Involvement of Inferior Vena Cava in Egyptian Patients with Budd-Chiari Syndrome: Frequency, Relation to Etiology, and Impact on Clinical Presentation

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By

Mohamed Gaber Mohamed Hassan

M.B.B.Ch.
Al-Azhar University

Under Supervision of

Prof. Dr. Mohammad Amin Sakr
Professor of Tropical Medicine
Faculty of Medicine-Ain Shams University

Prof. Dr.Ahmad Kamal El Dorry
Professor of Radiodiagnosis
Faculty of Medicine-Ain Shams University

Dr. Sara Mahmoud Abd El-Hakam
Lecturer of Tropical Medicine
Faculty of Medicine-Ain Shams University

Faculty of Medicine
Ain Shams University

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بسم الله الرحمن الرحيم

{قَالُوا سُبْحَانَكَ لا عِلْمَ لَنَا إِلاَّ مَا
عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ}

صدق الله العظيم
(البقرة:32)

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LIST OF ABBREVIATIONS

Abbrev.	Meaning
ACAs	Anticardiolipin Antibodies
ACL IgG	Anticardiolipin IgG
ACL IgM	Anticardiolipin IgM
ALB	Albumin
ALP	Alkaline phosphatase
ALT	Alanin amino-transferase
AMM	Agnogenic myeloid metaplasia
ANA	Anti nuclear antibody
APAs	Antiphospholipid antibodies
APC	Activated protein C
APCR	Activated protein C resistance
APS	Antiphospholipid syndrome
APTT	Activated partial thromboplastin time
AST	Aspartate amino-transferase
AT III	Antithrombin III
BCS	Budd-Chiari syndrome
BD	Behcet Disease
BM	Bone marrow
BUN	Blood urea nitrogen
CD	Color Doppler
CDUS	Color Doppler ultrasound
CML	Chronic Myelogenous leukemia
CT	Computed Tomography
DB	Direct bilirubin
DSV	Digital subtraction venography
DVT	Deep venous thrombosis
ELTA	European liver transplant association
ESR	Erythrocyte sedimentation rate
FISH	Fluorescent in-situ hybridization
FV	Facor V
FVa	Acivated factor V
FVLM	Factor V Leiden mutation
Hb	Hemoglobin
HCC	Hepatocellular carcinoma
Hetero	Heterozygous
Homo	Homozygous
HVOO	Hepatic venous outflow obstruction
HVs	Hepatic veins
INR	International normalized ratio
IVC	Inferior vena cava

LIST OF ABBREVIATIONS

Abbrev.	Meaning
IVCO	inferior vena cava obstruction
IVCT	inferior vena cava thrombosis
JAK2	Janus tyrosine kinase-2
LA	Lupus Anticoagulant
LAP	Leukocyte alkaline phosphatase
LCF	Liver cell failure
LF	Liver cell failure
LHV	Left hepatic vein
LMWH	Low molecular weight heparin
MF	Myelofibrosis
MHV	Middle hepatic vein
MOVC	Membranous obstruction of IVC
MPDs	Myeloproliferative disorders
MRI	Magnetic resonance imaging
MRV	Magnetic resonance venography
MSCT	Multislice CT
MTHFR	Methylenetetrahydro-folate reductase
OCPs	Oral Contraceptive Pills
PC	Protein C
PCR	Polymerase chain reaction
PGM	Prothrombin gene mutation
PLT	Platelets
PNH	Paroxysmal nocturnal hemoglobinuria
PS	Protein S
PT	Prothrombin time
PTFE	Polytetrafluoroethylene
PTT	Partial thromboplastin time
PV	Portal vein
PCV	Polycythemia vera
PVT	Portal vein thrombosis
RHV	Right hepatic vein
SAAG	Serum-ascites albumin gradient
SD	Standard deviation
SLE	Systemic lupus erythematosus
TB	Total bilirubin
TIPS	Transjugular Intrahepatic Portosystemic Shunt
VOD	Veno-occlusive disease
VTE	Venous throboembolism
WBCs	White blood cells
WHO	World Health Organization

