

# The Analysis of Histopathological Features of Patients with Chronic Viral Hepatitis C. A Comparative Study with Chronic Viral Hepatitis B

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Currently, with all existing diagnostic methods, the liver puncture biopsy remains the gold standard to diagnose chronic hepatitis. The histopathological diagnosis of the liver puncture biopsy sample includes several elements: the determination of necro-inflammatory activity, the determination of the fibrosis staging and showing the suggestive elements for different etiology (ground glass hepatocytes for the virus B infection; bile duct lesions, portal inflammatory infiltrates and steatosis for virus C infection).

The aim of the study was to analyze the frequency of the histopathological lesions at 2 groups of patients with chronic viral hepatitis C and B in order to identify the distinctive elements for the different etiology.

We have taken in study a total number of 106 patients at which we analyzed three characteristics that appear more frequent in virus C infection than in virus B infection: lymphoid follicles (62,3%/28,5%), bile duct lesions (48,23%/19,04%) and macrovacuolar dystrophy (65,8%/61,9%). These three lesions are histologic parameters useful to diagnose the hepatic disease caused by the hepatitis C virus infection.

**Keywords:** hepatitis C virus infection, hepatitis B virus infection, histological features

## Introduction

The hepatitis proves itself to be profoundly implanted even in our days in the population of all countries representing one of the biggest problems of the human pathology with profound repercussions, sometimes irreversible, on the human health and with a powerful impact on the entire society.

The hepatitis virus B and C infections represents an important health problem with implications on the morbidity, mortality and high social costs.

The introduction on large scale of the new methods for the serologic diagnostic has raised the problem of the opportunity of the histopathology diagnostic in postviral chronic hepatitis. But despite of the modern methods of diagnostic, the liver biopsy remains the “gold standard” in the chronic hepatitis diagnosis. Liver biopsy may confirm the clinical diagnostic and enables to exclude numerous diseases which can manifest as “chronic hepatitis” [1, 2].

We have followed the frequency of the lesions which appear on the liver biopsy with the aim of quantification the histological features which discriminates the hepatitis C virus infection from hepatitis B virus infection.

## Material and methods

We have taken in study a number of 106 patients with ages between 18 and 65 years diagnosed with chronic viral hepatitis B or C in 1999-2005 period in the 1st Medical Clinic of Targu Mures.

The total number of patients was divided in two groups on the basis of clinical, serological and histological investigations as it follows: The first group (group 1) includes a

number of 85 patients with tests positive for HCV-ARN and anti HCV antibodies and the majority of them presenting elevated levels of aminotransferases with a medium value of 134,81+/-6,2. The second group (group 2) of patients includes a number of 21 patients with positive tests for Ag HBs, negative serology for hepatitis C and the majority of them presenting elevated levels of aminotransferases with a medium value of 114,83+/-16,4.

The exclusion criteria from the study were the age bigger than 65 years or under 18 years, the alcohol consumption more than 20mg/day, the existence of an autoimmune hepatic disease (autoimmune hepatitis), primary biliary chirosis, congenital jaundice, storage hepatic diseases, the presence of B and C or B and D coinfection or the presence of the clinical or paraclinical signs of chirosis.

After taken the informed consent it was made the liver biopsy using the aspiration technique with 0,8-1,6mm gauge needle and for the lesions quantification it has been used the Knodell score system.

At all the patients it has been quantified the values of the necroinflammation and fibrosis scores and it was mentioned the histological changes as micro and macrovacuolar hepatocyte steatosis/dystrophy, bile duct lesions, ground glass hepatocytes, lymphoid follicles in portal tract, sanded nuclei.

## Results

The gender repartition of the two groups highlights the predomination of the feminine gender as it follows 61,1% in group 1 and 52,38% in group 2. The patients average age analysis shows a mean age of 46+/-1,8 years in the group 1

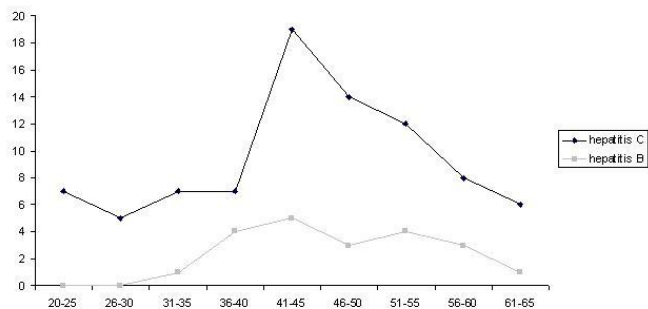


Fig.1. The distribution by age of C and B hepatitis

and 44+/-4,2 in the group 2. Also there is a predomination of the patients with ages between 40-50 years in group 1 and 35-45 years in group 2 (Figure 1).

In table I. there are presented the frequency of the histological features obtained on the liver biopsy for the patients with chronic C hepatitis versus chronic B hepatitis.

On the biopsy samples we identified the presence of the lymphoid follicles in a proportion of 62,3% in the group with chronic hepatitis C compared with 28,5% for the group with chronic hepatitis B. Analyzing the presence or the absence of the lymphoid follicles based on the fibrosis severity and the histological activity index, we observed the presence of a direct relationship between the increasing frequency of the portal lymphoid follicles and the necroinflammation grade the highest incidence being at the patients with moderate and severe necroinflammation (Table II, III).

The epithelial lesions of biliary ductus were present in 42,45% of all patients taken in study ( 48,23% in group 1 versus 19,04 in group 2).

