

Oral Lichen Planus and Hepatitis C virus Infection: an Epidemiological Study of 149 Cases

Liquen Plano Oral e Infección del Virus de la Hepatitis C: un Estudio Epidemiológico de 149 Casos

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ABSTRACT: The objective of this investigation was to assess the prevalence of oral lichen planus (OLP) in Moroccan patients infected with hepatitis C virus (HCV) from the Hepatology service of Ibn Sina University hospital of Rabat. The study group consisted of 149 patients with HCV infection. All patients with clinical features of OLP were submitted to the service of oral surgery for confirmation. Among the 149 HCV-infected patients of the study group, 35 patients had OLP which represents a prevalence of 23.5%. Two out of these 35 patients with OLP-HCV association had cutaneous lichen planus (CLP) as well. Our findings indicate that there is a significant association between OLP and HCV infection especially for reticular and erosive types of OLP.

KEY WORDS: lichen planus, oral, HCV, hepatitis C.

INTRODUCTION

The relationship between hepatitis C virus (HCV) infection and oral lichen planus (OLP) remains a matter of controversy. OLP is a chronic inflammatory disease characterized by relapses and remissions (Epstein *et al.*, 2003) that occurs in approximately 1% to 2% of the general population (Epstein *et al.*; Miller *et al.*, 2001). It is a cell-mediated immune condition of unknown etiology (Epstein *et al.*).

HCV is a single-stranded, positive-sense RNA virus. It is a bloodborne pathogen, and important routes of transmission include blood transfusion, percutaneous exposure from contaminated needles, and occupational exposure to blood. After acute HCV infection, the proportion of patients who may remain chronically infected is estimated to be as high as 85% to 90% (Chainani-Wu *et al.*, 2004). A large proportion of these chronically infected individuals are asymptomatic carriers who may be unaware of being infected.

An association between OLP and HCV infection has been reported in the literature, especially in

Mediterranean areas and Japan (Chainani-Wu *et al.*). If this is a true association, OLP in certain populations can be used as a marker of HCV infection in asymptomatic patients, leading to diagnosis and early treatment and possibly a better prognosis.

This article reports the results of an epidemiological study that aims to investigate the prevalence of this association in Moroccan patients within the Hepatology service of Ibn Sina University hospital of Rabat.

MATERIAL AND METHOD

This study appears in the cross-sectional epidemiological investigation. It was conducted for a period of six months between November 2004 and May 2005.

The study was performed within the Hepatology service of Ibn Sina University hospital of Rabat in

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collaboration with oral surgery Service of the center of consultation and dental treatment of Rabat (CCDT).

The study group consisted of 149 patients with HCV infection from the Hepatology service of Ibn Sina University hospital of Rabat. 8 patients out of 149, who had an OLP, had been submitted from the CCDT of Rabat and have been revealed carriers of hepatitis C.

The diagnosis of HCV infection was based on the presence of the anti-HCV antibodies by means of a third generation enzyme-linked immunosorbent assay (ELISA). For 126 patients, confirmatory diagnosis was made by detection of serum HCV-RNA by means of polymerase chain reaction (PCR), whereas for the 23 remaining patients, we didn't get the results of this test. Patients with HCV infection having antibodies against any other type of viral hepatitis were excluded from this study. All patients with clinical features of OLP were submitted to a biopsy to confirm the diagnosis.

RESULTS

The study group consisted of 149 patients with HCV infection. 60% of these patients were female and 40% were male; the median age was 55 years old (23- to 90-year-old range). One percent of the patients were less than 33 years old, 63% were between 30 and 60 years old, while the remaining 36% were more than 60 years old. 28 patients out of 149 (19%) were under treatment of HCV (2 patients were treated with &-interferon and 26 patients were treated with &-interferon associated with ribavirin). 31% of the patients had been treated for HCV-infection but still had HCV RNA in serum. 50% of the patients were waiting for the beginning of the treatment.

Among the 149 patients of the study group, 35 patients (23.5%) had OLP and have been named subgroup B. 43% of these patients were female and 57% were male; the age was between 33 and 80 years old: 63%

