Original Paper

Histological Alterations in the Hepatic Parenchyma in Infections with the Hepatotrop Virus B

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ABSTRACT This study included 116 cases of liver serologically confirmed biopsies, which were clinico-pathologicaly assesed. We evaluated the portal and intraloburlarly inflammatory infiltrate, the injury of segmental bile ducts, the hepatocytic necrosis, fibrosis stage and other additionally histopathological aspects. This results sustain the importance of histopathological evaluation for diagnosis and therapeutic management for the lesions.

KEY WORDS *Viral Hepatitis B, liver biopsies, staging*

Introduction

B hepatotropic virus is an atypical hepadnavirus, because although it is one of the smallest human pathogens, it causes a more chronic condition than other viruses. The genome of the hepatitic virus B, consisting of 3,200 base pairs, was initially sequenced in 1979 (10), but the function of some of the encoded proteins is still unclear. As hepatitis C and HIV, hepatitis B mutates at a high rate and as the disease progresses, new viral species evolve and lead to the formation of new types of disease (4).

Material and method

In our study we included 116 cases of liver biopsies, all serologically confirmed. The liver fragments were fixed in formalin, paraffin-embedded, then sectioned at 5 microms. Sections were marked using standard (Hematoxylin-eosin) and special (Gordon Szekely) stainings.

Results and discussions

In the group of patients selected, age ranged between 18 and 62 years (mean = 40.58 years) and the was a predominance of the female population (F: B=2,41:1). The age group with most cases ranged between 31 to 40 years - 35 cases.

Table 1: Distribution of cases according to age and gender

Age (years)	**Masculin**	**Feminin**	**Total**
11-20	5	0	5
21-30	15	4	19
31-40	22	13	35
41-50	23	6	29
51-60	15	10	25
61-70	2	1	3
Total	**82**	**34**	**116**

Although by definition, chronic hepatitis is characterized by the presence of necroinflammatory lesion lasting over 6 months, in practice the limit between acute and chronic forms is more difficult to distinguish, because acute viral hepatitis B may occasionally be prolonged and some forms of chronic hepatitis develop insiduosly, without the presence of a clinically apparent acute onset (3).

In the cases included in the study most portal tracts showed variat amounts of lymphoplasmocitic infiltrate. Although its arrangement in aggregates and follicles is more common in chronic hepatitis C (9), it was found in our group of patients with chronic hepatitis B in 17 cases. Inflammatory infiltrate was most commonly located in the portal tracts, but also intralobularly, arranged in small foci, in spots, often around altered hepatocytes or in the form of intrasinusoidal rows. Quantification of the inflammatory infiltrate revealed the following results: grade1 - 43 cases (mild inflammation), grade 2 - 37 cases (moderate inflammation), grade 3 - 25 cases (moderate-marked inflammation), grade 4 - 10 cases (marked inflammation).

The injury of segmental bile ducts characterized by vacuolation, necrosis and and the presence oflymphocytic inflammatory infiltrate was identified in 5 cases. In normal liver, few bile ducts are identified in the portal tracts, while in chronic hepatobiliary afections these structures are frequently modified (1).

Hepatocytic necrosis was present under several aspects:

- focal or spotty affecting a cell or a small group of cells - one or less per 10x objective- 12

cases, 2-4 foci per 10x objective -96 cases; 5-10 2-4 foci per 10x objective – 7 cases

- confluent necrosis with large areas of necrosis present and connective tissue containing inflammatory cells including macrophages and cellular debris - 6 cases

The notion of "piecemeal necrosis" was used to describe the disappearance of hepatocytes located at the boundary between liver parenchyma and connective structures (5). These areas of necrosis showed infiltration with numerous lymphocytes and other inflammatory cells and deletion of the lobular limiting plates and irregular outline of the parenchyma-mesenchyme interface. It was quantified in our study using the following scale:

- Mild (focal, few portal tracts) -32 cases
- Mild / moderate (focal, most portal tracts), 51 cases
- Moderate (continuous <50% of tracts or septa), 18 cases
- Sever (continuously> 50% of tracts or septa)- 11 cases

