CASE REPORT

Atypical variant of lichen planus mimicking normal skin histology

FLAVIA BADERCA1, RODICA LIGHEZAN1, AURORA ALEXA1, DELIA ZĂHOI2, M. RAICA1, D. IZVERNARIU1, LORENA ARDELEAN3

1)Department of Histology
2)Department of Anatomy
"Victor Babes" University of Medicine and Pharmacy, Timisoara
3)Private Practice of Dermatology, Timisoara

Abstract
We present the case of a 69-year-old Caucasian and non-smoker patient with erythematous, itchy, violaceous lesions on the ankles, wrists, lower legs, forearms and trunk developed within 15 months. Her condition was diagnosed as prurigo and she was treated for a long period of time with antihistaminic drugs, with no resolution of lesions. In October 2008, she presented to a Private Practice of Dermatology in Timisoara. The dermatologist noticed the development of violaceous lesions on her trunk. The patient had similar lesions on the ankles, wrists, lower legs, and forearms for the last eight months. At physical examination many hyperpigmented, 1 to 6 cm, thin plaques were present on the flanks, shoulders, and infra-mammary area. There was no vaginal involvement. This eruption had a good response to topical glucocorticoids, but recurred multiple times after discontinuation of treatment. A biopsy specimen showed some histopathological features of lichen planus.

Keywords: lichen planus, normal skin.

Introduction
Lichen planus is a common inflammatory disease of the skin, mouth, nails, and scalp [1–3]. The name “lichen” refers to the lichen plant, which grows on rocks or trees, and “planus” means flat. It was first described by Sir Erasmus Wilson in 1869 [4]. It affects about one to two percent of the general population [1–3].

The classification of lichen planus upon clinical criteria include annular, linear, hypertrophic, verrucous, atrophic, morphoeic, annular atrophic, vesiculo-bullous, erosive, follicular, pigmentous, buccal, actinicus lichen planus and lichen planopilaris [1, 5], all these being variants of the same pathological process, with pathognomonic histological features, modified by intensity and location of the process [6].

Usually, lichen planus is relatively straightforward to diagnose. Physicians can make the diagnosis in typical cases simply by looking at the rash. If necessary, a skin biopsy may be done to confirm the diagnosis.

In florid active stage, the classical lichen planus has five major histological features: hyperkeratosis, hypergranulosis, acanthosis, heavy band-like lymphocytic infiltrate in upper dermis and hydropic degeneration of epidermal basal layer.

This tell-tale appearance under the microscope can be valuable in ensuring that the rash or spots are lichen planus.

Persistent oral or vaginal lichen planus, with spots that thicken and grow together, can sometimes be difficult to distinguish clinically from whitish precancerous plaques called leukoplakia. A biopsy can be very helpful in this situation.

Widespread lichen planus with erosions in the mouth can also be confusing. A biopsy may be required to distinguish this from other conditions such as candidosis, carcinoma and aphthous ulcers in the mouth.

A skin biopsy is not always practical in children where it is preferable to initiate the treatment without histological confirmation. A biopsy is essential in all cases that fail to respond to adequate treatment [7]. But, with the passage of time, the active destruction of basal layer ceases and the chronic inflammatory infiltrate in the upper dermis reduces; the epidermis regains its normal configuration, making diagnosis of lichen planus hard to establish [6].

The aim of this study was to highlight the histopathological features of an atypical lichen planus and to compare the morphology of the skin affected by lichen planus with the normal histology of the skin.

Materials and Methods
Specimens
Human tissue samples were obtained from fresh surgical specimens of a 69-year-old Caucasian and non-smoker patient. The otherwise healthy woman noticed the development of the erythematous, itchy lesions on the ankles, wrists, lower legs, and forearms for the last 15 months. They expanded to the back, the shoulders, and the upper part of the legs and arms. The individual lesions were small and of ivory or reddish in color, with shiny papules and macules. The surface displayed prominent dilated pilosebaceous or sweat duct orifices.

