

HCV AND DRUG ABUSERS – morphological changes (Liver biopsy in CHC and heroin abuse)

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Abstract

The aim of the study was to evaluate the morphological changes in the liver biopsies from patients with chronic hepatitis C (CHC) and heroin abuse (HA). Material and methods: In the study were included 10 patients with CHC and HA (9 m, 1 f, mean age $24,2 \pm 3,26$ y) and 36 patients (25 m, 9 f) with no HA and CHC (n=22, mean age $32,68 \pm 11,41$ y) or chronic hepatitis B (CHB, n=14, mean age $24,00 \pm 3,66$ y). The diagnosis of chronic hepatitis was put according to standard criteria and liver biopsy was done in all cases. The grading of activity and staging of fibrosis by METAVIR, the presence of steatosis and depletion of glycogen content was evaluated after using HE, V. Gieson, Gomori and PAS stains. Results: In the group of HA patients with CHC were found more often moderate grade of inflammation (A2, 60%) and clinically significant stage of fibrosis (F2, 70%) while in the both groups of non- HA patients with CHC or CHB the prevalences of mild grade of activity (A1, 59% and 50%, respectively) and early stage of fibrosis (F1, 59% and 71%) were predominant. No significant differences were found in the comparison of HA patients with CHC and non- HA control groups regarding the presence of steatosis and decrease of glycogen contents in hepatocytes. In conclusion, our study showed that in liver biopsies of patients with CHC and heroin abuse there were more severe morphological changes including grading and staging of chronic hepatitis compared to the cases with CHC or CHB without history of drug abuse.

Keywords: liver biopsy, chronic hepatitis C, heroin abuse.

Introduction

It is well known that the addiction to heroin is related to a lot of short-term and long-term effects on the health of drug abusers. The main part of the long-term effects are related with the use of contaminated heroin, infected needles, syringes, spoons (1-17). The heroin addicted subjects are the main risk group for infection with hepatitis C virus (HCV). In literature various pathological changes in the livers of heroin abusers have been reported (18-22). They included quantitative and qualitative alterations of cellular organelles, extracellular matrix and hepatic vascular system like vacuole and fatty degeneration, changes in the cellular nucleus, membranes or intracellular content of glycogen, inflammation, fibrosis/cirrhosis, dysplasia, amyloidosis. All of them can be resulted by the HCV infection, heroin itself, and also by concomitant alcohol abuse, if present. In addition, the intensity of liver morphological changes is related to the duration of misuse. The aim of our study was to evaluate the morphological changes in the liver biopsies from heroin addicted patients with chronic hepatitis C.

Materials and methods

In the study were included 10 patients with chronic hepatitis C (CHC) and heroin abuse (HA) and 36 patients with no evidence of addiction to any psychoactive substances and CHC (n=22) or chronic hepatitis B (CHB, n=14) as controls. The diagnosis of chronic hepatitis was put according to standard criteria and liver biopsy was done in all cases. The morphological changes in liver samples were investigated through different scoring systems, after routine processing and haematoxyline-eosine (HE),

van Gieson and Gomori stainings for fibrosis, as well as PAS (Periodic Acid Schiff) stain for carbohydrates/glycogen (23-25). The severity of inflammation and stage of fibrosis were defined according to METAVIR, and also the presence or no of steatosis. The decrease in hepatocytes glycogen content using PAS staining was evaluated semiquantitatively into 4 grades as follows: 0 – no decrease, grade 1 – mild, grade 2 – moderate and grade 3 –severe glycogen decrease in hepatocytes.

Results

Demographic characteristics of the patients with and no HA and chronic hepatitis In the group of patients with CHC and HA, 9 cases (90%) were males and only 1 (10%) –female. Among all cases with no HA and CHC or CHB (n=36), 25 (69%) were males and the rest 9 cases (31%) – females. There was no significant difference by sex in comparison the cases with and no HA and chronic hepatitis. The mean age of HA patients with CHC was significantly lower compared to the cases with no HA and CHC ($t=5,246$; $p=0,029$) (tabl. 1). There was no difference between the mean ages of the patients with CHC and HA and those with CHB without HA. The average duration of the heroin abuse in cases with CHC was $6.00 \pm 1,83$ years (from 3 to 8 yrs) as in 7 of them the duration of heroin abuse was above 5 years.