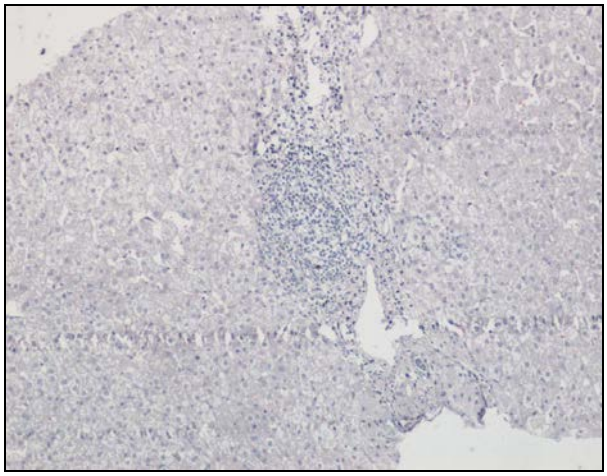

Figure 1: Chronic hepatitis B with the presence of moderate piecemeal necrosis. HE stain, 100x

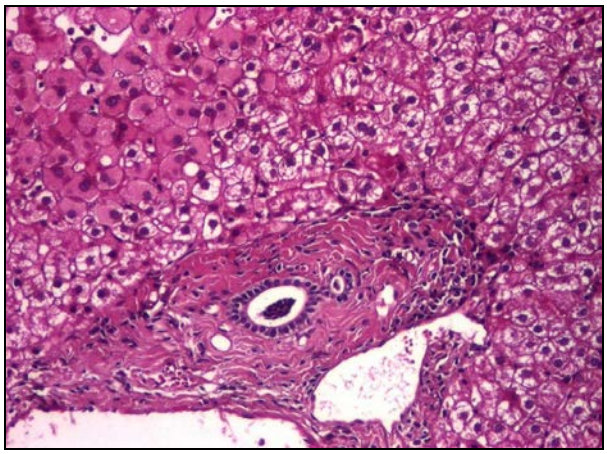

Figure2: Chronic hepatitis B with the presence of fibrosis in the portal tracts and pericellular focally; „ground glass" hepatocytes present, HE stain 200x

Fibrosis stage was assessed by the following criteria: pericellular fibrosis (focal or extensive) - 3 cases, pericellular fibrosis (focal or extensive) plus portal fibrosis - 11 cases, fibrosis of the bridges (thin porto-portal bridges) - 48 cases and fibrosis in thick porto-portal and portocentral bridges - 21 cases.

Out of the spectrum of changes identified, one is considered relatively specific: the presence of „ground-glass" hepatocytes. However, their etiology is heterogeneous and although most commonly caused by HBsAg, these hepatocytes could appear due to the presence of other diseases such as cyanamide treatment of alcoholism, Lafora disease (6) and epilepsy, type IV monoclonal glycogenosis (8). This histologically feature, characterized by the presence of partial or total changes of the cytoplasms which becomes fine granular, pale, often separated by a halo membrane, was shown in our study in 92 cases.

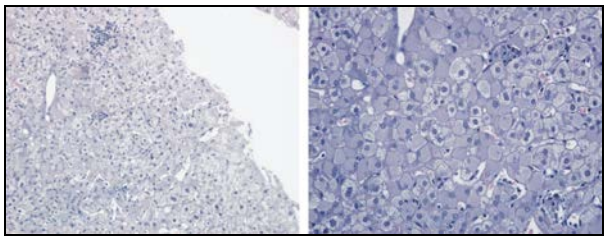

Figure 3: Chronic hepatitis B with the presence of „ground glass" hepatocytes. HE stain, 40x and detail 200x

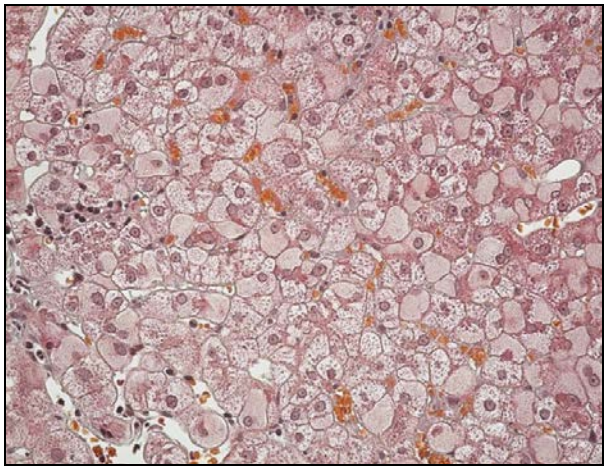

Figure 4: Chronic hepatitis B with the presence of „ground glass" hepatocytes, Gordon Szekely stain, 200x

