Journal of Korean Medical Science
Vol. 2, No. 4, P 259-262, Dec. 1987

Lichen Planus Specific Antigen and Antibodies

—In a Patient with Generalized Lichen planus—

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A 43-year-old man with generalized lichen planus demonstrated serum antibodies against autologous lesional skin. Indirect immunofluorescence using serum and papular lesional skin revealed a lichen planus specific antigen found only in the granular layer. The specific tissue antigen was not detected in normal skin from this patient, in normal skin from patients with skin disorders other than lichen planus or in skin from normal control persons. When titers of the serum antibodies against lichen planus antigen were examined before and after a successful therapy a positive correlation of the titer could be found in this patient.

Key Words: *Lichen planus, lichen planus specific antigen, serum antibody titer*

INTRODUCTION

Lichen planus is a papulosquamous disorder of the skin and mucous membranes of world-wide distribution. The cause of this disease remains unknown. There is little solid evidence to support the older hypothesis of viral origin, neurologic changes, or psychologic stress as sole causative factors. Evidence currently available suggests that cell-mediated immunity is centrally involved in the pathogenesis of lichen planus, and T lymphocytes either helper/inducer or suppressor/cytotoxic subsets are participants in generating the typical lichen planus lesions (Bhan et al., 1981; Simon et al., 1983; Naukkarinen et al., 1985).

Recently, a lichen planus specific antigen (LPSA) was demonstrated by indirect immunofluorescence (IIF) using patient's serum and autologous or allogeneic lesional tissues from patients with lichen planus (Olsen et al., 1983; Olsen et al., 1984; Camisa et al., 1986). This LPSA occurred mostly in the granular layer but not in the horny layer, basal layer, basement membrane zone, or in the dermis.

The objectives of this case studies were to further determine whether LPSA could be a marker unique to lichen planus, and to examine if there were any changes of serum antibody titer in different clinical stages of the disease.

CASE REPORT

A 43-year-old man was seen for an evaluation of papules over the trunk and extremities and for whitish patches on the oral cavity, which occurred during a 4 weeks period preceding his first visit. The patient initially noted several violaceous papules on the thighs which had spread to involve the abdomen, lumbar regions, extensor aspects of the arms, and anterior lower legs, numbering about twenty in each area, within a few weeks. He also had whitish patches developing on the buccal mucosa at about the same time. He had no history of drug intake or infection which could be relevant to the skin lesions. His family history and past history revealed nothing to note.

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Examination of the pruritic skin lesions showed polygonal, slightly scaly, red-violaceous, flat topped papules distributed almost symmetrically. Oral lesions on the buccal mucosa appeared as a lacy white network, extending to a part of the lower lip. Other physical findins were all in normal ranges.

Biopsy specimens taken from pruritic papules on the lower leg and buccal mucosal lesion showed findings consistent with lichen planus including hyperkeratosis, focal hypergranulosis of the epidermis, vacuolization of the basal cells, and band-like lymphohistiocytic infiltrate in the upper dermis encroaching upon the dermoepidermal junction. Direct immunofluorescence (DIF) with the above two different specimens demonstrated heavy deposits of fibrin and cytoid bodies stained with IgM, IgG, and C3, along the dermoepidermal interface. Under a routine IIF using rat tongue as the substrate, neither circulating basement membrane zone antibodies nor intercellular substance antibodies were detected.

Laboratory studies including a complete blood count with differential, ESR, urinalysis, stool examination, and chest roentgenogram were within normal ranges. The pattern of serum protein electrophoresis, the values of liver, kidney, and thyroid function tests, the level of fasting blood sugar, the serum concentrations of IgG, IgA, IgM, serum total hemolytic complement (CH50) and C3, C4 concentrations, antinuclear antibody, cryoglobulin, latex fixing rheumatoid factor, VDRL, and ASTO were all within normal limits or negative.

This patient, who showed a rare generalized form of lichen planus, was treated with intramuscular injection of triamcinolone acetonide (40 mg, biweekly) for systemic effect, with adjunctive intralesional triamcinolone acetonide for oral lesions, and topical corticosteroids (0.25% fluocortolone) for skin lesions. After 7 weeks of treatment most of the skin and oral lesions had subsided. A follow-up examination of the skin lesions 2 months thereafter showed no tendency of recurrence.