INTRODUCTION

Budd-Chiari syndrome (BCS) is a structural and functional abnormality of the liver caused by obstruction of the hepatic venous outflow from its origin in the hepatic sinusoids till the final drainage in the right atrium ***(Fu et al., 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).***

BCS can be classified as primary when obstruction of the hepatic venous outflow tract is the result of an endoluminal venous lesion (thrombosis or web). It is considered secondary when the obstruction results from the presence in the lumen of material not originating from the venous system (malignant tumor or parasite invading the lumen) or from external venous compression (abscess, cyst or solid tumor) ***(Okuda et al., 1998).***

External venous compression can be complicated by thrombosis, particularly when prothrombotic factors are present by chance (inherited thrombophilia) or by

association (inflammatory response secondary to an adjacent abscess) ***(Janssen et al., 2003).***

The risk factor leading to the occurrence of thrombosis could be recognized in more than 90% of cases with proper investigations ***(Valla et al., 2003).*** Obstruction of the hepatic venous outflow tract is classified according to its location: small hepatic veins, large hepatic veins, inferior vena cava (IVC) and combined obstruction of large hepatic veins and inferior vena cava ***(Ludwig et al., 1990).***

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

Designation	**Definition**
Small hepatic veins	Veins that can not 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).

BCS is commonly presented by classic triad of abdominal pain, tender hepatomegaly and ascites, but if IVC is involved, leg edema, fever, marked dilated veins over the trunk and ulcers in the peri-tibial areas difficult to heal may also be present ***(Okuda, 2002).***

Unlike the West, where isolated hepatic vein thrombosis is responsible for a majority of cases with BCS, in Africa and Asia, isolated IVC obstruction is the commonest cause of BCS. In various series, isolated IVC accounted for 39–78% of patients with BCS; on the other hand associated IVC obstruction with hepatic vein occlusion accounted for 60% patients with BCS. Hepatic vein thrombosis is commonly due to an underlying hypercoagulable state and presents more often with an

acute illness. In contrast, BCS due to IVC obstruction, also known as obliterative hepatocavopathy or membranous obstruction of IVC is frequently idiopathic and is associated with a milder, more chronic disease (***Vivek et al., 2009***).

Although less common in western countries, primary membranous obstruction of the IVC is the most common cause of BCS in South Africa and Asia, and is thought to be a consequence of IVC thrombosis ***(Okuda, 2002).*** For unknown reasons, 44-49% of patients with known membranous occlusion ultimately develop hepatocellular carcinoma (HCC), even in the absence of cirrhosis ***(Simson, 1982).*** On the other hand, HCC has not been reported to be a complication of hepatic vein thrombosis, except in Behcet's disease-associated BCS ***(Bayraktar et al., 1998).***

Membranous obstruction of the IVC (MOVC) was described at the first time by ***Nagayo 1909*** in Japanese patients and the term was first used by ***Bennett 1950***. It was reported to be the most common cause of BCS accounting for one-third of cases in Asian countries, including Taiwan, China, Japan and India, and also in South Africa ***(Wei et al., 2001).***

Thrombosis of the IVC occurs in association with various systemic and local diseases such as vasculitis, infection, malignancy, etc, but idiopathic thrombosis at the

hepatic portion of the IVC is the most common, particularly in developing countries. A major question or focus of interest is why the hepatic and supra-hepatic portion of the IVC is predisposed to thrombosis. It has been suggested that the respiratory movement of the diaphragm and coughing cause microscopic damage to the endothelial lining of the IVC. Turbulence also caused by the hepatic vein flow perpendicular to the IVC may contribute to thrombus formation in this part of the IVC ***(Okuda, 2002).***

An epidemiological survey conducted by a national study group in 1989 in Japan suggested the existence of about 300 patients with BCS, only 9 patient (5.7%) had hepatic vein thrombosis, and the remaining patients had IVC obstruction ***(Okuda, 2002).***

A previous study at Mayo clinic showed that IVC obstruction was very rare in the United States compared to developing countries ***(Okuda, 2002).***

In India, peri-caval filariasis was considered to be an important factor for inducing IVC thrombosis. Hypercoagulable conditions previously mentioned in BCS were observed in only a few cases of IVC thrombosis ***(Okuda, 2002).***