

Oral Lichen Planus as an Extra-hepatic Manifestation of Viral Hepatitis—Evaluation in Indian Subpopulation

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ABSTRACT

Background: Oral Lichen Planus (OLP) is considered to be associated with numerous systemic conditions one of which includes Chronic Liver Disease (CLD). Hepatitis virus B and C (HBV and HCV) have known to be important causative agents of CLD and can be prevalent in asymptomatic carriers that can make them difficult to identify. Off late, the association of viral hepatitis with OLP has been a subject of controversy due to conflicting reports. Indian studies on this regard are sparse to evaluate the same. Association between the hepatitis virus and OLP, if present and established, can be of great help to format a protocol for identifying carrier states of viral hepatitis due to HBV and HCV.

Methodology: Forty five cases of clinically and histologically confirmed OLP were subjected to a serological screening of hepatitis B and C viruses by detection of hepatitis B surface antigen and anti-hepatitis C virus antibodies.

Results: None of OLP cases were seropositive for the hepatitis viruses.

Conclusion: We could not demonstrate any association between OLP and viral hepatitis. This could be attributed to lower prevalence of hepatitis viruses compared to the countries hyper endemic for these viruses or genotypic variation of the viruses or other etiological factors contributing for the present group of patients.

Key words: Oral lichen planus, Hepatitis B virus, Hepatitis C virus, Extra hepatic manifestations

INTRODUCTION

Lichen Planus (LP) is a chronic inflammatory possibly autoimmune mucocutaneous condition. LP affects oral mucosa with a variety of clinical presentations that includes reticular, papular, plaque type, erosive, atrophic and bullous lesions [1,2]. Oral Lichen Planus (OLP) affects from 0.1%–4% of the world population [3] and in Indian population its prevalence rate is 2.6% [4].

The current etiological factors include genetic background, infectious agents [3], immune reactions [2], stress and autoimmunity [5]. OLP has been associated with numerous diseases like diabetes mellitus, hypertension, graft versus host reactions, lupus erythematosus, myasthenia gravis and hepatitis [3,5].

A possible association between lichen planus and chronic liver disease has been thought about ever since the simultaneous occurrence of erosive lichen planus along with severe liver disease has been reported, later, several studies have suggested the possible relation between the two conditions. The liver diseases so far found to be associated with OLP are of chronic nature especially Chronic Active Hepatitis (CAH) and primary biliary cirrhosis [3].

Hepatitis B & C infections are among the major aetiological factors of the chronic liver disorders. Individuals infected by these viruses would either suffer from acute viral hepatitis and/or become chronic lifelong carriers of the virus. The carriers are difficult to diagnose and become possible source for spread of infection. Patients may also suffer from cirrhosis of liver, hepatocellular carcinoma, liver failure and death [6,7].

Since the identification of hepatitis C, it has been associated with lichen planus in general and oral lichen planus in particular. Worldwide Studies of the association of HCV and OLP have conflicting results demonstrating a positive association in Japan [8], Italy [9], Southern Europe [10], France [11] and Spain [12] and a negative association with The Netherlands [13] and United Kingdom [14]. HCV association with LP has been found in the Indian population in one study. However, in India HBV infection is more prevalent, leading us to believe that a similar association with HBV could also exist. This study was thus aimed to evaluate a group of OLP patients for the

simultaneous presence of hepatitis B & C virus infections.

MATERIAL & METHODS

A total of 45 cases of clinically and histopathologically confirmed OLP were included in the study of which 31 were males and 14 were females. The patients had reported and were diagnosed with OLP at the outpatient block of departments of Oral Medicine and Radiology, KLEVK Institute of Dental Sciences, Belgaum and SDM College of Dental Sciences, Dharwad, India. Detailed case history and consent was obtained from the patients. Patients who were on antiviral therapy for any other systemic illness were excluded from the study.

PROCEDURE

Following aseptic procedures, 5ml of intravenous blood was drawn. The serum was separated by centrifugation for 5min at 1000 rpm and stored at–20°C. It was then subjected to ELISA using 3rd generation ELISA kit, EliscanTM HBs (M/S RANBAXY DIAGNOSTICS, New Delhi, India) and Eliscan TM HCV (M/S RANBAXY DIAGNOSTICS, New Delhi, India) respectively using automated ELISA system.

