

Unilateral depigmented lesions on the right arm

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A 36-year-old male patient presented with asymptomatic skin lesion on the right arm for one year. The lesion started as a small hypopigmented lesion, that slowly increased in size and become depigmented. There was no previous history of similar lesion, and there was no family history of similar condition. General condition of the patient was good, and there was no history of systemic diseases. There was also no history of previous trauma or intradermal injection at the site of the lesion.

Cutaneous examination revealed well-demarcated, whitish to bluish, atrophic patches and macules distributed in a linear pattern on the posterior aspect of the right arm just above the elbow region. The large patch measured about 1.6 x 2.1 cm, while the small one was less than 1 cm in diameter (Fig. 1). The lesions were slightly firm in consistency but the surface was mostly smooth. Examination of other body areas showed no similar lesions. Hair, nail and mucous membranes

were absolutely normal. Routine laboratory investigations were irrelevant.

What is the clinical diagnosis?

1. Vitiligo
2. Morphea
3. Lichen sclerosus et atrophicus
4. Atrophoderma of Pasini and Pierini
5. Macular atrophy

An incision biopsy was performed from the edge of the lesion including a part from normal skin. Histological examination showed hyperkeratosis, thinning of the epidermis and loss of the rete ridges (Fig. 2). The basal layer showed basal cell vacuolization and vacuolar alteration in focal areas. The papillary dermis shows pigmentary incontinence, edema and hyalinization of papillary dermal collagen (Fig. 3). The dermal inflammatory infiltrate was mild to moderate and

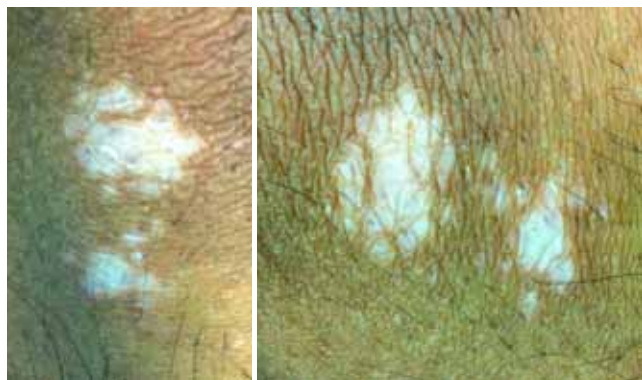


Fig. 1 A well-demarcated, whitish to bluish, atrophic patches and macules on the posterior aspect of the right arm.

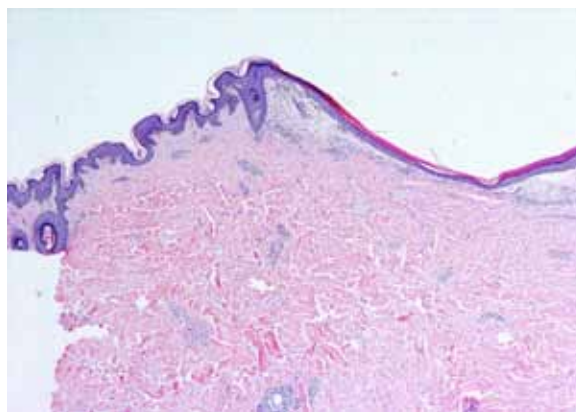


Fig. 2 Skin biopsy showed hyperkeratosis, thinning of the epidermis and loss of the rete ridges (H&E x100).

composed mainly of lymphocytes and histiocytes and more localized below the hyalinized collagen (Fig. 4). Special staining for elastic fibers showed scanty elastic tissue in the dermis, while special staining for melanin showed normal melanin concentration in the basal layer.