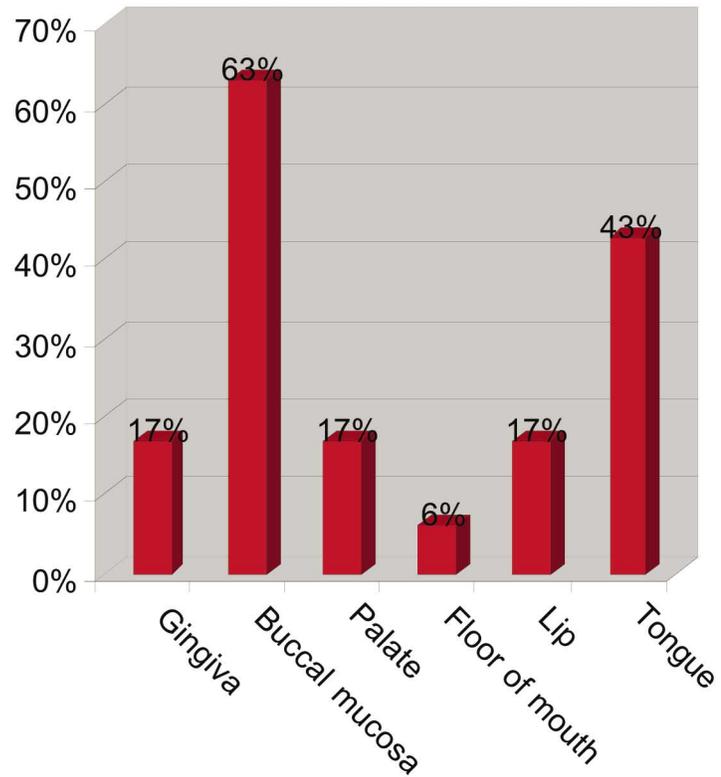


Fig. 1. Distribution of the patients of the subgroup B according to the localization of the OLP.

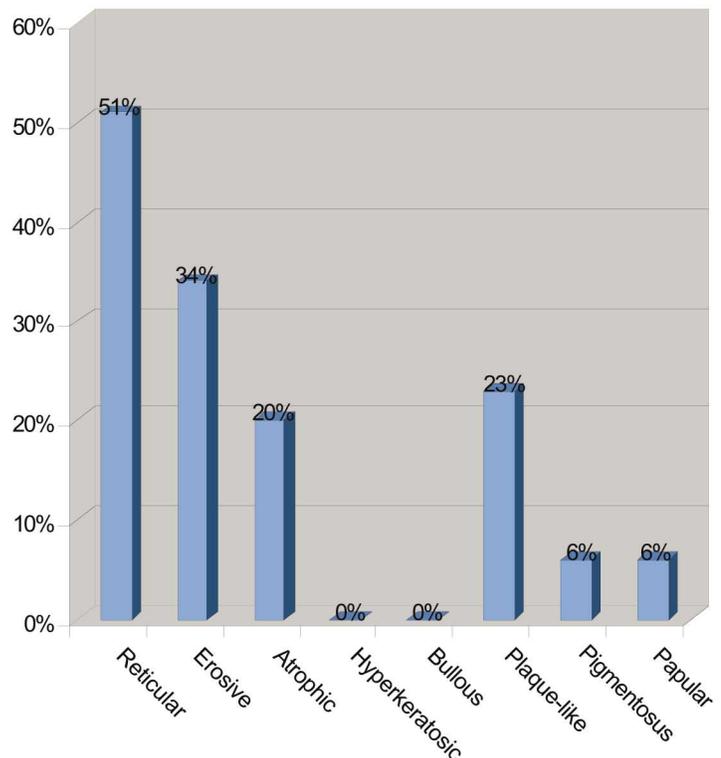


Fig. 2. Distribution of the patients of the subgroup B according to the type of the OLP.

were between 33 and 60 years old, while the remaining 37% were more than 60 years old. 57% of the subgroup B had not yet started the treatment, 17% have been under treatment during the period of the study (interferon + ribavirin) and 26% had been already treated.

Among the 35 HCV-infected patients with OLP association, 2 had a CLP as well and 8 others had non diagnosed dermatologic disorders. The buccal mucosa, and tongue involvement were more prevalent in patients with HCV infection (Fig. 1).

The reticular and erosive types of OLP were more prevalent among patients with HCV infection (Fig. 2). The diagnosis of the OLP has been confirmed by the anatomopathological exam for 27 patients. While for the 8 remaining patients, they only have been clinically diagnosed.

DISCUSSION

In recent years, both mucosal and cutaneous lichen planus have been reported to occur in the setting of chronic HCV infection (Ghodsi *et al.*, 2004).

In this study that we performed on a group of 149 patients infected with HCV, 35 (23.5%) patients had OLP as well. In addition, 2 out of these last had CLP.

This prevalence showed to be similar to the ones found around the Mediterranean basin that ranged from 14% (Rebora, 1992) to 28% (Mignogna *et al.*, 1998). However, a similar study (Cuha *et al.*, 2005) conducted in Brazil showed a very low prevalence of the OLP (1.5%). The study group consisted of 134 patients with HCV-infection (58% were female, 42% were male) ranging from 17 to 80 years old. In the literature, the frequency of the OLP-HCV association changes considerably; indeed, the prevalence of the anti-HCV antibodies regarding the patients with LP varying from 0% in England to 63% in Japan (Ghodsi *et al.*). Whereas, the prevalence of the OLP in HCV-infected patients varies from 1.5% in Brazil to 20% in the Scotland (Chainani-Wu *et al.*; Cunha *et al.*). However, there are few studies that investigated the prevalence of OLP in HCV patients in comparison with those that assessed the prevalence of HCV infection in patients with OLP (Cunha *et al.*).