RESULT

The study group of 45 patients comprised of 31 males and 14 females. The common age groups affected by OLP were between the ranges of 41-50 years and 21-30 years. 15 of the reported cases gave a positive history of recent stressful conditions. The medical history of the patient's revealed 4 patients suffering with diabetes mellitus, 3 having hypertension, 1 having contact dermatitis and 1 another having hypotension. 14 patients amongst the study group were tobacco abusers, 10 taking the smokeless form and 4 in the smoke form. An additional 8 patients were betel nut chewers.

Intraoral examination revealed 29 patients having the reticular form of OLP. 7 presented with plaque type, 4 atrophic type, 2 erosive type, 1 papular and 2 ulcerative form but all the cases had peripheral radiating and interlacing striae as seen in reticular type. 5 patients with OLP also presented with skin lesions. None of the patients were seropositive for hepatitis B or hepatitis C viral infection.

DISCUSSION

Out of the 45 clinically and histologically confirmed OLP patients evaluated for HBV and HCV in the serum using ELISA, none of the patients showed seropositivity for both the viruses.

Till date there have been many published reports which have proposed the possible association between OLP and chronic liver disease such as that with primary biliary cirrhosis and with chronic active hepatitis [15].

India has been found to have intermediate endemicity for Hepatitis B with HBsAg prevalence between 2%–7% per annum, with more than 1,00,000 Indians dying due to illness related to HBV infection according to the World Health Organization report. The prevalence of HBV is more than that of HCV which is at 1.8% in India [16].

The first report of a possible relation between HCV and OLP was established in 1991 by Mokin et al., [15]. In the present study all the patients were found to be seronegative to anti HCV antibody thus contradicting the report of an association between OLP and HCV. Many studies during recent years have focused on the relationship between OLP and HCV. Studies performed in Southern Europe, Spain, Japan, and Brazil have found significantly higher prevalence of HCV infection in OLP patients compared to their matched controls. Whereas studies from America, United Kingdom, France, The Netherlands, Nepal, Nigeria and Germany did not find a significant association between HCV and OLP [17]. The results of strong association were in the geographic areas considered to be hyperendemic areas for HCV. No association has been found in geographic areas with low HCV prevalence such as India [18,19] where a prevalence of 1.8% has been reported [16].

A possible explanation to this could be the genotypic variation of the infecting virus which may also play a role in variability of association of OLP and HCV [17]. A study conducted by Lodi G et al., to detect the HCV subtypes in OLP suggested that 51 % were infected by 1b sub type and 27% were affected by 2a subtype [19]. In India, another study conducted by Chowdhury A et al., [20] suggested the presence of HCV types 1b in 9.5%, 3a in 38.1%, 3b in 28.6%, and an unclassified one in 23.8%. The above mentioned varied results in diverse populations are suggestive of a non-uniform prevalence of viral subtypes and this could be attributed to the possible negative outcome of our study. The ELISA kit used by us could not categorise the variations in the subtypes of the hepatitis C virus.

In the present study, none of the 45 patients were infected by HBV, thus indicating no association between OLP and HBV infection. A similar finding to that of Ibrahim and co workers who found no difference in the prevalence of HBV in OLP patients in comparison to controls [17]. HBV has been traditionally considered to be the most prevalent viral infection associated with chronic liver disease in India [18]. After the advent of HBV vaccination there may have been some reports of individuals developing LP or LP like lesions following hepatitis B vaccination as stated by, Schupp P and Vente C [21], Agrawal A and Sheno SD [22]. The reports have postulated the lesions to be lichenoid reactions to the vaccines used. Till date about 15 cases of LP occurring after hepatitis B vaccination have been reported in the literature irrespective of the type of vaccine used [22].

There have been Indian studies suggesting a weak to absolutely no association between the HCV infection and lichen planus. These

studies have not evaluated OLP but have considered dermal lichen planus [23,24]. The present study although include cases pertaining to OLP with 5 of them having dermal manifestations, yet all of those were seronegative for HCV.

With the above stated findings and the plausible reasons for the outcome of this study, the authors would like to conclude the absence of any association between OLP and hepatitis B & C viral infections.