In August 2008, she presented herself to a Private...
Practice of Dermatology in Timișoara, where the dermatologist noticed an extensive eruption, predominantly on dorsal aspects of extremities and trunk, consisting of ivory to red and violaceous papular nodules covered with a thick, adherent scale. These lesions were characterized by round, flat-topped, flesh colored papules, 2 to 5 mm in diameter that occurred in groups but did not coalesce and had a scaly surface. The patient had similar lesions on her ankles, wrists, lower legs, and forearms for the last 15 months, but in these regions, the pruritic-thickened papules were excoriated, hyperpigmented, and often covered with a crust. At physical examination, many hyperpigmented, 2 to 5 mm, thin plaques were present on the flanks, shoulders, and infra-mammary area. Their color varied from ivory to bright red to violaceous to brown and their surface was smooth or slightly verrucous.

She also complained of an irritation of the tongue, but the dermatologist noticed only few small white plaques. There was no vaginal involvement. Lymphadenopathy and hepatosplenomegaly were absent.

A complete blood count, comprehensive metabolic panel, and thyroid function were normal. Urine analysis and serum chemistry, including sugar and liver function tests, were all normal. Serology for hepatitis B and C virus was negative. Antinuclear antibody was negative and rapid plasma reagin test was non-reactive. Serum protein electrophoresis and immunofixation showed no monoclonal increase in immunoglobulins.

A review of systems was negative for fever, chills, weight loss, or fatigue. Past medical history and family history were not remarkable.

In order to confirm the diagnosis, a skin biopsy was taken from a lumbar lesion. The biopsy was immediately fixed in 4% v/v buffered formalin and sent for histopathological examination. Specimens were embedded in paraffin, and step sections were stained with routine Hematoxylin–Eosin method.

Sections were examined under oil immersion with a ×100 objective on a Nikon Eclipse E-400 microscope, and images were captured using a Coolpix 995 digital camera and a DN-100 digital imaging system (Nikon Instruments, Surrey, United Kingdom).

Histological sections were reviewed independently by two pathologists and then discussed for consensus.

Results

Gross pathology

The resected specimen was represented by a skin biopsy measuring 1 cm in its largest dimension. Visual inspection of the biopsied specimen, 10×5×2 mm in size, showed the presence of three papulomatous lesions, 2 to 4 mm in diameter. The slides were stained with Hematoxylin–Eosin.

Light microscopy

The case was analyzed for the presence of the following features: interface pattern; rete ridge pattern; cytoid bodies, defined as round or ovoid, eosinophilic homogeneous masses, approximately 10–20 µm in diameter, found in the lower epidermis or upper dermis; wedge-shaped hypergranulosis, basal squamatization, basal epidermotropism, defined as lymphocytes in the lower epidermis with scant or absent spongiosis, epidermal atrophy, follicular plugging, eosinophils, basement membrane thickening and elastic fiber density in the papillary dermis.

Scanning magnification discloses a relatively normal epithelium.

In normal epithelium, on histologic sections, basal cells were seen as a single row of cells above the basement membrane that showed minor variation in size, shape and melanin content. Basal cells were elongated or cuboidal, and with melanin in their cytoplasm because of pigment transfer from neighboring melanocytes. The nucleus was round or oval with coarse chromatin and with an indistinct nucleolus. The spinous layer was composed of several cell rows. The suprabasal keratinocytes were polyhedral, relatively basophilic and with a round nucleus. Melanin was noticed scattered in many of these keratinocytes. The upper superficial cells were larger, flattened, eosinophilic, and oriented parallel to the surface. An intercellular space of constant dimensions was present between each cell.

At epidermal level, basal cells were not arranged uniformly in a single layer on basal lamina compared to the normal epithelium. The basal cells have lost polarization, being not regularly, densely packed on basal lamina. The epidermis demonstrates mild basal vacuolar change and slight liquefaction of the basal cell layer accompanied by apoptosis of the keratinocytes.

There were no differences between normal skin aspects of spinous layer and the histologic appearance of the spinous layer in our case.

