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Original Research Article

Comparative evaluation of the presence of serum antibodies SMA, Anti DNA, ANA and RF in the oral lichen planus and oral lichenoid drug and contact reactions

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Abstract

Introduction: Oral lichenoid reactions (OLR) are referred to a group of diseases that clinically and histologically could not be differentiated from the oral lichen planus (OLP) diseases. In the recent years, the two groups of diseases have been considered as T-Cell mediated inflammatory diseases. The aim of this study was to gather more information to help better distinguish these two lesions.

Method and Materials: In this descriptive-analytical study, blood samples were taken from 80 patients (59 females and 21 males) and sent to the laboratory for histopathological diagnosis based on WHO criteria. After separating the blood sera of the samples, the sera were evaluated by enzyme linked immunosorbent assay (ELISA) for the presence of ANA, anti-DNA, RF, and SMA auto-antibodies. Data statistically was analyzed with SPSS using the chi-squared test and t-test (p value= 0.05).

Results: The mean ages were 48.62 and 49.38 for OLP and OLR patients, respectively. There were no significant differences in ANA and RF blood levels (p value= 0.05). Anti-DNA and SMA antibodies were not detected in the blood samples. No significant differences were noted in the blood levels of these antibodies (p value= 0.05).

Conclusion: According to the results of the present study, no significant differences were observed between the OLP and OLR patients in relation to the presence or absence of ANA, anti-DNA, RF, and SMA auto-antibodies in the blood samples.

Keywords: Auto-antibodies, Autoimmune disease, Oral lichen planus, Oral lichenoid reaction.

1. Introduction

Lichenoid reactions are a group of lesions that have different etiologies but have similar clinical and histopathological presentation. Histopathological assessment could not differentiate various lichenoid reactions from each others. Lichenoid reactions are classified as follow [1]:

1) Lichen planus
2) Lichenoid contact reaction
3) Lichenoid drug reaction
4) Lichenoid reaction of graft versus host disease.

Lichen planus is a chronic autoimmune disease which can affect the oral mucosa, skin and genital mucosa, scalp and nail [2]. The disease has most often been reported in third to seventh decade of life in females [3]. Oral lichen planus is also observed in children although it is rare [4,5]. The prevalence of oral lichen planus in different population ranges between 0.38% to 2.6% [6,7]. Clinically, oral lichen planus can appear as white striations (Wickham's striae), white papules, white plaque, erythema, erosion or blisters [8]. The buccal mucosa, dorsum of tongue and gingival are

mostly affected. Oral lichen planus usually presents as a symmetrical and bilateral lesion or multiple lesion. It can appear in six types of clinical variants namely reticular, popular, plaque like, erosive, atrophic and bullous [8,9] and some variants can co-exist in the same patients. Burning sensation and sometimes pain usually accompany the erosive, atrophic or bullous type lesion [10]. There have been many similarities between lichen planus and drug lichenoid reaction, lichenoid reaction associated with contact with restorative material, leukoplakia, lupus erythematosus and graft versus host disease (GVHD). Direct immunofluorescence can aid in distinguishing oral lichen planus from other lesion especially vesiculo-bullous lesion such as pemphigus vulgaris, benign mucous membrane pemphigoid and linear IgA bullous dermatosis [10]. Oral lichenoid reaction has clinical variants similar to those of oral lichen planus ones. It has been associated with numerous drugs, although only some of these have been confirmed. Drugs such as beta blockers, dapsone, oral hypoglycemic, non-steroidal anti-inflammatory drugs (NSAIDs), penicillamine, phenothiazines, sulfonylureas and gold salts have been associated with lichenoid reactions [11]. Other than drugs, lichenoid reactions have also been associated with dental materials. Lichenoid reaction as an allergic reaction to dental materials has been widely reported. Many studies have confirmed contact hypersensitivity to dental materials such as amalgam [12-14], dental composite [15] and dental acrylics presenting as lichenoid reactions [16]. Some studies also showed resolution of oral lichenoid lesions following replacement of causative restorations. In most cases, oral lichenoid reactions are not indistinguishable from idiopathic oral lichen planus, clinically or histologically [14,17].

