obstruction	Combination of obstruction in the large hepatic veins and IVC

The site of obstruction is in general easily determined through non-invasive imaging (Doppler-ultrasound, magnetic resonance (MRI), computed tomography (CT)) or conventional venography ***(Janssen et al., 2003).***

Recently, BCS has been classified according to the site of venous obstruction into 3 types and 6 subtypes ***(Zhang and Li, 2007):***

Type I: "IVC lesions":

a: Membranous lesions.

b: Short segmental occlusion (<5cm).

c: Long segmental occlusion (>5cm).

Type II: "lesions of HVs":

a: Membranous lesions.

b: Diffuse occlusion.

Type III:

Mixed type (type I & II).

The goals of treatment are to prevent extension of thrombosis in the hepatic veins and to alleviate venous obstruction in order to decrease hepatic congestion. Few patients respond to medical treatment (anticoagulation with or without thrombolytic therapy, diuretics). However, most of patients need more invasive procedures to restore the hepatic blood flow including percutaneous angioplasty with or without stenting, transjugular intrahepatic portosystemic shunt (TIPS) or shunt surgery ***(Slakey et al., 2001).***

Aim of the Work:

Primary Aim: To study the pattern of vascular involvement in Egyptian patients with BCS.

Secondary Aim: To demonstrate its relation to etiology and impact on clinical presentation in these patients.