Although steatosis is a feature commonly found in chronic hepatitis C (2), it is also described in B virus infections. According to the study of Minakari et al. (7) the steatosis found in chronic hepatitis B is due rather to metabolic host factors than viral factors. In our cases, steatosis

was characterized by the accumulation of lipid droplets in hepatocytes. The quantification of steatosis have taken into account the fatty invasion in the liver parenchyma as follows:

- Absent (40 cases)
- Mild (0-30% of hepatocytes) (26 cases)
- Moderate (30-60% of hepatocytes) (31 cases)
- Severe (> 60% of hepatocytes) (19 cases)

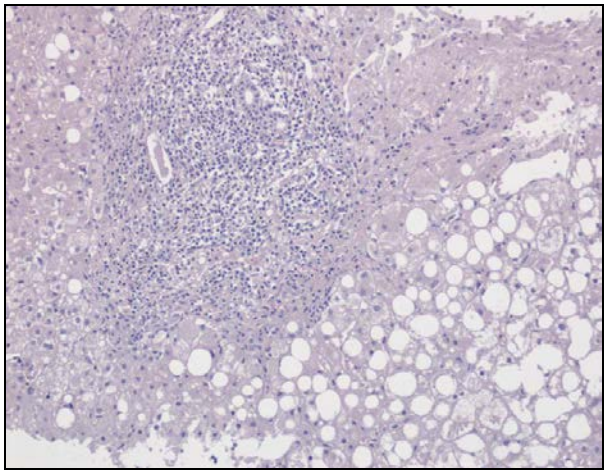

Figure 5: Severe steatosis, HE stain, 100x

Conclusions

Patients with chronic hepatitis B have different histological patterns. Most had mild inflammation and more than half had features suggestive for the etiologic diagnosis. Identification and clinical follow up of patients with hepatitic B virus infection is important because this disease has an increased risk of hepatocellular carcinoma development, even at young age.

References

1. Chen YK, Zhao XX, Li JG, Lang S, Wang YM, Ductular proliferation in liver tissues with severe chronic hepatitis B: An immunohistochemical study. World J Gastroenterol 2006; 12(9): 1443-6.
2. Comanescu V, Comanescu M. - Structura ficatului, aspecte anatomohistologice în hepatita cronică C" Sub redacţia: Moţa M, Popa S. INSULINOREZISTENŢA INDUSĂ DE OBEZITATE ŞI HEPATITA CRONICĂ VIRALĂ C - Ed. Medicală Universitară, 2009, pag. 23-38.
3. Diniz G, Aktaş S, Ortaç R, Unlü I, Vergin C., A comparative immunohistochemical study of HBsAg, HBcAg and CD57 in chronic hepatitis B pediatric patients with and without malignant disorders. Turk J Gastroenterol. 2003 ; 14(4): 234-8.
4. Foster Graham, Goldin R. D., Management Of Chronic Viral Hepatitis Ed a II-a , Ed Taylor & Francis 2005; pag. 63
5. Galle PR., Apoptosis in liver disease. J Hepatol. 1997; 27:405–12
6. MacSween RNM, Burt AD, Portmann BC, Ishak KG, Scheuer PJ, Anthony PP,eds. Pathology of the Liver. 5th ed. London: Churchill Livingstone 2007; p:425.
7. Minakari Mohammad, Molaei Mahsa, Shalmani Hamid Mohaghegh. Alizadeh Amir Houshang Mohammad et al., Liver steatosis in patients with chronic hepatitis B infection: host and viral risk factors.European Journal of Gastroenterology & Hepatology 2009; 21(5):512-6, 2009.
8. Moon WS, Yu HC, Chung MJ, Kang MJ, Lee DG, Pale bodies in hepatocellular carcinoma. J Korean Med Sci. 2000, 15(5):516-20.
9. Scheuer P, Lefkowitch JH, Liver Biopsy Interpretation, 6th ed. London: WB Saunders; 2000:155-6;
10. Servoss, J.C., Friedman LS. Serologic and molecular diagnosis of HBV. In: Martin P, Tran T., eds. Clinics in Liver Disease, Volume 8, Number 2. Philadelphia: Elsevier Science 2004.

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