



# Two cases with lichen planus pigmentosus inversus accompanying ankylosing spondylitis and diabetes mellitus

*Liken planus pigmentozusa eşlik eden ankilozan spondilit ve diabetes mellitusu olan iki hasta*

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## Abstract

Lichen planus pigmentosus (LPP) is an inflammatory dermatosis with an unknown etiology characterized by dark brown-black macules, papules and patches. LPP is considered as a rare variant of lichen planus (LP), but it differs from the LP by the absence of nail and oral area involvement and pruritus. LPP is most common on sun-exposed areas and less frequently seen in the axilla, inguinal or submammary regions. In the literature, very few cases have been reported to be associated with LPP. Herein, we reported two cases with LPP accompanied by ankylosing spondylitis and high levels of adrenocorticotrophic hormone along with diabetes mellitus.

**Keywords:** Lichen planus pigmentosus inversus, ankylosing spondylitis, diabetes mellitus, autoimmune diseases

## Öz

Lichen planus pigmentozus (LPP) etiolojisi bilinmeyen, koyu kahverengi-siyah makül, papül ve plaklarla karakterize enflamatuvar dermatozlardır. LPP lichen planus'un (LP) nadir görülen bir varyantı olarak düşünülmele birlikte tırnak ve oral bölge tutulumu görülmemesi ve kaşıntı olmaması ile LP'den ayrılır. LPP genellikle güneş maruziyeti olan bölgelerde ve daha az sıklıkla da aksilla, inguinal bölge ya da submammaryan bölgede görülür. Literatürde LPP'ye eşlik eden hastalıkla birlikte sunulan çok az sayıda olgu bildirilmiştir. Biz burada, ankilozan spondilitin ve serum adrenokortikotropik hormon yüksekliği ile birlikte diabetes mellitusun eşlik ettiği LPP'li iki olguyu bildirdik.

**Anahtar Kelimeler:** Liken planus pigmentozus inversus, ankilozan spondilit, diabetes mellitus, otoimmün hastalık

## Introduction

Lichen planus pigmentosus (LPP) is a chronic pigmentary disorder that shows diffuse or reticulated hyperpigmented macules<sup>1</sup>. LPP is categorized into many variants according to its location, distribution and morphology<sup>2</sup>. Sub-types such as actinic, linear, zosteriform and inversus have been defined so far<sup>3,4</sup>. The patches are usually symmetrical in distribution but may be found in a segmental, zosteriform, or blaschkoid pattern. The exact etiology is unknown. An autoimmune attack is generally accepted, as demonstrated by the inflammatory infiltrate of T-lymphocytes with varying populations of CD4+ and CD8+ cells, and the autoreactive

cytotoxic T-lymphocytes are implicated as the effector cells, which cause degeneration and destruction of keratinocytes<sup>5,6</sup>. Herein we report two cases of LPP in association with autoimmune disease such as ankylosing spondylitis and other disease such as diabetes mellitus.

## Case Report

Patient 1: A 32-year-old male patient with Fitzpatrick skin type 5, two-year pruritic papules on his right arm with a brownish-brown macules developed within 1 year on the face. He said that the lesions on the arm were treated when he applied a cortisone cream but then they recurred. There was no history

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of prolonged exposure on the lesion site. Medical history included the use diclofenac sodium tablets in ankylosing spondylitis for 8 years only in the presence of back pain. The examination revealed dark brown-black macules in the right/left malar region and the right axilla and, erythematous red-brown papules in the right forearm medial region. (Figure 1) There was no oral or nail involvement. The routine laboratory data were within normal limits.

Patient 2: A 55-year-old female patient with Fitzpatrick skin type 3 has developed brown reticular hyperpigmented macules around her breast



**Figure 1.** Brown-black macules in the malar region and the axilla, erythematous red-brown papules in the forearm



**Figure 2.** Brown papules were in the lumbar region and around the umbilicus with reticulated brown macules in both submammary regions

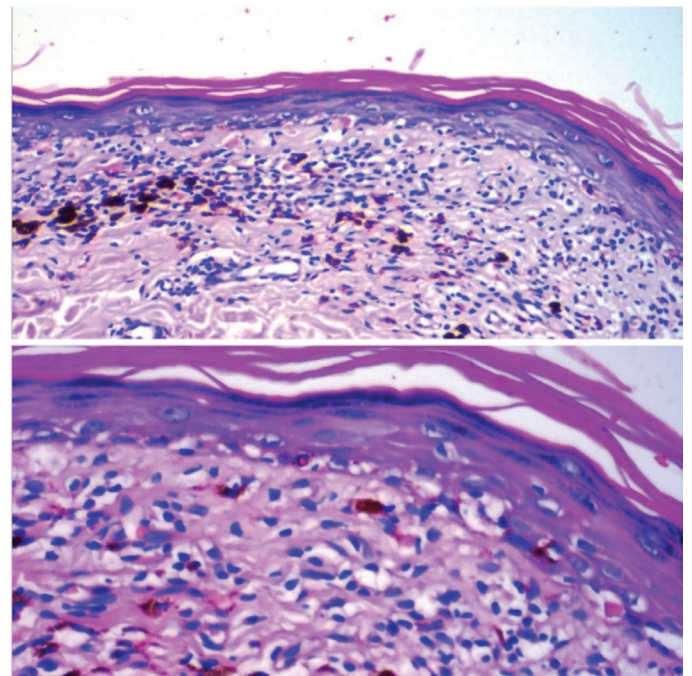
and navel and, red-brown papular lesions in the lumbar region in the last 6 months. No medication was used for treatment. No chronic disease was included in the medical history. During the examination, brown papules were seen in the lumbar region and around the umbilicus along with reticulated dark brown macules in both submammary regions. (Figure 2) The routine laboratory data of fasting glucose level was 283 mg/dL (n=70-99 mg/dL), adrenocorticotropic hormone (ACTH) (72.77 pg/mL) (n=7.2-63.3 pg/mL) and protein (++) and glucose (++) were tested positive in urine analysis. The patient was diagnosed with diabetes mellitus and was started antidiabetic therapy.