The granular layer of normal epithelium was composed of one to three layers of flattened cells containing intensely basophilic-stained granules known as the keratohyaline granules (Figure 1). Tricholemmal granules (hair follicles) were red in routine HE stained sections. In our case, an increased number of granular cells layers, with slight wedge-shaped hypergranulosis were observed (Figure 2).

The cornified layer was composed of multiple layers of polyhedral cells arranged in a basket-weave pattern (Figure 3). These cells were the most differentiated cells of the keratinizing system. In our case, the cornified layer was thicker, presenting slight, compact hyper-orthokeratosis (Figure 4).

The thin basement membrane of normal epithelium was replaced in our case by an uneven, band-like basement membrane, presenting focal thickening.

The epidermal-dermal junction was wavy on normal skin, with formation of rete ridges composed of loose connective tissue (Figure 5).

In our case, a slight vacuolar degeneration of dermal-epidermal junction and occasional areas of atrophic epithelium where the rete pegs were shortened and pointed (a characteristic known as saw teeth rete pegs) were observed.

Eosinophil colloid bodies (Civatte bodies), which represent degenerating keratinocytes, were very rare in the lower half of the surface epithelium and nearby dermal-epidermal junction.
In our case, there was no distinction between papillary and reticular dermis. The papillary dermis has shown homogenization and sclerosis. The collagen was distributed in fascicles, forming a hyalinized dermal superficial band, because of dermal fibrosis, an evidence for the lesion resolution (Figure 6). The dermal papillae were flattened and the connective tissue was intensely stained with eosin. In the upper dermis, we observed a small number of lymphocytes.

There was a sparse, superficial, perivascular, lymphohistiocytic infiltrate. The few mononuclear cells present in the dermis varied in proportions, without a clear tendency toward a specific cell type. Eosinophils were absent in the dermal infiltrate.
All these findings supported the diagnosis of an atypical variant of lichen planus, known as atrophic lichen planus.

**Discussion**

Lichen planus is a recurrent, inflammatory disease, not contagious, somewhat limited and of unknown origin. It is not a frequent disease that generally affects middle age adults, between 30 to 70-year-old. It is not common in very young or elderly people [8–10]. It is less common in children. It is seen in both sexes and common in very young or elderly people. It is middle age adults, between 30 to 70-year-old. It is not of unknown origin. It is not a frequent disease that generally affects middle age adults, between 30 to 70-year-old. It is unusual.

The pathophysiology is unknown and probably multifactorial with various components such as genetic, hormonal, autoimmune, and infectious influences, the disorder being likely to be related to an allergic or immune reaction [11].

The initial attack may last for weeks to months, and come and go for years. Some people have lichen planus inside the mouth, genital region, hair, and nails [12].

Lichen planus verrucous consists of confluent plaques, especially near the ankle, that are markedly thickened, sometimes quite dark in color, hard, rough, and wart-like.

Sometimes several lesions will arrange themselves as a straight or irregular line (linear lichen planus).

Annular lichen planus is a long-recognized clinical variant of lichen planus, but is often considered uncommon in occurrence. It is characterized by a ring-like configuration with violaceous annular plaques [12, 13]. The typical distribution and presentation of this variant have not been well described [14]. The annular lichen planus affects mostly Caucasian men, ranged in age from 24 to 76 years. Sites of involvement in order of decreasing frequency included: axillary region, penis, extremities, groin (including the inguinal creases and scrotum), back, buttocks, flanks, neck and eyelids. Frequently there are purely annular lesions. Some eruptions were macular, whereas the majority had a slightly raised edge with central clearing. Most patients present solitary lesions. None exhibited a linear Koebnerized response or generalized lesions. Most patients are asymptomatic. Annular lichen planus commonly involves the male genitalia but also has a predilection for intertriginous areas such as the axilla and groin folds. Eruptions typically consist of a few lesions localized to one or a few sites. Distal aspects of the extremities, and less commonly the trunk, may also be involved. Annular lichen planus is a subtype of lichen planus that may be more common than is reflected in the literature [14].

Another variant is the atrophic lichen planus, which can be seen on lower extremities or trunk as well-demarcated, white-bluish papules or plaques with central atrophy. This is the result of the epidermal thinning and the papillary dermal fibrosis occurring with the resolution of lichen planus [13, 15].