Table1. Mean age of the HA patients with CHC and control groups of cases with CHC and CHB.

groups \ age (years)	Mean	SD	Min.	Max.
HA patients with CHC	24,20	$\pm 3,26$	18,00	31,00
Patients with CHC without drugs	32,68	$\pm 11,41$	19,00	57,00
Patients with CHB without drugs	24,00	$\pm 3,66$	18,00	31,00

Liver morphological changes in the patients with and no HA and chronic hepatitis

The histological grades of activity and stages of fibrosis using METAVIR in all studied patients are presented on table 2 and fig. 1- 3. Among the HA patients and CHC, the moderate degree of activity (A2) was the most common (n=6, 60%), following by the mild grade A1 (in 3 cases, 30%) and severe grade A3 (in 1 case, 10%). In the both groups of cases with no HA, the portions of cases with mild degree of inflammation (A1) were the biggest (59% and 50% for CHC and CHB, respectively), following by that of moderate degree (32% and 29% for CHC and CHB, respectively) and severe grade (A3) was found in 2 and 1 cases with CHC and CHB, respectively. Among the patients with HA, the F2 stage was the most common (in 7 cases, 70%), following by the F1 stage (in 2 cases, 20%).

Table 2. Distribution of grades of activity and stages of fibrosis by METAVIR in the cases with and no HA and chronic hepatitis.

Evaluation according METAVIR	HA patients with CHC (n)	Patients with CHC drugs without	Patients with CHB drugs without	Total (n)
A0F2	0	0	1	1
A1F0	0	1	1	2
A1F1	0	9	6	15
A1F2	3	3	1	7
A2F0	1	1	0	2
A2F1	2	1	3	6
A2F2	3	4	1	8
A2F3	0	1	0	1
A3F0	0	1	0	1
A3F1	0	1	1	2
A3F2	1	0	0	1
Total	10	22	14	46

There was no case with advanced fibrosis (F3 or F4). On the opposite, among the cases with no HA and CHC or CHB, the prevalence of F1 stage was the highest (59% and 71% for CHC and CHB, respectively), following by that of F2 stage (32% and 21% for CHC and CHB, respectively). Only one case with F3 stage was found, from the group of cases with no HA and CHC.

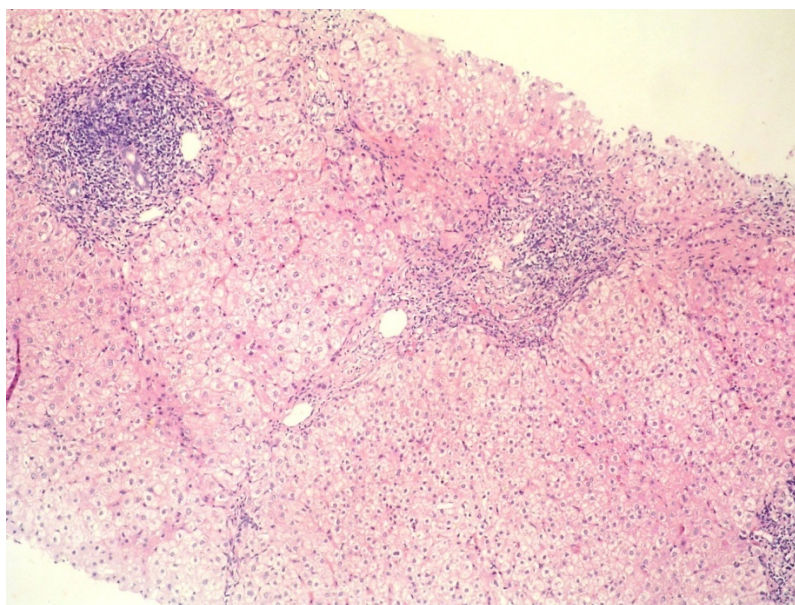


Figure 1. CHC without heroin abuse. Enlarged periportal spaces with marked round cell infiltrates with formation of lymphoid follicles, piecemeal necrosis and mild fibrosis. HE, x 100.

