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Original Research Article

Oral lichen planus and hepatitis C virus infection; a symbiotic relationship or a mere co-incidence?

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ABSTRACT

Background: Lichen planus (LP) is a common idiopathic chronic inflammatory immune mediated mucocutanous disease that effects stratified squamous epithelia and appendices. Hepatitis C virus (HCV) infection is quite common across the world. A couple of reports have suggested positive association of HCV infection and oral lichen planus (OLP) and most of the studies are usually confined to Mediterranean and south European countries. Due to high incidence and suspected alliance between these two diseases in Pakistan, the following study was conducted with the view that it may help clinicians to set guidelines for HCV testing of lichen planus patients.
Methods: Approximately 11500 patients from general population coming to dental diagnostics department of Fatima Memorial Hospital, Lahore (from March 2015-February 2016) were screened clinically for OLP and by ELISA for HCV infection. Out of these 11500 patients 103 were selected one of them incidental and the other pre-diagnosed or both incidental and both pre-diagnosed. These patients were unaware but had either one or both OLP and HCV infection which was confirmed clinically and by ELISA respectively.
Results: Majority of patients presenting for other dental complaints were unaware of these diseases process going on in them and was mostly an incidental finding by the clinician. Either one or both OLP and HCV infection were more conjoint in females comprising 77.7% of the total subjects. OLP alone was most common finding comprising 66.67% of the cases. HCV infection alone was present in 15.53% whereas 16.50% subjects showed presence of both OLP and HCV infection.
Conclusions: The current study could not detect statistically significant relationship between OLP and HCV infection in Pakistani population which could be due to genetic variation or may be geographic relationship.

Keywords: Association, Hepatitis C viral infection, Oral lichen planus

INTRODUCTION

Lichen planus (LP) is an immune-mediated disease affecting various organs including skin, oral cavity, genitalia, nails and scalp. Like all the immune-mediated diseases, LP also has a slight female predilection.[1] The cutaneous form of LP is rare with self-limiting pattern, however, the LP in the oral cavity can present with a chronic pattern which rarely goes into remission.[2] It can occur anywhere in the oral cavity but has preference for buccal mucosa, tongue, and gingivae. Clinically, oral lichen planus (OLP) can present as either bilateral white striations which is known as the reticular pattern. Along with white striations, it can also have an erythematous

patch, erosions, and bullae.[3] There are various types of OLP; reticular, erosive, atrophic, plaque-like, ulcerative and erythematous. Patients suffering from aggressive types of OLP such as atrophic or erosive disease commonly have substantial local morbidity. The disease has a negative impact on quality of life as it interferes with daily functions. Throughout the globe OLP has lichen planus (OLP) has gained significance as it is an established potentially oral malignant disorder.[4]

The answer to the question, 'what the etiology of the disease is?' is still unanswerable, but certain factors have been associated with the disease, for e.g., genetic factors such as Human Leukocyte Antigens like HLA-A3, A11, A26, A28, B3, B5, B7, B8, DR1, and DRW9. Various dental materials; metal or non-metal in nature, used for restorations are found to be associated with OLP. Various microorganisms such as gram-negative anaerobes, spirochetes, human papilloma virus, Epstein Bar Virus and Herpes Simplex Virus 6 have been studied as its etiology.[5,6] The pathogenesis is linked to the dysregulation of the cellular arm of the immune system. It is believed that apoptosis of basal cells of oral epithelium is mediated by T-cell auto-cytotoxic CD8 + T cells.[7] Furthermore, the presence of HCV-specific CD4+ and CD8+ lymphocytes in the sub epithelial connective tissue were reported suggesting a possible cause for pathogenesis of OLP. Several controversies exist regarding the relationship between OLP and HCV infection.[8]

HCV was first discovered in 1989. It was previously known as parentally transmitted or posttransfusion non-A non-B hepatitis.[9] It is an enveloped RNA virus ranging from 40 to 100 nm in diameter. The particle demonstrates a spherical shape with spikes attached to the surface. As far as its structure is concerned, it belongs to Flaviviridae family with genus Hepacivirus.[10,11] Almost 3% of the world population is chronically infected.[12] HCV infection is characterized by extremely high propensity of progression to persistent state. That may lead to chronic liver disease, such as cirrhosis and hepatocellular carcinoma with a leading indication for liver transplant in western countries.[13]

Across the globe in chronic HCV infection, a broad spectrum of extra hepatic manifestation has been observed that includes mixed cryoglobulinemia, membrano proliferative glomerulonephritis, autoimmune thyroiditis, non-Hodgkin's lymphoma, neuropathy and lymphoproliferative disorder. Some cutaneous manifestations such as porphyria cutanea tarda and leukocytoclastic vasculitis are also associated with chronic HCV infection.[14] Extra hepatic manifestations are quite common e.g. a large prospective cohort study suggested 74% of patients had at least one clinical extra-hepatic symptom. The extra hepatic manifestations could signify the first indication of this infection as the scarcity of HCV related specific symptoms in the patient. Furthermore, HCV can live in the extra-hepatic tissues and this may have an effect on HCV transmission, morbidity and treatment.[15]

METHODS

In this descriptive study, a total of 103 patients were selected from 11500 outdoor patients from the dental department (~0.1%) who were referred to the Oral Medicine Department, FMH College of Medicine and Dentistry, Lahore where the specialist examined all patients thoroughly for OLP, got them investigated and consulted for HCV infection when and where required. The patients were divided into three groups as following:

- Group A: Patients with OLP, pre-diagnosed or as incidental finding.
- Group B: Patients with pre-diagnosed, active HCV infection or as incidental finding due to classical clinical features of HCV (Hepatic encephalopathy, ankle edema, ascites, and hematemesis or variceal bleeding) further confirmed by ELISA.
- Group C: Patients presented with both diseases (one of them incidental and the other pre-diagnosed or both incidental and both pre-diagnosed).

