EXPRESSION OF E-CADHERIN IN RELATION TO APOPTOTIC PHENOMENA IN ORAL LICHEN PLANUS LESIONS.

(A clinical and immunohistochemical study)

Thesis

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Conclusions

1. The decrease in E-cadherin expression correlates to the increase in apoptotic cell count in OLP lesions.

2. There in no difference in E-cadherin expression in various clinical presentations of OLP.

3. Alteration in E-cadherin expression in OLP lesions when compared to normal specimen does not augment the idea of dysplastic changes in OLP lesions.

Aim of the Study

The aim of this study was to evaluate:

1- The difference in the expression of E-cadherin adhesion molecule in cases of atrophic and papular oral lichen planus compared to normal mucosa.

2- The relation of E-cadherin expression to the histopathological finding of apoptosis in OLP lesions (Atrophic and Papular).

Introduction

Oral lichen planus (OLP) is a chronic inflammatory disease whose etiology has not yet been fully understood. It is characterized by immunoreactivity directed against the keratinocytes of the basal cell layer and mediated by cellular infiltrate consisting mainly of T-lymphocytes. The key events in the pathogenesis of lichen planus (LP) is a modification of a surface antigenemia of the basal keratinocytes which, in the presence of a particular structure of histocompatibility antigens, are recognized by the immune system as being non-self. This in turn starts as a chain reaction which ends by the destruction of the keratinocytes themselves ***(Gombos and Serpico,1984).***

There is evidence that the activated T cells attach to the basal epithelium and produce death of these cells by apoptosis. The basal cells of the epithelium undergo flattening and hydropic degeneration, their nuclei are injured at an early stage of the mitotic cell cycle and intercellular spaces appear. Some basal cells continue to differentiate normally, some regenerate, and there is repopulation from the margins of the lesion ***(Scully and El-kom,1985).***

The molecular basis for any biological or pathological phenomena was found to be largely dependent on the expression and function of a variety of cell adhesion molecules that mediate the interaction of cells with each other and the components of the extracellular matrix as well as, other cell surface receptors ***(Obrink,1986 and Dedhor et al.,1998).***

Cell-cell binding is a fundamental property of multicellular organisms and tissues, since it plays an essential role in organogenesis,

physical transport, signal transmission or transduction as well as immunological function Errors is the phenomenon lead to pathological changes ***(Shimoyama et al.,1989).***

Among the known adhesion molecules, Cadherin are Ca+2 dependant transmembrane glycoprotiens that mediate homotypic adhesion interaction between epithelial cells. Cadherin could participate in cell-cell interaction, by the formation of junctional complex, cell polarization, stratification and the formation of tight tissue sheets. Cadherin receptors are associated with a variety of cytoplasmic proteins and cytoskeletal components e.g. plakoglobin and catenin, which are cytoplasmic proteins linked to the actin cytoskeleton. The connections stabilize the adhesion junctions between epithelial cells ***(Behrens et al.,1993).*** Lacking the expression of E-cadherin produces precocious induction of programmed cell death (apoptosis) ***(Hermiston and Gordon,1995).***

As OLP lesions are characterized by basal cells apoptosis, it was found of interest to investigate any possible alterations in an important adhesion molecule as E-cadherin with such lesions.

Review of Literature

Lichen planus (LP) is an inflammatory mucocutaneous condition that usually exhibits a distinctive morphology. It was first described clinically by the British physician , Erasmus Wilson, in 1896 and histologically by Dubreuilh in1906. Wilson thought that the lesion looked similar enough to lichens, which are small plants consisting of symbiotic algae and fungi growing on rocks ***(Murrah and Perez,1999).***

The prevalence of lichen planus is unknown, but it is estimated to occur in less than 1 percent of the population. Estimates of the prevalence vary among different populations, but the condition does not appear to exhibit a racial predilection. ***(Boyd and Neldner,1991).*** LP was found to affect women more than men in a ratio of 3:2.It is primarily a disease of the middle aged, although it can affect people of all ages, ranging from young adults to the elderly. Most studies have revealed a mean age of 50 to 55 years. It is rarely seen in children ***(Molloaglu,2000;Wright,2001).***

The classic appearance of skin lesions includes violaceous polygonal flat-topped papules and plaques. Close examination reveals a reticulated pattern of white scales known as Wickham's striae. Early cutaneous lesions may be difficult to diagnose, often appearing as scattered erythematous papules. More developed and extensive lesions may mimic discoid lupus, psoriasis or secondary syphilis. The flexor surfaces of the extremities, particularly the wrists, are common locations for lichen planus. Another clue to the diagnosis is that lesions may occur in areas exposed to trauma, such as lacerations. This tendency is known as an isomorphic response, or Koebner's phenomenon. Lesions often resolve

with intense hyperpigmentation. Some physicians describe lichen planus with the six "Ps": ***p***ruritic, ***p***olygonal, ***p***lanar (flat-topped), ***p***urple ***p***apules and ***p***laques. While some patients may be asymptomatic, most experience intense pruritus, a hallmark of lichen planus. ***(Boyd and Neldner ,1991; Chung et al., 2001).***