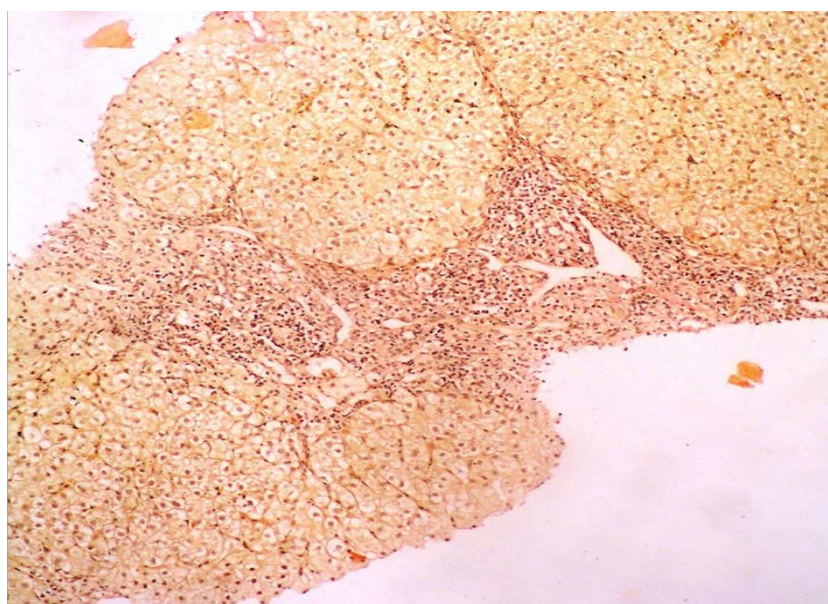


Figure 2. CHC and heroin abuse. There is moderate fibrosis in the enlarged periportal space, piecemeal necrosis and mild pericentral fibrosis. The collagen fibres are stained in pink / light red. Van Gieson staining, x 100

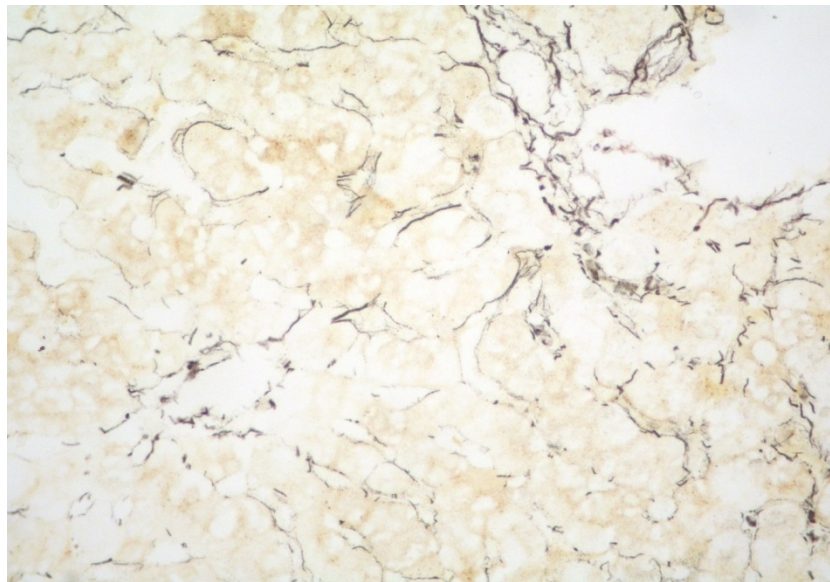


Figure 3. CHC and heroin abuse. A liver lobule, in which discrete reticular fibres (stained dark brownish to black) are seen. Gomori staining, x 400.

In addition, we performed comparative analysis of histological grades of activity and stages of fibrosis among the HA cases with CHC according to the duration of heroin abuse (> and < 5 y). We found that in cases with shorter duration of heroin abuse (n=3) the morphological changes tend to be milder regarding inflammation and fibrosis compared to the cases with duration of heroin addiction > 5 years.

We found no difference in the presence of steatosis between the HA cases with CHC and control groups. But steatosis was observed in four from the 7 HA patients and CHC with more than 5 years duration of the abuse and in no one with shorter duration of heroin addiction.

Using PAS staining, in the majority of HA patients with CHC mild to moderate grades of decreased glycogen content in the hepatocytes were found but without significant difference in comparison with control groups of cases (fig. 4).

