بسم الله الرحمن الرحيم

شبكة المعلومـــــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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CLINICAL AND BIOCHEMICAL SURVEY OF INTERFERON RESPONSE IN EGYPTIAN PATIENTS WITH PROVED CHRONIC HEPATITIS C

Thesis

Submitted In Partial Fulfillment
For Master Degree In Medicine

By

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Chronic Hepatitis

1- Introduction
2- Etiology
3- Classification & Histopathology
4- Clinical features & investigations
5- Special causes of chronic hepatitis (hepatitis B+Delta virus)
6- Autoimmune chronic hepatitis.
7- Drug-induced chronic active hepatitis
8- Genetic disorders.

Introduction

The term chronic hepatitis include a group of disorders that share a chronically active necroinflammatory process in the liver but differ in etiology, natural history, & therapy. The diagnosis of chronic hepatitis is applicable when unresolved necrosis and inflammation, with or without fibrosis are present for at least 6 months (Schiff, 1995)

Etiology

There are four well established causes of chronic hepatitis as :-

1- Viral

2- Autoimmune

3- Drug-induced

4- Genetic Causes

As well as other hepatobiliary diseases that may be mistaken for chronic hepatitis (Cholson & Bacon, 1993)

Classification and Histopathology

Chronic hepatitis is classified histologically into :- Chronic persistent hepatitis, Chronic lobular hepatitis, Chronic active hepatitis.

All cases of CPH don't necessarily follow a benign long-term course, and not all cases of CAH of mild to moderate severity histologically in variably progress rapidly to symptomatic cirrhosis (Shiff, 1995)

A- Chronic persistent hepatitis :

Was initially defined by DeGroote (1968) as a "Chronic inflammatory infiltration, mostly portal, with preserved lobular architecture and little or no fibrosis. Piecemeal necrosis is absent or slight.

Features of acute hepatitis may be surperimposed. The portal tracts are sharply delineated (Scheuer P.J., 1988). Inflammatory cells may extend beyond the portal tract but parenchymal cell necrosis, when present, is not extensive and inflammation within the lobule is slight. When these typical features are present, CPH (Chronic Persistent Hepatitis) can be distinguished readily from CAH (Chronic active Hepatitis)

If there is continuing diffuse lobular inflammation and cell necrosis, in the absence of significant portal tract inflammation, the disease usually is classified as CLH (Popper H. et al., 1981)

CPH occurs primarily in patients with chronic hepatitis B, hepatitis C infection and is less common in hepatitis D, autoimmune and drug induced chronic hepatitis, Wilson's disease, or α1-antitrypsin deficiency

(unless histologic status has been modified by treatment). In chronic hepatitis B carries, some hepatocytes exhibit a typical ground-glass appearance, manifested by a granular homogenous eosinophilic staining of the cytoplasm (Hadziyamis et al., 1973).

Those ground glass hepatocytes are pathognomonic for chronic hepatitis B infection, although similar cells may be seen in a few rare disorders (cyanamide ingestion, myoclonic epilepsy, type IV glycogensis) or confused with mitochondria-rich cells (oncocytes), which also occur in chronic hepatitis (Lefkowitch J.H. et al., 1980) but in chronic hepatitis C infection, steatosis is common and prominent lymphoid follicles with germinal centres often are found in the portal tracts, which may also contain damaged bile ducts, plasma cells and eosinophils are relatively un common (Scheuer PJ., 1992).

The variable degree of portal inflammation seen in CPH due to hepatitis C and B has prompted some pathologists to divide CPH into a mild and a marked category (Desmet VJ., 1988). In general CPH has a good prognosis but in some cases progression to CAH and cirrhosis and hepatocellular carcinoma has been documented (Lashner BA et al., 1988)

CPH also may occur by spontaneous regression from CAH or after treatment of CAH with corticosteroid or interferon. Such regression occurs spontaneously occasionally in hepatitis C, but is more common in chronic hepatitis B infection (Hopfu et al., 1990)

When this form of CPH shows fibrous septa with inflammatory activity but no piecemeal necrosis, it is termed **chronic septal hepatitis** by some authors (Sherlock S., 1976), The prognosis of CPH after treatment of

autoimmune or viral CAH is not always favorable, because there is a tendency to relapse when treatment is stopped (Shindo M. et al., 1991).

