



Unilateral unique Lupus tumidus: pathogenetic mystery and diagnostic problem

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Summary Lupus tumidus is a rare immunological disorder whose pathogenesis is not fully understood. Although on the one hand there are some differences in (1) the clinical morphology of lesions, (2) the histopathology picture, as well as in (3) serological profile of lupus tumidus patients at the current moment, the disease is regarded as a subform of chronic cutaneous lupus erythematosus. Differential diagnosis requires the exclusion of many diseases such as Jessner Kanoff lymphocytic infiltration, polymorphous light eruption, and reticular erythematous mucinosis. Differentiation between them is not always easy. The standard treatment regimen of patients with lupus tumidus is based on local and systemic application of corticosteroids, azathioprin, dapsone, mepacrine, chloroquine, and hydroxychloroquine. Modern treatment options include the use of pulsed dye laser, tacrolimus 0.1 % ointment and photophoresis. We present a 42-year-old patient with unilateral atypical form of lupus tumidus who was successfully treated with

systematically administration of hydroxychloroquine in combination with sunscreen SPF 50. After a 2-month course of treatment with hydroxychloroquine dosage of 200 mg per day and a break of 3 months between courses, we observed a complete remission.

Keywords Lupus tumidus · Treatment · Desquamation · Histopathology · Unilateral

Unilateraler ungewöhnlicher Lupus tumidus: pathogenetische Myserie und diagnostisches Problem

Zusammenfassung Lupus tumidus ist eine seltene Immunkrankheit, deren Pathogenese nicht vollständig aufgeklärt ist. Trotz einiger Unterschiede 1) im klinischen Erscheinungsbild, 2) in der Histopathologie und 3) im serologischen Profil wird die Erkrankung als Unter-

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form des chronisch-kutanen Lupus erythematoses eingeordnet. In der Differentialdiagnose sind zahlreiche Erkrankungen auszuschließen wie die lymphozytäre Infiltration Jessner-Kanoff, die polymorphe Lichtdermatose und die retikuläre erythematöse Muzinose (REM-Syndrom). Die Unterscheidung zwischen diesen ist nicht immer leicht. Die Standardtherapie für Patienten mit Lupus tumidus basiert auf der topischen und systemischen Gabe von Kortikosteroiden, Azathioprin, Dapsone, Mepacrin, Chloroquin und Hydroxychloroquin. Moderne Behandlungsoptionen sind auch gepulste Farbstoff-Laser, Photopherese und topisches Tacrolimus 0,1%. Wir berichten über einen 42-jährigen Patienten mit einer unilateralen atypischen Variante des Lupus tumidus, der erfolgreich mit Hydroxychloroquin 200 mg/d in Verbindung mit Lichtschutz (SPF 50) behandelt wurde. Nach 2-maliger Behandlung über 8 Wochen mit einer therapiefreien Pause von 12 Wochen erzielte der Patient eine Komplettremission.

Schlüsselwörter Lupus tumidus · Behandlung · Desquamation · Histopathologie · unilateral

Introduction

The term lupus erythematosus tumidus (LET) was first implicated in a publication by Gougerot and Burnier in 1930 to describe infiltrated, erythematous lesions with no clinical signs of desquamation or other superficial changes [1]. The frequency of lupus tumidus in patients affected by a disease that is currently regarded as a subform of cutaneous lupus erythematosus (CLE) seems to be underestimated and, in fact, there is a widespread view that it may even be more prevalent than discoid lupus erythematosus (DLE), for example (regarding some authors' collectives) [2–4]. A total of 250 cases have

already been described in the world literature, classified as lupus tumidus [5].

Nowadays, LET could be defined as a subtype of CLE with its own clinical, prognostic, and microscopic characteristics [4]. The features that differentiate LET lesions from those of other LE subtypes are the histopathological absence of desquamation, follicular plugs, or atrophy [4].

