ROLE OF ASCITIC FLUID COMPLEMENT 3 IN SPONTANEOUS BACTERIAL PERITONITIS

Thesis

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بسم الله الرحمن الرحيم

"يُؤْتِي الْحِكْمَةَ مَنْ يَشَاءُ وَمَنْ يُؤْتَ الْحِكْمَةَ فَقَدْ أُوتِيَ خَيْراً كَثِيراً وَمَا يَذَّكَّرُ إِلاَّ أُولُو الْأَلْبَابِ"

صدق الله العظيم

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Abstract

Ascites is the most common complication in patients with decompensated cirrhosis. Patients with cirrhosis and ascites show higher susceptibility to bacterial infections mainly because of the inadequate defense mechanisms. The most frequent and most severe one being spontaneous bacterial peritonitis (SBP). Prevalence of spontaneous bacterial peritonitis in cirrhotic patients with ascites is as high as 18%, with 40–70% associated mortality. Spontaneous bacterial peritonitis is probably related to several impaired defense mechanisms, such as depressed reticuloendothelial system, phagocytic activity, leukocyte dysfunction, reduced serum complement, and low bactericidal activity of ascitic fluid. Ascitic fluid complement 3 (C3) concentration and opsonic activities are important protective factors against SBP. The C3 component of complement tends to be reduced in cirrhosis .Patients with reduced ascitic fluid C3 concentration and reduced opsonic activities have been shown to be predisposed to SBP.

In our study, we evaluated the role of ascitic fluid complement 3 (C3) in SBP.

This was an analytic case control study on 100 patients which have liver cirrhosis, ascites at the age group of 40 to 75 years old They were 65 males and 35 females. Patients were divided into 2 groups:

Group A: 50 patients with cirrhotic ascites complicated by spontaneous bacterial peritonitis(ascitic fluid neutrophilic count>250 cells/mm^3).

#Group B: 50 patients with cirrhotic ascites not complicated by spontaneous bacterial peritonitis. Breif clinical assessment was done and CBC, PT, PC , Total protein &albumin, AST, ALT, FBS, PPBS, urea&creatinine , LDH were measured at the Serum. An ascitic fluid sample for C3, ascitic fluid culture, PMNLs, LDH and Total proteins & albumin was taken. Our results showed that: There is a statistically significant difference in the level of ascitic C3 between the two groups where ascitic C3 is lower in group A than group B with P value < 0.001. We concluded that the role of ascitic fluid C3 in the local defense against bacterial infection of ascitic fluid in cirrhotic patients. Ascitic fluid C3 is significantly reduced in cirrhotic patients with SBP. Prompt antibiotic therapy can be considered in cirrhotic patients with low ascitic fluid C3 level as a prophylactic measure against SBP. Also, ascitic fluid culture by the conventional method is significant but of low sensitivity, ascitic PMNLs was highly significant in diagnosis of SBP in cirrhotic patients.

Keywords:

Ascitic fluid complement 3, liver cirrhosis, Ascites, spontaneous bacterial peritonitis

Contents

List of Abbreviations

Ab	Antibody
ADH	Anti-diuretic hormone
A.F	Ascitic Fluid
AFB	Acid-Fast Bacilli
AFIs	Ascitic Fluid Infections
Ag	Antigen
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
AP	Alternative Pathway
APC	Antigen Presenting Cells
AST	Aspartate Aminotransferase
BA	Bacterascites
BT	Bacterial Translocation
Bp	Binding protein
C3	Complement 3
CAH	Chronic active hepatitis
CBC	Complete blood count
CNNA	Culture Negative Neutrocytic Ascites
CP	Classical Pathway
COPD	Chronic obstructive pulmonary disease
CoPV	Cobra venom factor
CT	Computed Tomography
DAF	Decay-accelerating factor
dl	Deciliter
DNA	Deoxyribonucliec acid
EDTA	Ethylene diamine tetra acitic acid
FBS	Fasting blood sugar
FHF	Fulminant hepatic failure
GALT	Gut-Associated Lymphoid Tissue
GFR	Glomerular filtration rate
GGT	Gamma-glutamyl transpeptidase