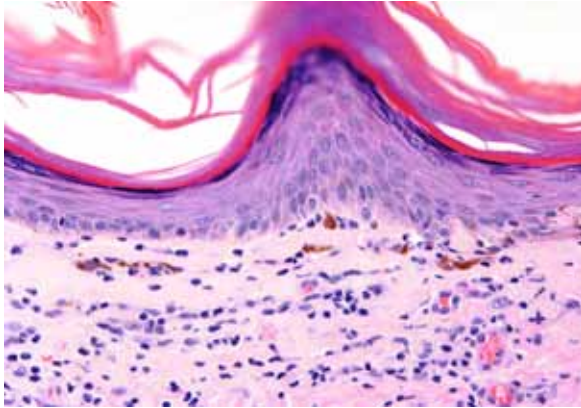


Fig. 3 The papillary dermis shows pigmented incontinence, edema and hyalinization of papillary dermal collagen (H&E x200).

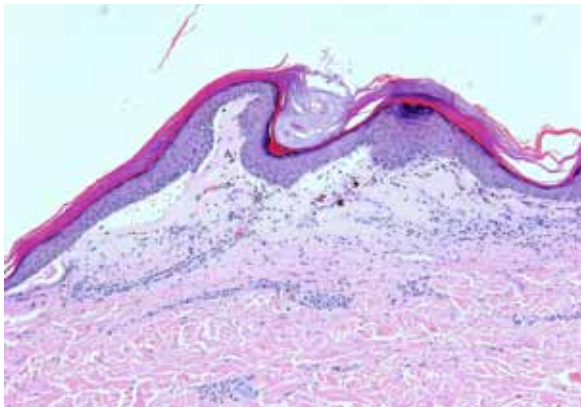


Fig. 4 The dermal inflammatory infiltrate was mild to moderate and composed mainly of lymphocytes and histiocytes and more localized below the hyalinized collagen (H&E x400).

DIAGNOSIS

Lichen Sclerosus et Atrophicus (Extragenital variant)

DISCUSSION

LSA was first described in the late nineteenth century by Hallopeau. It is an inflammatory dermatosis that primarily affects the vulvar, perineal and perianal skin of prepubertal,

perimenopausal and postmenopausal women.¹ The disease affects people of any age but is rare in childhood, with an estimated prevalence of at least 1 in 900 children. When present in children, the appearance of symptoms occurs between two and five years of age.²

Extragenital LSA can exist in isolation in 6% of cases, or in association with genital LS in 15-20% of presentations.³ Meffert et al. proposed that extragenital LSA represent about 16% of all cases and it was most commonly located on the neck, shoulders and upper portion of the trunk. It is generally asymptomatic, but it can occasionally be pruritic. Less common sites include the palms, soles, scalp and face.⁴

The etiology of LSA is still not clear, but there is evidence of association with HLA Class I antigens and with HLA-A29/B44, infections by human papillomavirus (HPV) and spirochete *Borrelia burgdorferi*, autoimmune and hormonal phenomena, and trauma.⁵ Immunological changes on the level of T and B cells have been also described. Thus an autoimmune phenotype has been observed in the case of vulvar lichen sclerosis involving increased levels of Th1-specific cytokines, dense T cell infiltration and enhanced BIC/miR-155 expression as well as auto-antibodies against extracellular matrix protein 1 and BP180 antigen (e5-e7). The pathogenetic relevance of these observations is unclear. Oxidative DNA damage and TP53 mutations (tumor suppressor gene) have also been described.⁶

The diagnosis of LSA is usually based on the clinical presentation of whitish patches and nodules that can coalesce into bigger areas (plaques). The lesions are typically found in the anogenital region, and usually they start with slight redness

as a first sign. White thickening, atrophic skin, lacerations and ecchymosis typically occur later in the course of disease.⁷ Scarring in the area of the clitoris and the labia minora may develop and possibly lead to complete burying of the clitoris, a narrow vaginal introitus resulting in dysparunia (pain during sexual intercourse) or also perianal stenosis and painful defecation.⁸

In males, sclerosis and narrowing of the foreskin may result in erectile dysfunction. LSA may be limited to the glans penis and prepuce or affect the penile shaft and scrotum. As a complication the meatus and urethra can also be affected potentially leading to urethral stenosis. Especially in children lichen sclerosus may manifest itself initially as slight redness followed by depigmentation of the skin.⁹