REFERENCES

- [1] Scully C and M El- Kom. Lichen planus: review and update on pathogenesis. *J of Oral Pathol.* 1985; 14: 431–58.
- [2] Mollaoglu N. Oral lichen planus: a review. *British Journal of Oral and Maxillofacial Surgery.* 2000; 38: 370–77.
- [3] Scully C, Beyli M, Feirero M, Ficarra G, Gill Y, et al. Update on oral lichen planus: Etiopathogenesis and management. *Crit Rev Oral Biol Med.* 1998; 9(1): 86–122.
- [4] GunaShekhar M, Reddy Sudhakar, Mohammad Shahul, John Tenny, Manyam Ravikanth, Manikyakumar N. Oral lichen planus in childhood: A rare case report *Dermatology Online Journal.* 2010; 16 (8): 9
- [5] Yamamoto T, Yoneda K, Ueta E, Osaki T. Cellular immunosuppression in oral lichen planus. *J Oral Pathol Med.* 1990; 19: 464-70
- [6] Pan CQ, Zhang JX. Natural history and clinical consequences of Hepatitis B virus infection. *Int. J. Med. Sci.* 2005; 2(1):36-40.
- [7] Lodi G, Porter SR and Scully C. Hepatitis C virus infection review and implications for the dentist. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1998; 86: 8-22.
- [8] Nagao Y, Sata M, Tanikawa K, Itoh K, Kameyama T. Lichen planus and hepatitis C virus in the northern Kyushu region of Japan. *Eur J Clin Invest.* 1995; 25: 910-4.
- [9] Gandolfo S, Carbone M, Carozzo M, Gallo V. Oral lichen planus and hepatitis C virus (HCV) infection: is there a relationship? A report of 10 cases. *J Oral Pathol Med.* 1994; 23:119-22.
- [10] Romero MA, Seoane J, Centelles PV, Diz-Dios P and Otero XL. Clinical and pathological characteristics of oral lichen planus in hepatitis C positive and negative patients. *Clin Otolaryngol.* 2002; 27: 22-26.
- [11] Jubert C, Pawlitsky JM, Pouget F, Andre C, DeForges L, et al. Lichen planus and hepatitis C virus-related chronic active hepatitis. *Arch Dermatol* 1994; 130: 73-6.
- [12] Bagán JoséV, Ramón C, Carozzo L, Diago M, Millán M A, Corset R, et al., Preliminary investigation of the association of oral lichen planus and hepatitis C. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1998; 85: 532-6.
- [13] Van Der Meij EH, Van Der Waal. Hepatitis C virus and oral lichen planus: a report from the Netherlands. *J Oral Pathol Med.* 2000; 29: 255-8.
- [14] Ingafou M, Porter SR, Scully C, Teo CG. No evidence of HCV infection or liver disease in British patients with oral lichen planus. *Int J Oral Maxillofac Surg.* 1998; 27: 65–66.
- [15] Klanrit P, Thongprasom K, Rojanawatsirivej S, Theamboonlers A, Poovorawan Y. Hepatitis C virus infection in Thai patients with oral lichen planus. *Oral Diseases.* 2003; 9: 292–297.
- [16] Theodore Sy, Jama MM .Epidemiology of Hepatitis C Virus (HCV) Infection. *Int J Med Sci.* 2006; 3: 41-46.
- [17] Nita Chainani-Wu. Hepatitis C virus and lichen planus: A review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2004; 98:171-83.
- [18] Sarin SK, Guptan RC, Banerjee K, Khandekar P. Low prevalence of hepatitis C viral infection in patients with non-alcoholic chronic liver disease in India. *J Assoc Physicians India.* Apr 1996; 44(4): 243-5.
- [19] Lodi G, Carozzo M, Hallett R, D'Amico E, Pattelli A, et al., HCV genotypes in Italian patients with HCV-related oral lichen planus. *J Oral Pathol Med.* 1997; 26: 381-4.
- [20] Abhijit Chowdhury, Amal Santra, Susmita Chaudhuri, Gopal Krishna Dhali, Sujit Chaudhuri, et al., Hepatitis C virus infection in the general population: A community-based study in West Bengal, India. *Hepatology.* 2003; 37(4): 802 – 809.
- [21] Schupp P, Vente C. Lichen planus following hepatitis B vaccination. *Int J Dermatol.* 1999; 38(10):799-800.
- [22] Agrawal Akhilesh, Sheno Shrutakirti D. Lichen planus secondary to hepatitis B vaccination. *Indian J Dermatol Venereol Leprol.* 2004; 70(4): 234–35.
- [23] Das A, Das J, Majumdar G, Bhattacharya N, Neogi DK, et al. No association between seropositivity for Hepatitis C virus and lichen planus: A case control study. *Indian J Dermatol Venereol Leprol.* 2006;72:198-200.
- [24] Prabhu S, Pavithran K, Sobhanadevi G. Lichen planus and hepatitis c virus (HCV) - Is there an association? A serological study of 65 cases. *Indian J Dermatol Venereol Leprol.* 2002;68:273-4.

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