Patients presenting with drug-induced lichenoid reaction (DILR) and lichenoid contact reaction (LCR) were excluded. None of the subjects selected had congenital or acquired disease. Neither patient had history of drug abuse, nor had any social habits (e.g. niswar, betel-nut).

The studied variables included age and gender. Subjects in all three groups underwent anti-HCV antibody test using ELISA method (Abbott's i1000SR and i2000SR 'ARCHITECT' immunoassay analyzer). Descriptive statistics were adopted to report the results by using SPSS 20.0 computer software.

RESULTS

A total of 103 patients were selected from 11500 outdoor patients from the dental department (~0.1%). The male to female ratio was 1:3.5 and it consisted of 23 (22%) males and 80 (78%) females.

In group A, there were 70 patients that consisted of 66.67% of the total study population. All of these had OLP only but no oral or systemic features of HCV infection. It included 16 (2.8%) males while 54 (75.7%) females and male to female ratio was 1: 2.8.

While in group B, 16 patients i.e. 15.53% of the total study population had HCV alone. None of them had symptomatic or asymptomatic OLP. There were 3 (18.8%) males while 13 (81.2%) females and male to female ratio was 1: 4.3.

In group C, there were 17 patients i.e. 16.50% of the total study population who had both OLP and HCV. It consisted of 4 (23.5%) males while 13 (76.5%) females

and male to female ratio was 1:3.2. This all is summarized in Table 1.

Table 1: Stratification of the patients according to gender and allocated group.

Groups	Males patient's %	Females patient's %	Total patient's %
A	22.8% (n=16)	75.7% (n=54)	66.67% (n=70)
B	18.8% (n=3)	81.2% (n=13)	15.53% (n=16)
C	23.5% (n=4)	76.5% (n=13)	16.50% (n=17)
Total	22.3% (n=23)	77.7% (n=80)	100% (n=103)

DISCUSSION

The association between HCV and OLP has been a centre of discussion over a long period of time. The first report indicating an association between chronic liver disease and OLP (ulcerative variant) was published in 1978.[16] The prevalence of patients suffering from both LP and chronic active HCV infection varies from 4.0% to 13.5%. However, the prevalence of anti-HCV antibodies in patients suffering from OLP ranged from 3.8 to 65%.[17]

Although the relation has been detected all around the world but the geographical variations with strong positive associations is quite evident in the East, Southeast Asia, South America and Mediterranean countries.[18] Carrozzo et al reported association of HCV with OLP as distinct subset among LP and is particularly associated with HLA-DR6.[19] There is significant variation in the prevalence of HCV in patients suffering from OLP, ranging from 3.8% in France to 62% in Japan.[20] This validates current study with literature from Europe but it varies highly from data of other parts of Asia.

There was no evidence of HCV infection in patients suffering from OLP in the British population whereas a relationship between cutaneous features of LP and hepatitis as low as 7.8% in a pool of 371 patients had been detected in Lahore, Pakistan that re-affirm low prevalence of both these conditions in the study group.[21] Dermatological presentation of various other cutaneous diseases was observed in 54% of the patients while no oral features of OLP were reported.[22] Keeping in mind that a majority of patients showed consistent signs of either disease instead of both presenting together reinforced the fact of a rare possibility of a concurrent pattern of both diseases presenting together. The ratio of male to female in the proposed study was 1:3.5, similar to studies performed in Saudi Arabia, Iran, and parts of India and Turkey.[23-26]

Liver disease may be diagnosed before, after or at the time of oral examination in patients who present with OLP, neglecting the role of either disease contributing to other.[27] However, data from Italy suggested possible contribution of HCV in the pathogenesis of OLP.[28] The association of HCV infection with OLP has been more prominently highlighted in the Mediterranean area.[29] The presence of anti-HCV antibodies in oral or cutaneous LP varies from 4-65% as studies conducted in southern Europe and Japanese population, whereas it is not so common in patients of OLP in Netherlands.[30] A study conducted in Sao Paulo suggested significant relationship between OLP and HCV but in the current study there was no significant association between OLP and HCV infection.[31] Despite the efforts of the authors the study had a few limitations. Genotyping which could further verify a negative co-relation between the two diseases could not be carried out due to lack of resources. As the study was a cross-sectional one, the patients were followed up with the intention to treat protocol and the possibility of OLP developing in patients with HCV later in life was not documented.

CONCLUSION

OLP may seldom occur in patients of systemic disease such as HCV. Although, cutaneous features are relatively low compared to oral features of LP in patients of HCV infection, both mucosal and cutaneous LP have been reported very rarely in patients with chronic HCV infection.

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