Annular atrophic lichen planus is the most unusual variant of lichen planus, and has both morphological features and configuration of annular and atrophic lichen planus in the same lesions.

The first case of annular atrophic lichen planus was reported by Friedman DB and Hashimoto K [16]. The second case was reported by Requena L et al.; since then, only a few reports have appeared in the literature [17, 18]. It is characterized by violaceous papules with progressive centrifugal extension and pigmented, atrophic hypopigmented centers and raised borders. It presents mixed pathological findings of annular and atrophic lichen planus [5, 12, 13, 19].

The course of annular atrophic lichen planus is chronic and tends to be resistant to treatment with topical glucocorticoids, retinoids, photochemotherapy, or immunosuppressive agents. In our case, the lesions were resistant to topical steroids [5, 13, 18].

Lichen planus can affect the genital skin, lesion called lichen sclerosus. This condition can be confused with sexually transmitted diseases, although lichen planus is neither sexually transmitted nor contagious.

Lichen sclerosus is a lymphocyte-mediated dermatosis, which appears in both sexes and was first formally described at the end of the nineteenth century by Hallopeau H and Darier J as a variant of lichen planus in a patient with coalescent papules on the trunk and forearms who also had pruritis and lichenification of the vulva [20], using the term “lichen plan atrophique” for it. It was followed by the histological description by Darier J who termed it “lichen plan sclereux” [21]. The terms leucoplakia and kraurosis vulvae present in older literature are a source of confusion. Balanitis xerotica obliterans, a term used for lichen sclerosus of the penis was only recently coded as part of lichen sclerosus. Not all lichen sclerosus are histologically atrophic, and the term “lichen sclerosus et atrophicus” has now been replaced with lichen sclerosus alone [22].

Initial lesions of lichen sclerosus are porcelain ivory white polygonal papules, which coalesce to form a discrete atrophic plaque that may be surrounded by an erythematous or violaceous halo. The surface of the plaque can present telangiectasia, erosions, fissuring, atrophy and wrinkling [22]. Early lesions may show folliculocentric keratin plugs overlying follicular ostia. Bullae may appear with or without underlying hemorrhage. A Koebner reaction is common. Late lesions show atrophy, loss of pigmentation, and loss of normal skin markings. Other processes may be concurrently present, specifically morsphenia, lichen planus, or atrophoderma of Pasini and Pierini [11, 23, 24].

The histological features consist of thinned epidermis with hyperkeratosis with keratotic plugs of the orifices of the hair follicles and dermal appendages, vacuolar degeneration of the basal layer and edema or sclerosis of the papillary dermis. Such changes in the basal layer eventually result in the loss of melanin and bulla formation. It presents a wide band of homogenized collagen below the dermo-epidermal junction and a lymphocytic infiltrate beneath the homogenized area. There may be small focal areas where the inflammatory infiltrate is close to the dermo-epidermal junction, similar to lichen planus. A few patients may have a thickened...
epidermis; these patients tend to have complicated disease that is not so responsive to treatment and may have a higher risk in the long term of developing an associated squamous cell carcinoma.

Cases of linear lichen sclerosus have been reported along the lines of Blashko [3]. Clinically, hypopigmented atrophic patches are observed, which may or may not be pruritic [23].

Lichen planopilaris is an uncommon inflammatory hair loss disease characterized by reactive lymphocyte destruction of the hair follicle and progressive scarring alopecia of the scalp. Perifollicular erythema, scaling, and groups of keratotic follicular papules are the commonly encountered clinical findings. In the early stages, diagnosis is made through clinical and histopathologic findings, morphologically being classified as a follicular lichen planus. However, in the later stages, only few specific signs are present [25].

The first characteristic change noted in the epidermis is thought to be an acanthosis, followed by intercellular edema, hyperkeratosis, wedge-shaped hypergranulosis, squamatization of the basal layer, and vacuolar degeneration of the basal layer cells with the formation of numerous cytoid bodies [11]. Pointed rete ridges are found more commonly in lichen planus included. Wedge-shaped hypergranulosis develops around intraepidermal follicles, namely, acrocytoma and acrotrichia. The rete and corneous layer are noted to be thickened, and the papillae enlarged [6].