While this "classic" form of cutaneous lichen planus is the most common, other variants do exist and exhibit various morphologies. Patients with hypertrophic lichen planus present with thick hyperkeratotic plaques commonly found on the anterior surface of the legs. In vesiculobullous lichen planus, patients exhibit blisters within the plaques, while the actinic type of lichen planus occurs on sun-exposed areas of skin. Cutaneous LP may undergo spontaneous resolution with 89% clearing within 2 years . However, about 20% of the cases may relapse ***(Scully and El-Kom,1985; Chung et al.,2001).***

While lichen planus often occurs only on cutaneous surfaces, it may also involve the nails, the scalp, the genital mucosa, and the oral mucosa. Nail involvement results in ridging,distal splitting, thinning, subungual hyperkeratosis,pteryguim formation, and permenant nail loss(***(Boyd and Nedlner,1991).***Scalp involvement results in scarring alopecia. Rarely there is laryngeal, esophageal,and conjuntival involvement ***(Eisen,1999; Surgeman et al.,2000a).***

Genital lichen planus may also exhibit various morphologies. In men, the classic lesion is visible as violaceous papules on the glans penis. In women, violaceous papules, hypertrophic lesions or erosions may occur, typically on the vulva. Erosive lichen planus may be very painful,

and in longstanding cases, may lead to alterations of the genital architecture ***(Lewis,1998).***

Oral lichen planus classically presents on the buccal mucosa as a white, lacy, reticular pattern. Papular, atrophic or erosive lesions may also occur. Erosive lesions, in particular, may be quite painful and lead to multiple complications such as secondary infections (particularly candida), and poor nutrition and dehydration secondary to pain. ***(Silverman et al.,1985).*** The condition presents usually as symmetrical and bilateral lesions, whereas sometimes it presents as multiple lesions in the mouth ***(Lozada-Nur and Miranda,1997).***

The most common type of OLP is the reticular form. Characteristically, it presents as slightly raised fine whitish keratotic lines that produce lace-like pattern ."Wikham's striae" are fine hyperkeratotic striations with an erythematous border radiating from the lesion that can get accentuated by stretching the surface mucosa. The lesion often occurs bilaterally in a symmetrical form on the buccal mucosa; also it may be seen on the lateral border of the tongue and less often on the gingiva and the lips . Reticular LP is likely to resolve in 41% of the cases ***(Scully and El-Kom,1985;Regezi and Scuibba,1999).***

A variant of reticular OLP is the plaque-like form,which clinically resembles leukoplakia but which has a multifocal distribution.These plaque-like lesions can range in presentation from smooth,flat areas to irregular,elevated areas.This variant is commonly found on the dorsum of the tongue and on the buccal mucosa ***(Thorn et al.,1988).***Both the reticular form and its plaque-like variant are usually asymptomatic***(Mollaoglu,2000).***

Erosive OLP is the second most common type.It presents as a mix of erythematous and ulcerated areas which are covered with a fibrinous plaque or a pseudomembrane. The periphery of the lesion is surrounded by the reticular pattern or finely radiating Wikham's striae.It is painful especially when the pseudomembrane or fibrinous plaque is disturbed.The lesions of erosive OLP migrate over time and tend to be multifocal***(Silverman et al.,1991;Bernard et al.,1993).***

Another two additional presentations are the atrophic and the bullous forms, which are considered variants of the erosive type.The atrophic form of OLP appears as diffuse,erythematous patches surrounded by fine Wikham's striae radiating from the periphery**.**The attached gingiva is frequently involved in this form of OLP which is referred to as "chronic desqumative gingivitis".It exhibits a patchy distribution,often over all four quadrants***(Bricker,1994;Lozada-Nur and Miranda,1997).*** Theses lesions may be also found on the dorsum of the tongue resulting in atrophy of the filiform and fungiform papillae so that it appears smooth and erythematous.This form can cause significant discomfort ***(Mollaoglu,2000).***

The bullous variant of OLP appears as small vesicles that tend to rupture easily.When they rupture they leave an ulcerated painful surface.This form is more rare than the other forms of OLP***(Zegarelli,1993).***The bullous form is commonly seen on the buccal mucosa,particularly in the lateral border of the tongue .The lesions are rarely seen on the gingiva and labial mucosa ***(Bricker,1994).***

The cause of increased oral cancer risk in OLP patients is unknown, although the oral mucosa affected by OLP may be more