Case report

We present an interesting case of a 42-year-old otherwise healthy male patient with no history of comorbidities and medication. Sporadic complaints in the form of redness in the face and back were reported, presented predominantly in spring and summer, as the lesions persist until late fall and fade gradually. The complaints were made over a period of 3–4 years. Lack of improvement of the clinical symptomatology after application of topical corticosteroid creams and ointments with combination of antihistamines were reported. Unilateral redness and swelling proximal to the left lower eyelid with involvement of the left cheekbone in the form of an erythematous plaque was clinically established within the dermatological examination (Fig. 1a). Conglomeration of single erythematous papules with mild urticarial edge in the periphery with tendency for conflation was observed in the area of the left sweat channel in the back (Fig. 1b). The conducted paraclinical and imaging diagnostic procedures were within the normal range. Antinuclear antibodies were negative. Lack of significant changes in the epidermis with the presence of a minor, barely noticeable atrophy of the epidermis were observed histologically by the performed two biopsies (Fig. 2a, b). Superficial and deep perivascular and periadnexial lymphocytic infiltrate, diffuse deposition of mucin (positive staining with Alcian blue) between collagen fibers in the reticular dermis

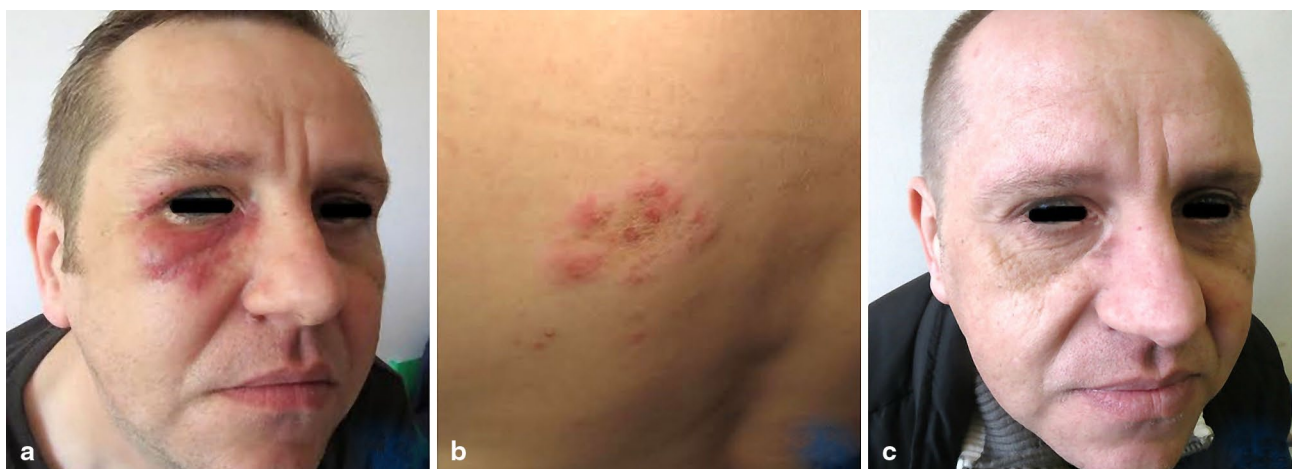


Fig. 1 a Clinical manifestation of unilateral redness and swelling proximal to the left lower eyelid with involvement of the left cheekbone in the form of an erythematous plaque. b Conglomeration of single erythematous papules with mild urticarial

edge and tendency for conflation in the area of the left sweat channel in the back. c Clinical manifestation of the complete remission achieved by a 2-month systemic administration of hydroxychloroquine in combination with sunscreen SPF 50