The diagnosis of oral lichen planus is usually made by clinical and histological evaluations. In classic lesions, it is possible to make a diagnosis based on its clinical appearance alone. The diagnosis of oral lichenoid reaction is difficult and the pathognomonic features of oral lichenoid reaction required further evaluations [10]. Although the exact etiology is unknown, oral lichen planus is recognized as a chronic disease of cell-mediated immune damage to the basal keratinocytes in the oral mucosa that are recognized as being antigenically foreign or altered [18]. Management of oral lichen planus remains palliative and topical corticosteroids remains the treatment of choice although several other medications have been studied including retinoids, tacrolimus, cyclosporine and photodynamic therapy [10]. Clinical transformation of oral lichen planus and lichenoid reactions deserved continued clinical follow up and must be histopathologically evaluated to rule out dysplasia and carcinoma involvement. For the purpose, not only the primary biopsy is essential, but also the frequent biopsies along with symptom alterations especially in the ulcerative and plaque like forms is critical [19].

Nowadays, autoantibodies and autoimmune diseases have been implicated in the development of various lesions especially neoplasm and precancerous lesions [20,21]. Some autoantibodies may involve in the development of the lesion, although the lesions have not the characteristics of a classic autoimmune disease, some studies has considered the oral lichen planus as an autoimmune disease [22]. The world health organization, has categorized oral lichen planus as a precancerous condition [23]. In histopathological evaluation of oral lichen planus, a band-like layer of T lymphocytes infiltrate along with macrophages and degeneration of basal cell layer are observed. The cellular presentations are associated with cell mediated immune system [24-25]. Majority of the T cells are activated CD8+ lymphocytes. At present, oral lichen planus and lichenoid reaction are taken into account as T-cell mediated inflammatory diseases [26,27]. The world health organization, has described at least three clinical and one histopathological criterion for distinguishing between the two groups of lesions. Lichenoid reactions have typical features as follow: definite etiology, unilateral, erythematous view (ulcerative or erosive), and in histopathological staining with toluidine-blue accompanied with degranulated mast cells. Otherwise the condition would fall into oral lichen planus diseases. In the present study we sought to gain more information about the immunological aspects of the two diseases to find further distinguishing criteria [28].

2. Materials and methods

The study is a descriptive-analytical research that was conducted on patients referred to our private clinic and oral and dental department of Isfahan dentistry faculty. After completing the medical history questionnaire and written consent from each patient, a biopsy sample was also taken to confirm the diagnosis. The biopsies were also used for treatment purposes. Prophylactic treatment was carried as needed under the supervision of their specialists. 24 hours before sampling, 10 mg trialuoprazine was prescribed for each patient to alleviate the work stress. On the morning of sampling day (7 hours before the initiation of sampling), dexametazon was administered to the patients. 2 incisional biopsies were taken from each patient. One biopsy was evaluated by hematoxylin and eosin (H&E) staining method and the other sample were assessed by direct immunofluorescence (DIF) method. DIF method was performed on frozen sections of biopsy and the fluorescently stained sections were evaluated under fluorescent microscopy. Various immunoglobulins (Ig) and the complements C3 and C4 were evaluated in samples by

using of the DIF method (Euro Immune,). The sample for H&E method was store in formalin solution, and that for DIF method was stored in Michell solution or physiological serum prior staining.

The biopsies were prepared under local anesthesia by using of a number 15 Bisory blade by an oral medicine specialist. The biopsy samples for H&E staining were placed in 10% formalin and sent for histopathological evaluation and the biopsy samples for DIF staining were immersed in Michell solution or physiological serum and sent to pathology laboratory.

After confirmation of OLP and OLR diseases, 10 cc of fasting blood sample was obtained from each patient. Serum aliquots were prepared from the blood samples and were assessed for the presence of autoantibodies ANA, Anti DNA, RF, and SMA. The presence of the autoantibodies was explored by using of ELISA methods (Binding Site Co.). Histopathological evaluation of the specimens by using of H&E staining differentiated OLP lesions from OLR that has degranulated mast cells. Clinical presentation of the lesions including unilateral or bilateral pattern, ulcerative and erythematous types or white and keratotic types and/or a combination of them, history of systemic diseases and hepatitis C, medications, the presence or absence of dental restorative materials were carefully taken into account by experienced pathologist to differentiate between OLP and OLR according to the WHO criteria.

