

ORAL MANIFESTATIONS IN LIVER DISEASES

Crînguța Paraschiv, Cristina Gavrilesco, Irina Cotea, Irina Eșanu, Rodica Ghiuru,
D.Munteanu

The University of Medicine and Pharmacy „Gr. T. Popa” Iași, Faculty of Dental Medicine
Department of Internal Medicine

Abstract: Chronic hepatitis C infection is a worldwide health problem because it causes chronic hepatitis, cirrhosis, and hepatocellular carcinoma. Chronic liver diseases may induce several oral manifestations due to impairment of coagulation, thrombocytopenia or association with diabetes mellitus but hepatic C virus can give rise to a broad spectrum of nonhepatic manifestations.

Aim. The purpose of this report was to evaluate the association between oral manifestation and chronic viral hepatitis.

Material and methods. We examined 230 patients suffering from chronic hepatitis C and 150 patients with chronic hepatitis B virus infection. We investigated the possible associations between HCV and oral diseases.

Results. The prevalence of lichen planus, sialadenitis and abnormal salivary secretion was higher in patients with HCV infection than in patients with chronic hepatitis B. The periodontal disease was more frequent in patients with HCV probably due to the high prevalence of diabetes mellitus.

Conclusions HCV infection is a relatively common infection worldwide. It is usually an asymptomatic disease with normal or minimally elevated transaminases. HCV infection is associated with a number of extrahepatic manifestations that may include oral diseases such as lichen planus or sialadenitis. The HCV positive patient may require particular management when dental treatment is required due to bleeding disorders, defective metabolism of many drugs and the risk of nosocomial transmission of HCV.

Key words: hepatitis C virus infection, oral diseases, lichen planus.

INTRODUCTION

Chronic hepatitis C infection is an worldwide health problem because it causes chronic hepatitis, cirrhosis, and hepatocellular carcinoma. The biological and social impact of HCV infection is remarkable. Persons become infected mainly through parenteral exposure to infected material by blood transfusions or injections with nonsterile needles. Persons who inject illegal drugs, people who snort cocaine with shared straws, and health care workers who are at risk for needle stick and other exposures are at highest risk for HCV infection.

Acute hepatitis occurs in a minority of HCV infected patients at 6-12 weeks after the contact with the virus, but viral RNA is detectable at 1 week after exposure. The clinical manifestations are nonspecific (fatigue, loss of appetite, nausea) and are present in only c25% of patients, 75% of the infected persons showing no sign of acute hepatic disease. HCV infection tends to cause chronic infection. Over 70% of infected patients have elevated transaminases for longer than 6 months, but when serum HCV RNA is used as a marker of persistent infection up to 100% of patients have chronically been infected. [1].

Most patients with acute and chronic infection are asymptomatic, often with persistently normal liver function tests or only slightly elevated levels of transaminases

However histopathological changes are present in all infected persons, even those apparently healthy, and serum transaminases levels do not correlate with histological appearance. For these reason many infected persons remain undiagnosed and can transmit the virus through parenteral routes mentioned above, including through dental maneuvers [2]. After 10-20 years 20% -50% of patients with chronic hepatitis evolves to cirrhosis, the percentage of patients who develop cirrhosis is positively correlated with increasing age of contagion, the duration of infection, alcohol consumption, genotype 1b high level of viremia, coinfection with hepatitis B or HIV. Progression to liver fibrosis is faster in immunocompromised persons. Approximately 15% of patients with chronic HCV develop in the medium-de18 25 years, although cases of hepatocellular carcinoma without previous cirrhosis have been reported.

Hepatitis C may have effects not only on the liver, but also on various nonhepatic tissues joints, muscles, neural and gastrointestinal tissues, and skin. Although the extrahepatic manifestations have not a high-frequency they may have a significant impact on patient prognosis, affecting the duration and quality of life. Several cutaneous manifestations have been associated with chronic HCV liver disease some showing a definite correlation - essential mixed

cryoglobulinemia, porphyria cutanea tarda, lichen planus, others more rare, possibly related to HCV infection - panarterita nodosa urticaria, erythema nodosum, erythema multiforme. [3]. Manifestations caused by HCV in the oral cavity are lichen planus, Sjogrens syndrome and sialadenites, mouth cancer.