While for the observed clinical form of OLP in patients infected with HCV, we found that the most frequently clinical forms of OLP of our study group are those of the reticular (51%) and erosive (34%) OLP. Here again, the epidemiological studies report conflicting results. In Italy, Gandolfo *et al.* (1994) showed that among ten cases of OLP-HCV association, all patients presented oral erosions. Almost 59% of the patients with erosive OLP in the study performed by Carozzo *et al.* (1996) were HCV-positive, whereas only 13,2% of those with nonerosive OLP presented with HCV infection. Dupond *et al.* (1998), in a study performed with 28 erosive OLP patients, found positivity for anti-HCV in 29% of them. However, Mignona *et al.* (2000) in a study that aims to evaluate the clinical forms of OLP between the seropositive and seronegative, did not reveal significant difference between these two groups for erosive and atrophic forms. The reticular form was more frequently in HCV-positive patients.

The sites of involvement the more frequent of OLP in our study group are buccal, tongue, gingival and labial mucosa with respective rates of 63%, 37%, 17% and 17%. According to the study conducted by Romero *et al.* (2002), the sites of involvement of OLP in HCV positive patients in relation with HCV negative patients are: gingiva, 71.4% versus 23.6%; tongue, 57.1% versus 29.1%; and lip mucosa, 28.6% versus 7.3%. The results of this study reinforce the need for liver examination in all patients with OLP, particularly those showing lesions on the gingiva with multiple intraoral locations affected. However, other studies show that the sites of OLP don't seem to be related to the HCV, since the OLP have been noticed anywhere in the oral mucosa (Bagan *et al.*, 1998).

Several hypotheses have been suggested for the co-occurrence of OLP and hepatitis C. However, there is still no definitive explanation for this association. Some authors believe that the concomitant occurrence of OLP and hepatic disease caused by HCV could be the result of a lichenoid reaction to the medication used in the treatment of hepatitis C, mainly α -interferon (Gandolfo *et al.*). In our study, 57% of the patients presented OLP even if they were not under treatment when the oral examination has been taking place. However, we observed a case of regression of the OLP after some weeks of the treatment with α -interferon and ribavirin. Based on information in the literature and for unknown reasons, the effect of α -interferon therapy on HCV-associated LP differs markedly from case to case (Carrozzo, 2008). α -interferon has been reported to have no influence (Pawlotsky *et al.*, 1995), to ameliorate

(Doutre *et al.*, 1992, 1996; Nagao *et al.*, 1999), or to trigger or worsen LP lesions (Nagao *et al.*, 1996; Varela *et al.*, 2000; Guijarro Guijarro *et al.*, 2001). In a small series of four OLP patients on long-term follow up after a-interferon treatment, a clinical and histological improvement of the oral lesions was noted after 3 years; similar to what was observed in the liver of patients responding to the anti-viral therapy (Nagao *et al.*, 1999). Ribavirin was reported to increase the risk of adverse cutaneous reactions, often of a lichenoid type (Sookoian *et al.*, 1999), and it apparently both worsened and improved LP (Manjón-Haces *et al.*, 2001; Harden *et al.*, 2003; Nagao *et al.*, 2005) but there are no large studies evaluating in details the impact of therapy for HCV infection on LP (Carrozzo).

It has been suggested that geographic localization could explain the different association between HCV and OLP. These may include the prevalence of HCV infection, the prevalence of other etiologic factors of OLP, differences in genetic susceptibility to HCV induced OLP, and differences in the genotypes of HCV (Chainani-Wu *et al.*). At present, there is not enough information to determine if HCV genotype plays a role in development of OLP (Chainani-Wu *et al.*).

Carrozzo *et al.*, (2001) in a study performed in Italy, showed that OLP patients with HCV infection had a statistically significant higher frequency of HLA class II allele HLA-DR6 than patients with OLP and without HCV infection. This could partially explain the peculiar geographical heterogeneity of the association between HCV and LP.

The results of our study indicate that there is an association between OLP and HCV infection especially for reticular and erosive forms. This allows us to conclude that OLP has to be used as a marker of HCV infection in asymptomatic patients, leading to diagnosis and early treatment and possibly a better prognosis. More studies are necessary for a better understanding of the relationship of OLP and HCV infection.

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RESUMEN: El objetivo de esta investigación fue evaluar la prevalencia de liquen plano oral (LPO) en los pacientes marroquíes infectados con hepatitis C (VHC) del Servicio de Hepatología del Hospital Universitario Ibn Sina de Rabat. El grupo de estudio consistió de 149 pacientes con infección por el VHC. Todos los pacientes con características clínicas de LPO se presentaron al servicio de cirugía oral para su confirmación. Entre los 149 pacientes infectados por VHC del grupo de estudio, 35 pacientes presentaban LPO, una prevalencia de 23,5%. Dos de estos 35 pacientes con LPO asociado al VHC tenían también liquen plano cutáneo (LPC). Nuestros hallazgos indican que existe una asociación significativa entre la LPO y la infección por el VHC, especialmente para los tipos de LPO reticular y erosivo.

PALABRAS CLAVE: liquen plano oral, VHC, hepatitis C.

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