Cirrhotic Retinopathy

essay

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Dedication

I would like to dedicate this essay to my family, namely, my mother, my father, my wife,my kids,my brother and my sister for their patience, support and help.

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List of Abbreviations:

Abbreviation	Meaning
AIDS	Acquired immunodeficiency syndrome.
ALT	Alanine transaminase.
AST	Aspartate transaminase.
AMP	Adenosine monophosphate.
CRALBP	Cellular retinaldehyde binding protein.
ERG	Electroretinogram.
GABA	Gamma amino butyric acid.
GFAP	Glial fibrillary acidic protein.
GLAST	Glutamate/ aspartate transporter.
GLUT	Glucose transporters.
GS	Glutamine synthetase.
HBV	Hepatitis B virus.
HCC	Hepatocellular carcinoma.
HCV	Hepatitis C virus.
HIV	Human immunodeficiency virus.
ILM	Inner limiting membrane.

INF- α	Interferon Alfa.
Kir	Inwardly rectifying K+ channel.
LDL	Low density lipoproteins.
MCT2	monocarboxylate transporter.
mfERG	Multifocal electroretinogram.
NASH	Non alcoholic steatohepatitis.
PAT	Parentral antischistosomal therapy.
PCR	Polymerase chain reaction.
RBP	Retinol binding protein.
RNFL	Retinal nerve fiber layer.
RPE	Retinal pigment epithelium.
SVR	Sustained viral response.
TIPSS	Transjugular intrahepatic portosystemic stent shunt.
WHO	World Health Organization.

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Introduction

Cirrhosis is a complication of many liver diseases that is characterized by destruction of the hepatocytes and their replacement with fibrous scar tissue that disrupts many important liver functions. The remaining viable cells multiply in an attempt to replace the destroyed cells. This results in clusters of newly-formed liver cells (regenerative nodules) within the scar tissue***. (Chow and Chow, 2006)***

There are many causes of cirrhosis; such as viruses, chemicals (alcohol, fat, and certain medications), toxic metals (iron and copper), and autoimmune liver disease. ***(Schuppan and Afdhal, 2008)***

World Health Organization.(WHO) estimates that about 3% of the world's population has been infected with Hepatitis C virus (HCV)and that there are more than 170 million chronic carriers who are at risk of developing liver cirrhosis and/or liver cancer.

Interferon Alfa(INF-alpha) therapy has been known to cause a variety of ocular lesions. Typical lesions include cotton-wool spots and retinal haemorrhages at the posterior fundus, particularly around the optic disc, secondary to retinal ischaemia, which usually appear within 3 months of the onset of therapy. ***(Ansari et al, 2010)***

Clinically, the ophthalmic pathologies of cirrhosis involve xerophthalmia and night blindness since liver is the organ where vitamin A is deposited. Vitamin A deficiency is a well-documented state in alcoholic cirrhosis. Colour blindness may be seen especially in alcoholic type ***(Ondre et al., 2005)***, and fundus picture may show exudates and

haemorrhage.

Cirrhotic retinopathy is suggested to be caused by the high level of serum ammonia in patients with liver insufficiency. The primary pathological alterations are found in Müller cells. These changes are thought to be associated with severe edema and necrosis of Müller cells ***(Reichenbach et al., 1995b),*** accompanied by reductions in the amplitudes of the scotopic a- and b-waves of the electroretinogram. ***(Eckstein et al., 1997)***

A study including patients with liver cirrhosis underwent routine ophthalmological examination and Electroretinogram(ERG) before and after successful liver transplantation. Laboratory parameters, including ammonia, aspartate aminotransferase (AST), bilirubin and cholinesterase, were compared. The data from that study suggests the recovery of Müller cells from cirrhotic retinopathy. ***(Uhlmann et al., 2003)***

Aim of the Work

The aim of this study is to review the effect of liver cirrhosis and its treatment on the retina and whether these changes are reversible or not.

Liver cirrhosis

Cirrhosis is the final stage attained by various chronic liver *diseases after years or decades of slow progression. There are, however, ways to prevent cirrhosis, because the diseasesthat most commonly lead to it progress slowly, and measures are available to prevent and treat them.Moreover, most cases of hepatocellular carcinoma (HCC) arise in a cirrhotic liver, so cirrhosis prevention is, in fact, also HCC prevention. The risk of developing HCC depends on the underlying disease:It is low, for example, when the underlying disease is autoimmune hepatitis(2.9% in 10 years)* ***(Manns MPet al. 2010.),*** *and high when the underlying disease is chronic hepatitis B with a viral burden greater than* 10^7 *copies/mL (19.8% in 13 years)* **(*Chen CFet al. 2011.).*** *Aside from chronic viral hepatitis, fatty liver disease due to any of the very common underlying disorders (obesity, diabetes, alcohol abuse) commonly progresses to cirrhosis and thus merits both specialized medical treatment and close* follow-up by the primary-care

The etiology of cirrhosis

Cirrhosis can arise in consequence of an exogenous/toxic, infectious, toxic/allergic, immunopathological/autoimmune, or vascular process or an inborn error of metabolism. The commonest causes of cirrhosis in Germany are alcoholic and non-alcoholic fatty liver disease and viral hepatitis (B or C). Cirrhosis is rising in importance as a public health problem.

the number of deathsfrom cirrhosis per 100 000 population doubled from 5 in 1980 to 9.9 in 2005 ***(StatistischesBundesamt. Todesursachenstatistik. Gesundheitsberichterstattung des Bundes 2011.).***

Autopsy studies have revealed fatty liver disease in 70% of overweight persons and in 35% of persons of normal weight. They have also revealed cirrhosis in 18.5% of overweight diabetics***(Neuschwander-Tetri BA et al., 2003).***

Cirrhosis and HCC due to chronic hepatitis C are among the main indications for liver transplantation in Western industrialized countries. From 1988 to 2010, viral hepatitis was the underlying cause of liver disease in 39% of liver transplant recipients—hepatitis B in one-third of cases, and hepatitis C in two-thirds***(European Liver Transplant Registry. 2012.).***

The diagnosis of liver cirrhosis

Cirrhosis is histologically characterized by fibrous septa between the portal

fields; it comes in micro- and macronodular forms***(Schuppan D, Afdhal NH et al.,2008).*** The condition is diagnosed by its characteristic findings on clinical examination, laboratory tests, and ancillary studies.

The typical findings in cirrhosis include

- cutaneous signs of liver disease,
- a firm liver on palpation, and
- certain risk constellations such as:
  – metabolic syndrome
  – heavy alcohol consumption
  – exposure to hepatotoxic substances
  – use of hepatotoxic medications***(Berg T. et al.,2009).***

The early signs of cirrhosis in B-ultrasonography include inhomogeneity of the hepatic tissue, irregularity of the hepatic surface, or enlargement of the caudate lobe. Portal hypertension leads to splenomegaly.

In advanced liver disease approaching the stage of cirrhosis, thrombocytopenia is seen, along with impaired hepatic biosynthesis (as shown by, e.g., low concentration of albumin and cholinesterase and an elevation of the international normalized ratio [INR]) and impairment of the detoxifying function of the liver (as shown by, e.g., elevated bilirubin concentration). The transaminase concentrations are generally in the normal range or only mildly elevated***(Berg Tet al.,2009).***There is no well-defined threshold value of any laboratory test that can be used to determine when screening for cirrhosis should be performed.