No mater the etiology chronic liver disease impacts many systems of the body. The coagulation pathway is one such system. The liver synthesizes many of the clotting factors necessary for hemostasis. In addition, vitamin K, a fat-soluble vitamin, requires proper liver function to be adequately absorbed from the intestines. Furthermore cirrhotic patients may have thrombocytopenia due to hypersplenism or treatment with interferon. In patients with liver disease, the resultant impaired hemostasis can be manifested in the mouth as petechiae or excessive gingival bleeding with minor trauma. This is especially suggestive if it occurs in the absence of inflammation. Therefore, special care must be taken during any type of surgery, oral or otherwise; severe hemorrhage can ensue as a result of the paucity of clotting factors

We draw attention to the increased prevalence of diabetes in patients with chronic liver disease due to the severity of liver disease or to the treatment with interferon. HCV is also acting as an independent diabetogenic factor [4]. For the dentist this association has important implications because diabetes is associated with significant changes in the system somatognat: increased frequency of periodontal disease, stomatitis, candidiasis, cheilitis, oral leukoplakia, dental caries.

AIM

The purpose of this report was to evaluate the association between oral manifestation and chronic hepatitis and to assess if the etiology may act as an independent risk factor for their development. At the same time we tried to investigate the clinical and biological characteristics of the patients with chronic hepatitis B and C and oral manifestations.

MATERIAL AND METHOD

To reach that goal we conducted a study over a period of 4 years which included patients diagnosed with chronic liver disease by clinical examination, liver function tests, morphological examination. All patients were examined for antibodies (Ac) HCV using a second generation immunoenzymatic assay (Beckman ACCESS HCV-Ab) and for HBs antigen

(HBsAg Beckman ACCESS immunoassay test. The study group consisted of 230 patients diagnosed with chronic liver disease of viral etiology C. The control group included 150 patients with chronic liver disease of hepatitis B viral etiology. In all patients we investigated the presence of gingival bleeding, oral lichen planus, xerostomia, sialadenitis, stomatitis, periodontal disease. We also investigated the prevalence of diabetes. Statistical methods included chi-squared and t-test analysis.

RESULTS

Comparative analysis of the studied groups is shown in Table I. There were no significant statistically differences between patients regarding age, severity of liver disease assessed by the prevalence of cirrhosis and liver transaminases levels.

Table I. Clinical characteristics of the studied patients

	Hepatitis C	Hepatitis B
Number of patients	230	150
Age	51,2±6,4 years	55,3±4,3 years
Symptomatic	16 (69,56%)	14 (93,33%)
Elevated transaminases	80,9% (118±23 UI/L)	93,3% (137±16 UI/L)
Cirrhosis	63 (27,39%)	49 (32,66%)
Gingival bleeding	40(17,39%)	23 (15,33%)
Lichen planus	8 (3,47%)	2 (1,33%)
Dry mouth	68 (29,56%)	16 (10,66%)
Sialadenitis	27 (11,73%)	2 (1,33%)
Periodontal disease	14(60,86%)	69(46,66%)
Oral candidiasis	46 (20%)	10 (6,66%)
Diabet zaharat	50 (21,73%)	8 (5,33%)

However we noted that the majority of patients with B viral liver disease were

symptomatic and had elevated transaminases, while in the group with

hepatitis C virus infection 34.44% of patients had no symptoms, while liver function tests were not modified in 19.1% patients. The prevalence of diabetes was higher in patients with HCV liver disease (21.73% vs. 5.33%) and this did not correlate with the severity of the disease.

Regarding changes in the oral cavity we founded:

Of the 230 patients with chronic viral liver disease C, 3.47% respectively 8 patients were diagnosed with lichen planus, The prevalence of lichen planus was higher in hepatitis C group (with no

differences between hepatitis and cirrhosis) than in the hepatitis B group (1,33% but with 0 cases of oral lichen). Of the 8 patients 3 had only oral lesions, and in other 3 cases the oral lesions were accompanied by changes in the skin. 2 patients from hepatitis C group as well as 2 patients from hepatitis B group had only cutaneous lichen involvement. Among patients with lichen, five had chronic hepatitis and three had cirrhosis, but in two cases of serum transaminase levels were normal. (Table II)

Tabel II. Prevalence of lichen planus

Pathology	Patients	Prevalence of LP	
		număr	%
HCV Hepatitis	150	5	3,33
HCV Cirrhosis	80	3	3,75
	Total: 230	8	3,47
HVB Hepatitis	92	1	1,08
HBV Cirrhosis	58	1	1,72
	Total: 150	1	1,33