Based on the features, patients were divided into two groups. Group I consisted of 40 cases of OLP and Group II also included 40 cases of OLR. Serum samples were obtained from the patient to explore the presence of the autoantibodies ANA, Anti DNA, RF, and SMA as described above. The findings of the study were analyzed by the statistical tests, t and X2.

3. Results

In the present study, collectively 80 blood samples from OLP (40 samples) and OLR (40 samples) patients were evaluated by using of ELISA method. The mean ages were 48.63 and 49.38 years in patients with OLP and OLR respectively. Patients with OLP lesions consisted of 14 men (35%) and 26 women (65%). Patients with OLR lesions comprised of 7 men (17.5%) and 33 women (82.5%). The most locations that are frequently affected by OLP and OLR depicted in table 1.

Table 1: Frequency of the afflicted locations

Lesion Location	Oral lichenoid reactions	Oral lichen planus
Tongue	1 (%2.5)	4 (%10)
Buccal mucosa	14 (%35)	19 (%47.5)
Gingiva	5 (%12.5)	2 (%5)
Lip	4 (%10)	0 (%0)
Tongue and buccal	9 (%22.5)	4 (%10)
Tongue and gingiva	7 (%17.5)	11 (%27.5)

ANA was present in 17% (n=7) of patients with OLR and in 15% (n=6) of patients with OLP; There was no statistically significant difference in the serum concentration of ANA between OLR and OLP patients (P value < 0.05).

There were no observations of Anti-DNA and SMA in the two groups of patients. About 7.5% (n=3) of patients with OLR were positive for RF antibody and 7.5% (n=3) of patients with OLR were also positive for RF antibody. The amount of the serum RF antibody levels was not different between the two groups of patients (P value < 0.05).

4. Discussion

Oral lichen planus as a relatively common disorder of oral cavity has been considered by researchers. Researchers have pursued convenient treatment approaches, given that the white and red lesions of the disease potentially transform into malignant lesions.

In the recent year, researcher have sought to the separation and categorization of the idiopatic white and red lesions of the disease, or those lesions of the disease that are associated with etiologies such as systemic diseases (cardiovascular and diabetic diseases), drug consumption (especially NSAIDs), chronic hepatitis (especially hepatitis C), amalgam restorations, Sensitivity foods, Graft versus host disease. If the clinical aspects of the lesion were as unilateral, red lesions (erythematous and ulcerative), presence of degranulated mast cells in toluidine blue staining, the disease would be OLR, otherwise the disease would be OLP. This classification is accordance with WHO criteria [23].

In the present study, we selected those patients that had a similar histopathological and clinical appearance, to differentiate between them through immunological evaluations according to the presence of aforementioned autoantibodies.

To the best of our knowledge, in the present study, for the first time OLP and OLR patients are compared based on the presence of autoantibodies. Previously, the presence of the autoantibodies had been evaluated in OLP patients in comparison with control subjects, although there is a controversial between researchers in this regard.

Although, Lundstrom *et al* studied that there are significantly higher levels of ANA, RF, AMA and SMA in OLP patients than in healthy control subjects [28]. The concentration of the autoantibodies in the serum of patients with erosive form of oral lichen planus were significantly increased in comparison with those in healthy controls and patients with reticular oral lichen planus [29].

In the present study, the amount of the autoantiboies ANA, AMA, SMA, and RF were not different between patients with OLP and OLR. However, RF was present in 7 patients (17.5%) with OLR and in 6 patients (15%) with OLR. Anti-DNA and SMA were negative in both groups of the patients.

According to the findings of the present study, it may be concluded that there is no specific immunologically differences between the two groups of patients. Further studies required to elucidate the presence of the autoantibodies ANA, AMA, SMA, and RF in the groups of patients especially in comparison with normal subjects.

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