HBV	Hepatitis B virus
HCC	Hepato cellular carcinoma
HCV	Hepatitis C virus
HIV	Human Immunodeficiency Virus
HRF	Homologus restriction factor
HRP	Horseradish peroxidase
Ig	Immunoglobulin
IL	Interleukin
IV	Intravenous
L	Litter
LDH	Lactate Dehydrogenase
LP	Lectin Pathway
M cells	Macrophage cell
MAC	Membrane Attack Complex
MASP	Mannan-Binding Lectin associated Serine Protease
MBL	Mannan-Binding Lectin
MC	Mixed Cryoglobulinaemia
mg	Milligram
MLN	Mesentric Lymph Nodes
MNB	Monomicrobial non Neutrocytic Bacterascites
NeF	Nephritic factor
NO	Nitric Oxide
NSAIDs	Non steroidal anti inflammatory drugs
P	Properdin
PAMP	Pathogen-Associated Molecular Pattern
PBC	Primary-biliary cirrhosis
PC	Prothrombin concentration
PD	Peritoneal dialysis
PMNL	Polymorphonuclear Leucocytes
PPBS	Post prandial blood sugar
PRR	Pattern Recognition Receptor
PT	Prothrombin Time
PVS	Peritoneovenous shunt

SAAG	Serum Albumin-Ascitic fluid albumin Gradient
SBEM	Spontaneous bacterial empyema
SBP	Spontaneous Bacterial Peritonitis
SLE	Systemic lupus erythrematosis
SRBC	Sheep Red Blood Cell
TB	tuberculosis
TCC	Terminal complement complex
TIPS	Transjugular Intrahepatic Portosystemic Shunt
TLC	Total leucocytic count
TLR	Toll like receptor
TNF	Tumor necrosis factor
TP	Terminal Pathway
WBC	White blood cells

List of Tables

List of Figures

INTRODUCTION

Cirrhosis represents a late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules. It is generally considered to be irreversible in its advanced stages, at which point the only treatment option may be liver transplantation **(Asrani SK et al, 2013).**

Ascites (fluid retention in the abdominal cavity) is the most common complication of cirrhosis. It is associated with a poor quality of life, increased risk of infection, and a poor long-term outcome, this may be visible as increase in abdominal girth **(Dan et al, 2012)**

Spontaneous bacterial peritonitis (SBP) is defined as an acute bacterial infection of ascitic fluid despite the absence of an obvious source for the infection **(Lata Jet al., 2009).**

The presence of SBP, which almost always occurs in patients with cirrhosis and ascites, is suspected by signs and symptoms, such as fever, abdominal pain, or altered mental status or hypotension , though some patients are asymptomatic and are detected when they undergo paracentesis after being admitted to the hospital for another reason.A low clinical suspicion for SBP does not obviate the need for testing **(Chinnock et al, 2013).**

Spontaneous bacterial peritonitis is probably related to several impaired defense mechanisms, such as depressed

reticuloendothelial system phagocytic activity, leukocyte dysfunction, reduced serum complement, and low bactericidal activity of ascitic fluid **(Yildirim B, Sari R, Sezgin N**, **2002).** Ascitic fluid complement 3 (C3) concentration and opsonic activities are important protective factors against SBP. The C3 component of complement tends to be reduced in cirrhosis **(Sherlock S, Dooley J**, **2002)** and patients with reduced ascitic fluid C3 concentration and reduced opsonic activities have been shown to be predisposed to SBP **(Garcia Tsao G, 2005)**.

This study was designed with the aim to compare the level of ascitic fluid C3 concentration in cirrhotic patients with and without spontaneous bacterial peritonitis (SBP), to determine its possible protective role against this infection.

AIM OF THE WORK

To compare the level of ascitic fluid C3 concentration in cirrhotic patients with and without spontaneous bacterial peritonitis to determine its possible protective role against acquiring infection.

ASCITES

Définition:

Ascites **"Ascites" Dictionary.com: Oakland, 2010).**

Is a gastroenterological term for an accumulation of fluid in the peritoneal cavity. These medical condition is also known as peritoneal cavity fluid, peritoneal fluid excess, hydroperitoneum or more archaically as abdominal dropsy.

Eighty percent of cases of ascites are caused by hepatic diseases, in the remaining 20%, cancer, inflammation, pancreatic, renal or cardiac disease can be found **(Hwangbo et al., 2007).**

Etiology:

The cause of ascites may be classified pathophysiolo-gically into ascites with normal peritoneum and ascites with diseased peritoneum **(Hwangbo et al., 2007).**

A) Causes of Ascites with Normal Peritoneum:

1) Portal hypertension:

- Cirrhosis.
- Hepatic fibrosis.
- Congestive heart failure.
- Budd-Chiari syndrome.
- Portal vein occlusion.
- Constrictive pericarditis.