Hepatocyte steatosis was present in a percentage of 65,09% of all the patients taken in study, and was present in 65,8% cases in the group with chronic hepatitis C compared with 61,9% from the group with chronic hepatitis B.

The microvacuolar dystrophy is a lesion that characterizes some forms of ethanolic hepatopathy and occasionally can appear in viral hepatitis, but in the two study groups this lesion was absent probably due to the exclusion from this study of the patients with chronic alcohol consumption.

Analyzing the presence of the sanded nuclei we identified this lesions in the both groups taken in study with the highest predominance at the patient with chronic viral C hepatitis in a proportion of 56,4% compared to 38,09% in those with chronic hepatitis B.

Table I. Histologic features in HCV and HBV infections (HCV – hepatitis C virus; HBV – hepatitis B virus)

Histologic features	HCV	HBV
Lymphoid follicles	62.3% (53/85)	28.5% (6/21)
Bile duct lesions	48.23% (41/85)	19.04% (4/21)
Macrovacuolar steatosis	65.8 % (56/85)	61.9% (13/21)
Microvacuolar steatosis	0	0
Sanded nuclei	56.4% (48/85)	38.09%(8/21)
Ground glass hepatocytes	30.5% (26/85)	71.4% (15/21)

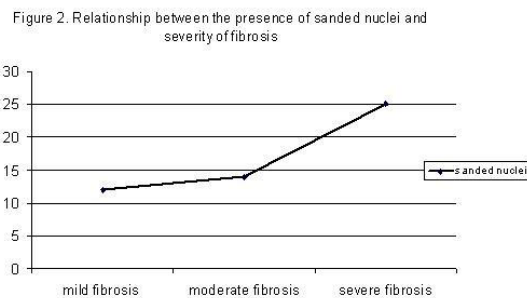


Fig. 2. Relationship between the presence of sanded nuclei and severity of fibrosis

Correlating the presence of the sanded nuclei with the severity of the fibrosis at the patients with hepatitis C we observed the increasing frequency of these lesions as the fibrosis severity grows (Figure 2).

The ground glass hepatocyte usually reflects the presence of the viral antigens in the hepatocyte nuclei, being a marker of viral replication. The lesion is more characteristic for hepatitis B but it can be present in other viral hepatic diseases (hepatitis C) or in alcoholic hepatitis. In this study we observed that the frequency of this lesion in hepatitis C is not small, yet this is present in 30,5% of cases.

Discussions

Up to date the hepatitis C virus was not identified in the hepatic tissues and there are no hepatocellular lesions identified through electron microscopy corresponding to those induced by Ag HBs (ground glass cells), lesions that could allow the microscopic identification of the hepatitis C virus.

In our study with two groups of patients with chronic hepatitis C, respectively B, we analyzed the incidence of six histological lesions separately in the two groups. According to obtained data the presence of the lymphoid follicles and of the bile duct lesions was significantly increased at the patients with chronic C hepatitis compared to hepatitis B. The obtained data shows that the macrovacuolar steatosis represents a histological lesion that is more frequent associated with the chronic viral C hepatitis.

Table II. Relationship between lymphoid follicles and necroinflammation in the group with hepatitis C virus infection (HCV – hepatitis C virus).

HCV group	Minimum necroinflammation	Mild necroinflammation	Moderate necroinflammation	Severe necroinflammation
Lymphoid follicles	5	9	25	14
%	9.4%	16.9%	47.1%	26.4%

Table III. Relationship between lymphoid follicles and necroinflammation in the group with hepatitis B virus infection (HBV – hepatitis B virus)

HCV group	Minimum necroinflammation	Mild necroinflammation	Moderate necroinflammation	Severe necroinflammation
Lymphoid follicles	2	3	9	7
%	9.5	14.2	42.8	33.3

The steatotic lesions are an indicator for C virus cytopathogeny which interferes with numerous metabolic links [3, 4, 5]. Although the macrovacuolar dystrophy is a lesion characteristic for hepatitis C, in this study we haven't found a significant difference concerning its incidence, this lesions appearing with a high frequency in both types of hepatitis B and C. Other studies suggests a possible role of the hepatitis C virus itself in the pathogenesis of steatosis an indicated a close relationship with fibrosis [6].

Although the microvacuolar steatosis can appear occasionally in chronic viral hepatitis C (being a lesion characteristic for alcoholic hepatopathy), it was missing in both groups of study probably due to the exclusion of the patient with antecedents of alcohol consumption.

The presence of sanded nuclei respectively of macrovacuolar dystrophy reflects the metabolic effect of C virus on hepatocytes, the incidence of these lesions being greater to the group 1 and has a positively correlation with the grade fibrosis.

The presence of the ground glass hepatocytes is more frequent in hepatitis B, being characteristic for this, but it can be found in other chronic viral hepatitis.

### Conclusions

1. Although there are not pathognomonic for hepatitis C, the high incidence of the lymphoid follicles, biliary duct

lesions and macrovacuolar steatosis shows the probability of a hepatitis C virus infection rather than a hepatitis B virus infection.

2. The presence of sanded nuclei correlates positively with the severity of hepatic fibrosis at the patients with viral hepatitis C, although these lesions aren't specific for viral C hepatitis.
3. There is not fully elucidated the proportion of immune aggression that may induce a number of lesions (lymphoid follicles, bile duct lesions) or the citopathic effect of the virus that is responsible for other lesions (hepatic steatosis and sanded nuclei).

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