B- **Chronic Lobular hepatitis** :-

The histologic pattern of spotty parenchymal necrosis and inflammation (with acidophil bodies) with minimal or mild portal inflammation is termed chronic lobular hepatitis (Scheuer PJ., 1988) (Bianchil., 1987)

In most cases, the onset is typical of acute hepatitis but it is followed by striking and often multiple biochemical (amino transferase) relapses or low-grade persistent aminotransfuse elevations, 67.5% of these cases occur with hepatitis B infection, and 19% with NANB hepatitis (Liaw YF. et al., 1982).

C- **Chronic active hepatitis** :-

It is a much more serious, progressive lesion than CPH, it is often associated with piecemeal necrosis which defined as "the destruction of liver cells at an interface between parenchyma and connective tissue, together with a predominantly lymphocytic or plasma cell infiltrate".

In some cases lymphocytes actually invaginate or invade the hepatocytes (em peripolesis). This form of cell necrosis occurs by cell fragmentation (also known as apoptosis) (Kerr JFR et al., 1979) and was initially observed in so-called autoimmune forms of chronic hepatitis, thus the term piecemeal necrosis came to be synonymous with chronic progressive liver disease, it may be seen in other disorders, as primary

biliary cirrhosis, inflammatory bowel disease and sclerosing cholangitis (Schiff., 1995). Today the term CAH is used both pathologically and clinically.

Although some studies report that cirrhosis may develop in patient whose initial biopsy shows only piecemeal necrosis (DeCroote J et al., 1978) others, believe that the more reliable prognostic histologic features are confluent areas of necrosis that form zones of parenchymal collapse, bridging portal trials and central veins (Okuno T et al., 1983), this pattern of necrosis was originally termed subacute hepatic necrosis which has been replaced by the more descriptive terms, (briding hepatic necrosis or multi lobular necrosis), series of studies from the Mayo clinic demonstrates that patients with liver biopsy evidence of bridging and multi lobular necrosis are of high risk for progression to cirrhosis and death from hepatic failure (Soloway RD et al., 1972) (Schiff, 1995), but the more active the disease and the longer it lasts, the greater is the likelihood of cirrhosis developing. CAH is divided into mild, moderate and severe forms according to the severity and extent of the necroinflammatory process (Black M., 1975).

CAH may be particularly likely when hepatitis B is super infected with hepatitis D (Verme G et al., 1986). Also CAH is the typical lesion observed in autoimmune hepatitis, drug-induced hepatitis, Wilson's disease, and α_1-antitrypsin deficiency. The histologic features of hepatitis B or C that are seen in CPH also are present in CAH. In CAH due to chronic hepatitis B infection, in contrast to CPH, there is cytoplasmic (rather than nuclear) expression of core antigen with low levels of expression of both surface and antigen (Naoumov NV. at al., 1990).

Autoimmune hepatitis has no pathognomonic histologic features, although cirrhosis frequently is established at the time of initial presentation (Hay JE., 1989).

Drug-induced CAH may be indistinguishable from viral and autoimmune forms, unless a hypersensitivity reaction is suggested by features such as granulomata, cholestasis, bile duct lesions and eosinophilia. The diagnosis is supported if the disease regresses after stopping medication.

Wilson's disease, as a cause of CAH, is suggested by the finding of steatosis, glycogen nuclei and Mallory bodies and strongly supported by staining for Cu or Cu-associated protein (Stremmel., 1991), but measurement of liver Cu concentration is the more reliable diagnostic test (Lef Kowitch JH., 1982) (Schiff., 1995).

α_1-antitrypsin deficiency, when manifest as CAH, may be diagnosed at the light microscopy level by finding diastase-resistant PAS+ve globules, these inclusions can be detected specifically by immuno-chemical staining for α_1-antitrypsin and also identified by electron microscopy (Bianchi, 1987) but it occasionally undetectable until late in the disease, thus measurement of the serum α_1-antitrypsin phenotype is the most reliable means of diagnosis (Jacobson, 1985).

Chronic hepatitis can progress to cirrhosis :

An active post necrotic cirrhosis may be present when histologic material is first obtained in patients with chronic hepatitis and is