Histological features of established lesions of LSA include hyperkeratosis, follicular plugging, thinning of the epidermis, and vacuolar alteration of the basal layer. There is a broad zone of subepidermal edema with homogenization of collagen and poor staining in hematoxylin and eosin preparations. Later in the lesions, this zone becomes more sclerotic in appearance and shows more eosinophilia.¹⁰ Basement membrane thickening also occurs. Expression of collagen IV and VII is increased. There is dilatation of thin-walled vessels in the zone and sometimes hemorrhage. Beneath the edema there is a diffuse, perivascular infiltrate of lymphocytes, predominantly of T-cell type in the mid dermis. This infiltrate is sometimes quite sparse in established vulval lesions and it may contain a few plasma cells and histiocytes. Mast cells and liberated mast cell granules are also present.¹¹

Nowadays, dermoscopy and confocal microscopy are good choices for patients with face

involvement without biopsy; they greatly help the diagnosis of LSA if the patient refuses biopsy due to concerns with the cosmetic appearance. The dermoscopy shows a whitish plaque with comedo-like openings on the surface of the lesion, while the confocal microscopy reveals hyperkeratosis, atrophy of the epidermis, dark and round structures containing bright amorphous material, and scattered inflammatory cells, as well as coarse collagen in bundles.¹²

Many authors have described coexistent LSA and morphea.¹³ Morphea and LSA coexisting in the same biopsy specimen has also been described. With sequential biopsies, several investigators have reported transition from LSA to morphea or vice versa.¹⁴ However, other investigators believe that there are enough clinical and histologic differences between LSA and morphea to argue that they are distinct diseases and those coexistent lesions are coincidental.¹⁵ It is possible that LSA case could progress to en coup de Sabre, and may be a transitional form of linear scleroderma en coup de Sabre.¹⁶

Linear form of LSA is uncommon and it was described in 1995 by Izumi and Tajima.¹⁷ Thereafter, a handful of cases of linear LSA have been reported, among which some developed in a pattern corresponding to the lines of Blaschko. Kim and Lee¹⁸ summarized 6 cases of linear LSA along the Blaschko's lines, and this occurred on the trunk, limbs or face. Out of the 3 reported cases of linear LSA that appeared on the face, one case showed facial lesion following the Blaschko's line without any oral mucosal lesion, and the other 2 cases showed additional oral mucosal involvement.

The recommended initial treatment of LSA is a three-month application of potent to ultra-potent

topical corticosteroids. Randomized studies show that application of potent to ultra-potent topical corticosteroids significantly improves LSA in 75 to 90% of patients, compared to roughly 10% in placebo groups.¹⁹ If the initial three-month treatment with topical steroids does not lead to the desired full remission in male patients with genital lichen sclerosus, a complete circumcision should be recommended, especially in uncomplicated cases in early stages (without involvement of meatus and urethra). This procedure is reported to lead to permanent, lifelong remission (recovery) in 90 to 100% of cases.²⁰

Calcineurin inhibitors (tacrolimus and pimecrolimus) are second choice treatment options, but the effect are inferior to those seen with topical corticosteroids.²¹ Treatment with sex hormones, especially with testosterone is obsolete, because it is not more but rather less effective than corticosteroids and has many side effects.²²

Systemic treatment is occasionally indicated in refractory cases. Successful treatment with etretinate (0.5-1 mg/kg) given for 14 to 18 weeks followed by a maintenance dose of 0.25 mg/kg was described in two small randomized studies.²³ In some cases cyclosporine 3-4 mg/kg/day was administered for 3 months or methotrexate 10-15 mg/week for 6-8 months.²³

In patients with LSA the risk of developing a squamous cell carcinoma in the genital area is slightly increased, and is defined with an estimated lifetime risk of approximately 4 to 5%. This risk seems to be significantly decreased by consistent long-term treatment.²⁴ The mechanism of malignant evolution is unknown. Unlike squamous cell carcinoma in the genital area that is associated with human papilloma virus (HPV), oncogenic HPV can typically not be detected in

carcinomas associated with LSA. It is assumed that p53 oncogenes, chronic inflammation and oxidative DNA damage are responsible for malignant transformation.²⁵

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