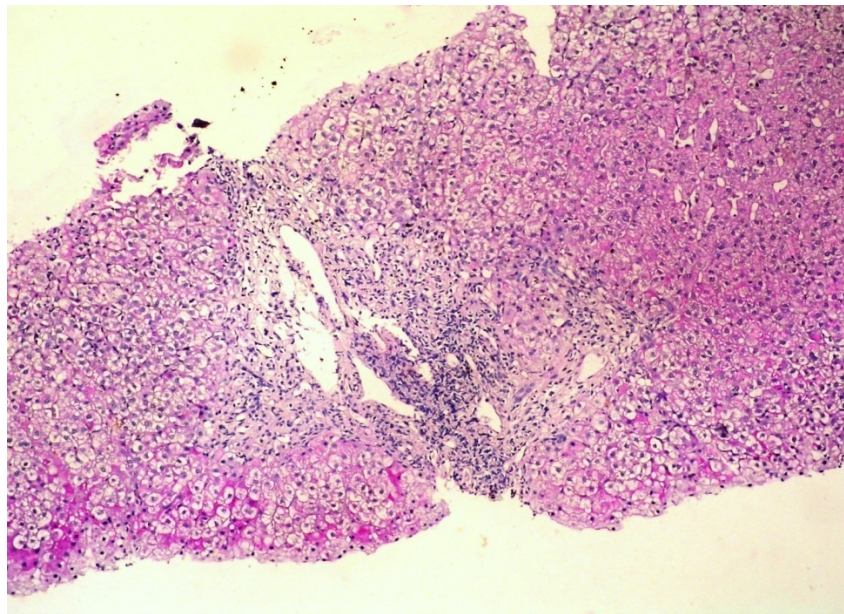


Figure 4. CHC and heroin abuse. Enlarged periportal spaces with moderately presented round cell infiltrates, piece meal necrosis. In the cytoplasm of small part of the hepatocytes pink stained (PAS positive) glycogen content is observed (sign of deminished glycogen content). PAS staining, x 100.

Discussion

The liver biopsy is the gold standard for evaluation the severity of liver damage in patients with chronic liver diseases. Beside grading of activity and staging of fibrosis, it gives opportunity to assess other features, which also have clinical significance. In this study we aimed to evaluate the morphological changes in liver biopsies from heroin addicted patients with CHC and to compare with those in cases with CHC and CHB without history for addiction to any drugs. Our small group of HA cases with CHC included mostly very young males with mean duration of heroin misuse of 6 years. The mean age of the studied cases was similar to that of control cases with CHB, but significantly lower in comparison with the mean age of non-HA with CHC. The young age of our HA patients with CHC confirms that heroin addiction is strong risk factor for hepatitis C virus infection. The evaluation of severity of liver damage using METAVIR showed some substantial differences between the HA cases with CHC and control cases with CHC and CHB. Regarding the grading of activity, in over half of the HA patients we found moderate inflammation while in the both control groups of non-HA patients the mild inflammation predominated. About the staging of fibrosis, we found that all studied HA and non-HA patients with chronic hepatitis, except one from the control group with CHC have no severe fibrosis or cirrhosis. Nevertheless, among the HA cases with CHC the clinically significant stage F2 was established more often in comparison with the both groups of non-HA cases with CHC or CHB. In the last the early stage of fibrosis the early stage of fibrosis (F1) was found to be more common. There were no peculiar differences when compared the liver biopsies of the HA CHC patients and non-HA CHC or CHB cases concerning the presence or no of steatosis and the

depletion of glycogen content in the hepatocytes, evaluated by PAS staining. When compared the severity of liver damage according to the duration of heroin misuse, we found that in cases with duration of heroin abuse less than 5 years the morphological changes tend to be milder regarding inflammation and fibrosis compared to those with longer duration of heroin abuse. The literature data for the morphological changes and severity of liver damage in HA patients with CHC on liver biopsies are scanty. In contrast, in several studies the light microscopic and ultrastructural changes in liver autopsy samples of intravenous heroin addicts have been reported (18-22). The authors summarized that heroin abuse induces significant morphologic changes in the liver tissue, including vesicular and fatty changes, reduction in the amount of glycogen in hepatocytes, chronic hepatitis, cirrhosis and the severity of these changes increases with years of heroin abuse.

In conclusion, our study showed that by the patients with CHC and heroin abuse the morphological changes, found in the liver biopsies including grading and staging of chronic hepatitis were similar to the ones, found by the cases with CHC or CHB without history of drug abuse, who were significantly older. Thus this could be the basis for establishing a group of patients with specific behavior problems and chronic liver diseases in the future. Further studies are needed to clarify the influence of heroin abuse on the severity of liver damage in chronic hepatitis C and to estimate the future chronic disease burden for the society.

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