Some authors suggested that the most important finding was that Langerhans' cells appear in increased numbers in the epidermis very early in the disease, even preceding the experience of lymphocytes there and then that the appearance of lymphocytes is followed by destruction of keratinocytes in the lower portion of the epidermis and by general epidermal hyperplasia, including hypergranulosis and hyperkeratosis [6, 26].

In florid stage, the papillary dermis shows a lichenoid or band-like, predominantly lymphocytic infiltrate. The papules result from a mononuclear cells proliferation in the papillae that become edematous to a variable degree and in some instances to the degree of vesculation. Eosinophils are absent in the dermal infiltrate of lichen planus. The central point of the depression usually corresponds to the sweat-duct orifice, the depression resulting from resorption and degeneration of the infiltration; the sweat-glands are not affected. The vessels of the papilla show dilatation.

With time, the inflammatory-cell infiltrate disappears and the epidermis regains its normal configuration [6].

The pathological examination of annular lichen planus shows typical features of lichen planus at the active border, whereas epidermal thinning and fibrosis of the dermal papillae are observed in the centre of the lesion. In both sites, the elastic fibers are destroyed in the papillary dermis, because of lytic activity of the inflammatory cells [16]. Our case was consistent with these features [5, 18].

Histologically, a compact orthohyperkeratosis recovers the thinned epidermis. Vacular degeneration of the basal layer is common, especially in earlier lesions; when extensive, it may cause bullae formation. Follicular occlusion by a cornified plug may lead to atrophy and disappearance of appendageal structures. The papillary dermis becomes homogenized and edematous soon after onset, and hyalinized and sclerotic over time. Elastin may be modified so as to stain poorly with Orcein [16]. Examination of early lesions showed that elastolysis had already begun in the heavy cellular infiltration that is why some authors conclude that the annular configuration resulted from the elastolytic activity of the inflammatory cells with the formation of foci of localized acquired cutis laxa [16]. Melanocytes are reduced. A mononuclear lichenoid infiltrate may be dense and extensive or patchy in older lesions [11].

The histological features of annular atrophic lichen planus are an admixture of both, atrophic and annular lichen planus histology. Histology showed features of lichen planus in the active border of the lesion and a pattern of resolved lichen planus in its center. Elastic fibers had been destroyed in the papillary dermis both in the border and in the center of the lesion, resulting in an atrophic appearance of the lesion. Annular atrophic lichen planus is an uncommon variant of lichen planus that results from elastolytic activity of inflammatory cells with formation of areas of localized acquired cutis laxa [12, 17].

On the atrophic patch, flattening of the epidermis is seen, with loss of rete ridges and fibrotic changes in the dermis. Elastic stain revealed decreased elastic fibers in the upper dermis of the atrophic lesions with deterioration of elastic fibers due to elastolysis in the upper reticular dermis, which is the characteristic finding of atrophic annular lichen planus [12, 13].

Our patient had lesions similar to those observed in the patients reported in the literature. She improved with topical steroid therapy, which is often effective in the treatment of lichen planus. Topical tacrolimus has also been reported to be successful in this condition [18].

Conclusions

In this paper, we highlight that in cases of lichen planus with such a unique nature of presentation, it is of major importance the systematic work-up for an accurate diagnosis and classification, which must integrate the histological analysis with the clinical data. At epidermal level, basal cells were not arranged uniformly in a single layer on basal lamina compared to the normal epithelium. There were no differences between normal skin aspects of spinous layer and the histologic appearance of the spinous layer in our case. The thin basement membrane of normal epithelium was replaced in our case by an uneven, band-like basement membrane, presenting focal thickening. In our case, a slight vacuolar degeneration of dermal-epidermal junction and occasional areas of atrophic epithelium where the rete pegs were shortened and pointed (a characteristic known as sawtooth rete pegs) were observed.

References