In all these cases, skin biopsies showed some examples of hyperkeratinized stratified squamous epithelium, irregular acanthosis and hypertrophy in the epithelial layer, hydropic degeneration in basal lamina, papillary edema, perivascular inflammatory infiltration and pigmentary incontinence with melanophages (Figure 3).

Mometasone furoate 0.1% cream (2 times/day) treatment was used for both of the two patients and then they were monitored.

## Discussion

LPP is most commonly seen in the upper extremities and the trunk such as the face and neck, and rarely in the lower extremities and the flexural areas. In 2001, Pock et al.<sup>4</sup> found that in a case of 7 patients, 90% of the patients developed lesions on intertriginous areas, which was defined as LPP-inversus. Variants of LP can be present in patients with LPP, such as the common papular type or rare types like bullous or actinic LP. Usually, there is no pruritus, and involvement of oral mucosa is rare as in LP<sup>1</sup>. In two of our patients, typical LP papules were associated with the disease and there was no pruritus. No mucosal or oral involvement was found in both patients.



**Figure 3.** Hyper-keratinized squamous epithelium, hydropic degeneration in basal lamina and perivascular inflammatory infiltration and pigmentary incontinence with melanophages (hematoxylin and eosin, x400)

Although the etiology of LPP is unknown; drugs, sun exposure, internal malignancy, liver diseases, impaired carbohydrate metabolism have been proposed as pathogenic factors<sup>7</sup>. Some researches proposed that LPP was a Koebner phenomenon, which develops as a result of wearing tight clothing<sup>8</sup>. Some researchers reported that cytotoxic activity induced by CD8 T lymphocytes against basal keratinocytes played a role in the etiology<sup>9</sup>.

LPP is considered to be among dermatoses that cause acquired hyperpigmentation. The differential diagnosis should include erythema discroicum perstans, actinic lichen planus, Riehl melanosis and fixed drug eruption. In our first patient, hyperpigmented macules in sun-exposed areas were considered to be differential diagnosis. However, the lesions in the axillary area proved otherwise. The patient was asked about the cutaneous drug reaction due to the history of diclofenac sodium in ankylosing spondylitis, but since these lesions developed in the no medication period and pigment incontinence was prominent in the histopathological findings and consistent with LPP, the medical history was not considered as the etiology of the disease. Recent studies have shown that LPP inversus also plays a role in T lymphocyte-induced cytotoxic activity against basal keratinocytes as in classical LP<sup>7</sup>. Kashima et al.<sup>10</sup> reported that the immunohistochemical studies of two Japanese patients with LPP-inversus revealed CD8 (+) T-cell infiltration with keratinocyte damage in the epidermis and upper dermis, and a high content of CD1a (+) cells in the epidermis, focal expressions of human leukocyte antigen (HLA)-DR on keratinocytes. Kanwar et al.<sup>1</sup> reported a linear deposition of immunoglobulin M or C3 in the basal membrane in the direct immunofluorescence study. It is known that the same autoimmune mechanism where cytotoxic T-cell response is generated and genetic predisposition and autoimmunity of ankylosing spondylitis and LPP are also responsible for the etiopathogenesis in ankylosing spondylitis, which is one of the sero-negative spondyloarthropathies, genetically associated with HLA-B27<sup>11</sup>.

Bhat et al.<sup>12</sup> found that 26% of 30 clinically diagnosed LPP patients reported associations such as hypertension, diabetes mellitus, hypothyroidism and epilepsy. Karn et al.<sup>13</sup> found that thyroid peroxidase autoantibodies were significantly higher in 54 patients with LPP compared to the control group. In the second patient we reported, diabetes mellitus was associated with LPP with elevated levels of serum ACTH. LPP has been associated with endocrinopathies in a study from Mexico, including type two diabetes in 38%. These associations may be due to the chronic inflammatory state in patients with LPP, which may produce insulin resistance<sup>14,15</sup>.

Although the lesions are generally resistant to treatment in LPP, oral steroids, topical corticosteroid and tacrolimus are used<sup>16</sup>. Spontaneous remission may occur in some cases or the disease may persist for many years despite treatment.

In the literature, there are previous reports of some diseases accompanying LPP such as antinuclear antibodies, frontal fibrosing alopecia, acrokeratosis of Bazex, head and neck carcinomas, hepatitis C infection and Nephrotic syndrome<sup>17-20</sup>. We have reported these cases in order to draw attention to fact LPP is not only caused by immune dysregulation but also associated with autoimmune diseases such as ankylosing spondylitis and carbohydrate metabolism disorders such as diabetes mellitus in the etiology.

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## Ethics

**Informed Consent:** Informed consent was obtained from our patient.

**Peer-review:** Externally peer-reviewed.

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