CLINICAL EXPERIMENTS

In Vitro Demonstration of LPSA

IIF tests employing two autologous skin specimens taken from fully developed papular lesions, serum (diluted 1:8) obtained before the treatment, and goat antihuman polyvalent antiserum (Meloy Co., Springfield, USA) revealed that the patient contained antibodies reactive to epidermal cells. The fluorescence

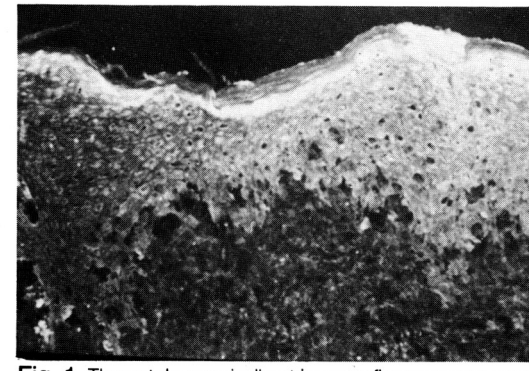

Fig. 1. The autologous indirect immunofluorescence assay demonstrates deposits of immunoglobulin (polyvalent) in the granular layer of the epidermis (x200).

patterns noted on the above substrates were consistently associated with intense staining of the granular cell layer of the epidermis with much less intense diffuse cytoplasmic staining patterns in the upper squamous cells of the epidermis (Fig. 1). Serum antibodies were also detectable on the cytoid bodies deposited at the papillary dermis. However, antibodies to dermal cells, basement membrane zone, or horny layer were not noted. IIF with serum from lichen planus patient revealed no positive reactions with normal skin taken from the flank of the patient, normal and lesional skin taken from each two patients with pemphigus vulgaris, bullous pemphigoid, and chronic eczema, as well as skin from two normal persons. Conversely sera (diluted 1:8) from these controls failed to demonstrate antibodies to the granular layer with the same substrates of lichen planus lesional skin.

Utilizing immunoglobulin class specific secondary reagents, it was shown that antibodies to the LPSA from this patient's serum tested were mostly IgM and IgG. However, the patient's serum did not have IgA type antibodies to the LPSA.

Titration of Serum Antibodies to the LPSA

To examine a possible change of the antibody titer against LPSA, the patient's sera were collected before and 8 weeks after corticosteroid therapy when the clinical remission was evident. The IIF assay, utilizing the above papular lichen planus lesions as the substrates and a polyvalent antiserum, showed that there was a significant difference in the titer of the antibodies between the two different phases of the lichen planus in this patient. From a serum sample obtained at the time of his first visit

the titer was 1:64, but the titer of a serum sample taken at the time of clinical remission was decreased to 1:16. Negative controls including normal serum as the primary reagent and omission of the primary incubation with the serum resulted in negative findings.

DISCUSSION

Regarding the pathogenesis of lichen planus there is no universally agreed hypothesis. However, the autoimmune pathogenesis, even controversial, is still attractive (Black, 1977; Fellner, 1980; Hsiao et al., 1986; Shuttleworth et al., 1986). In fact, there are reports of patients who have lichen planus with one or more autoimmune diseases, such as myasthenia gravis (Aronson et al., 1978), systemic lupus erythematosus (Ahmed et al., 1982), primary biliary cirrhosis (Epstein, 1984), morphea (Connelly and Winkelmann, 1985), and pemphigus vulgaris (Lee et al., 1987). Recent studies suggested that lichen planus represents a cell—mediated immunological response to an induced antigenic changes in the epidermal cells in a genetically predisposed individual (Bhan et al., 1981; Naukkarinen et al., 1985; Black, 1977; Hsiao et al., 1986).

Results from recent IIF studies of patients with classic skin and mucous membrane lichen planus, using autologous and allogeneic lichen planus lesions as substrates, gave evidence of circulating antibodies directed against as-yet-unidentified antigen (s) in the granular layer (Olsen et al., 1983; Olsen et al., 1984; Camisa et al., 1986). The clinical experiments with this patient further confirmed the presence of specific antigen in lesional skin as reported previously. The LPSA was found mainly in the granular layer but not in the horny layer, basement membrane zone, or in dermal skin components (Fig. 1). The specificity of the LPSA was confirmed in several ways. Firstly, serum from this patient reacted with LPSA in autologous lesions. Secondly, anti-LPSA serum failed to cross react with normal skin remote from the lesional sites in this patient and skin from patients with non-lichen planus dermatoses or normal controls did not contain antibodies to the LPSA. The antigenic characteristics of this LPSA in the granular cells seems not to have any relation to that of the "induced antigenic changes in the epidermal cells" (probably on the cell membrane) mentioned above.

The DIF assay did not demonstrate any fluorescence in the granular layer as seen in the IIF method. The inability to detect antibodies bound to the LPSA in the biopsy materials may be due to the fact that the amount of bound immunoglobulin was below the limit of resolution for DIF, perhaps, caused by the low *in vivo* affinity of the antibodies.

Although the LPSA is associated with lichen planus and the serum titer was somewhat correlated with the disease activity, this may be a secondary phenomenon which can be observed during the process of autoimmune repair mechanism unique in lichen planus.

The autoimmune pathomechanism relevant to the development of lichen planus, and the nature of LPSA will further be elucidated through more sophisticated immunologic studies of the pathologic epidermal cells.

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