Analyzing the patients who associated lichen planus to hepatitis C viral chronic disease we found that lichen occurred in 75% in patients aged over 60 years, in whom the evolution of liver diseases was longer. In 3 cases lichen planus was diagnosed at the same time with the liver

diseases and in the remaining cases it was diagnosed in 4-8 years after the diagnosis of chronic hepatopathy. Among patients with lichen, five had chronic hepatitis and three had cirrhosis, but in two cases serum transaminases levels were normal. (Table III)

Table III Clinical and biological features of patients with chronic liver disease and lichen planus

Patients	Sex	Age	Pathology	TGP (UI/l)	γ globuline (g/l)	LP	Years LP
1	F	73	HCV CH	132	25	Oral erosive	8
2	F	72	HCV CH	128	28	Oral erosive and cutaneous	5
3	M	70	HCV HC	154	26	Oral reticular	5
4	F	68	HCV HC	140	30	Oral reticular and cutaneous	8
5	M	55	HCV HC	148	25	Oral reticular	0
6	F	64	HCV CH	152	32	Oral reticular and cutaneous	0
7	F	69	HCV HC	139	27	cutaneous	4
8	M	55	HCV HC	132	26	cutaneous	4
9	F	63	HVB HC	165	28	cutaneous	5
10	M	67	HVB CH	157	26	cutaneous	7

Dry mouth was recorded almost 30% of patients with HCV liver disease compared to 10% in the control group. Dry mouth has a number of consequences, including altered taste, increased risk of fungal infection, increased caries risk, and increased prevalence of traumatic ulceration due to lack of lubrication. Patients with severely impaired salivary flow also have difficulty with eating, swallowing, and speech. The former can result in decreased food intake and poor nutrition. Sialadenitis was present in 11.72% of patients with hepatitis C.

Gingival bleeding was found with the same frequency in the two groups studied. All these patients had cirrhosis. Among patients with gingival bleeding 72.5% of those with HCV infection and 76.66% of those with HBV infection had hypersplenism with thrombocytopenia.

Oral candidiasis was more common in patients in the study group (20% vs.

6.66%), but note that 86.95% of patients with hepatitis C and candidiasis as well as 80% of those with hepatitis B and candidiasis had diabetes mellitus.

Periodontal disease was diagnosed in a higher percentage in the study group, probably due to a higher prevalence of diabetic patients, all of them being diagnosed with periodontitis in both groups studied.

DISCUSSIONS

Our study draws attention to some extrahepatic manifestations of HCV infection localized in the oral cavity. Outside lichen planus, xerostomia and sialadenitis, some studies have reported association of HCV infection with Sjogren syndrome, with oral cancer and Behcet syndrome. The common presence of gingival bleedings in patients with chronic liver diseases requires coagulation tests before invasive dental maneuvers.

Also be cautions in the administration of drugs: central nervous system depressants (barbiturates, opiates), hepatotoxic drugs (tetracycline, phenylbutazone) or drugs that can aggravate gingival bleeding (aspirin). More frequent presence of diabetes cause high prevalence of periodontal disease and candidiasis in these patients.

CONCLUSIONS

HCV is a major public health problem because it causes chronic hepatitis,

cirrhosis, and hepatocellular carcinoma (HCC). Chronic hepatitis C virus can remain asymptomatic for a long time, but patients can present a number of extrahepatic manifestations such as those in the oral cavity. Dentist has an active role in detecting infection with hepatitis C. On the other hand, given the risks, the dental treatment of patients with known chronic HCV liver disease raise special problems.

REFERENCES:

1. Van der Poel Cl., Cuyppers H.T., Reesink H.W.: Hepatitis C virus: six years on, *Lancet* 1994; 344:1475-9
2. Hervees., Savoye G., et al: Chronic hepatitis C with normal or abnormal aminotransferase (ALT) levels. Is it the same hepatitis_ *Gastroenterology* 1999; 116(4):A1221.
3. Sanchez Perey, De Castro M., Buezo G.F., et al: Lichen planus and hepatitis C virus: prevalence and clinical presentation of patients with lichen planus and hepatitis C virus infection. *J of Dermatology* 1996; 134:715-719
4. Mason A.L., Lau J.Z., et al: Association of diabetes mellitus and chronic hepatitis C virus infection. *Hepatology* 1999;299:328-333