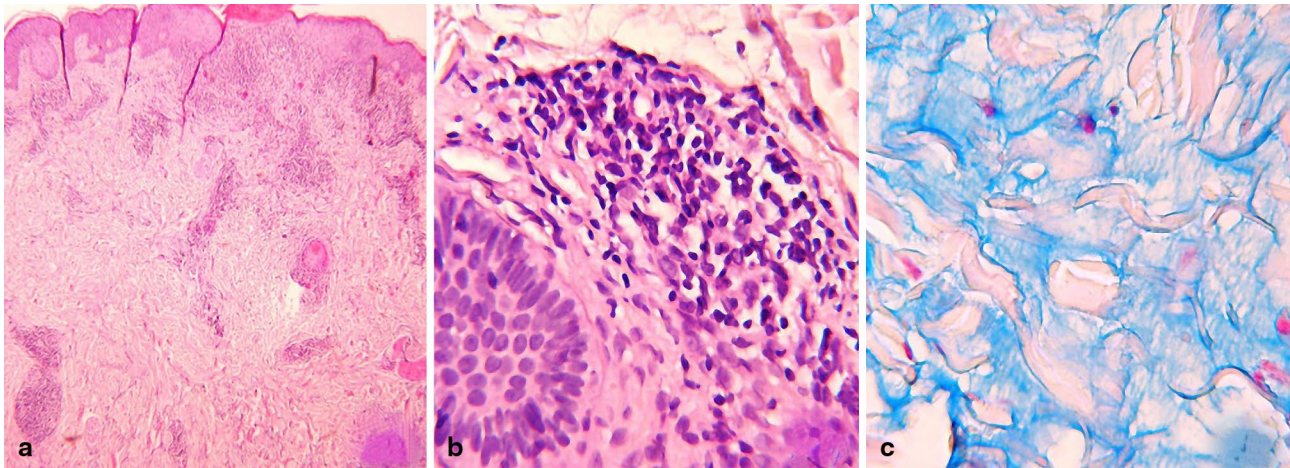


Fig. 2 **a, b** Histopathological findings (HE 10×2)—presence of a minor atrophy of the epidermis. Superficial and deep perivascular and periadnexal lymphocytic infiltrate. **c** Diffuse de-

position of mucin (positive staining with Alcian blue) between collagen fibers in the reticular dermis

were also established (Fig. 2c). The described histological findings correspond to the histopathological diagnostic criteria for LET. We observed a complete remission after a 3-month course of treatment with the administration of hydroxychloroquine 200 mg/daily and local application of sunscreen with SPF 50 (Fig. 1c).

Discussion

The differential diagnosis in the described-as-lupus-tumidus case includes Jessner Kanoff lymphocytic infiltration, polymorphous light eruption, and reticular erythematous mucinosis [2]. The main distinguishing features between Jessner Kanoff lymphocytic infiltration and lupus tumidus are the lack of photosensitivity and unsuccessful response to antimalarial therapy, which is destined to fail [4]. Other author collectives contest these statements [6, 7]. According to studies performed in the past decade, Jessner Kanoff lymphocytic infiltration is classified within the spectrum of lupus and, in particular, could be considered as a form of LET [4]. Research by Weber et al., which was focused on the photoprovocation of the patient and reported on patients with Jessner Kanoff lymphocytic infiltration, demonstrated that all the patients developed cutaneous lesions after photoprovocation and observed a latency period of over 48 h before the appearance of the lesions; this occurs in all forms of cutaneous lupus erythematosus [4, 8]. Histopathological evaluation of the lesions revealed a perivascular and periadnexal infiltrate indistinguishable from LET, as well as interstitial mucin deposits and an unaltered epidermis [8]. Actually, there were no significant clinical, pathological, or photobiological differences between Jessner Kanoff lymphocytic infiltration and LET [8]. Other authors confirm the thesis that there are no differences between lupus tumidus and Jessner Kanoff lymphocytic infiltration [9]. Jessner lymphocytic infiltration is now generally considered as a subtype of LET [4].

The lesions of patients with LET also heal without scarification or hypopigmentation [4]. It is important to determine the course and behavior of the lesions after sun exposure, as this is beneficial to the differentiation between LET and polymorphous light eruption [4]. In LET, the lesions do not appear immediately, but rather after a latency period between 24 h and several weeks [4]. The characteristic erythematous and sometimes indurated plaques tend to persist throughout the summer and even into the late autumn [4]. The clinical lesions in patients with polymorphous light eruption develop soon after sun exposure, and improvement is obtained within a few days if there is no further exposure [4].

There are no data in the literature that compare the features of polymorphous light eruption and LET [4]. Histopathologically, polymorphous light eruption can also be difficult to differentiate from CLE, as the two diseases may share certain common features, such as (1) perivascular lymphocytic infiltrate, (2) mild vacuolar changes in the basal layer, (3) epidermal atrophy, (4) and follicular plugging [10, 11].

Differentiation from reticular erythematous mucinosis is also not always easy and possible. According to del Pozo et al. one of the important features, helpful in the differentiation, is the deposition of IgM in the basal membrane [12].

After the disease was initially described in 1909, limited case reports and series exist, considering the treatment options in patients with lupus tumidus, as a separate entity, or as a subform of CLE [4].

Different regimens are reported with various degrees of success, including topical and systemic application of corticosteroids, azathioprin, dapsone, mepacrin, chloroquine, and hydroxychloroquine [13, 14]. Application of topical corticosteroids combined with sunscreens of SPF 15 or greater is reported as satisfactory enough in 45% of patients, whereas complete remission as a result of systemic administration of antimalarial therapy with hydroxychloroquine sulfate, chloroquine phosphate,

and mepacrine hydrochloride, achieved 91% [13]. A course with hydroxychloroquine sulfate at dosage 4 mg/kg/per day with duration of 4–6 weeks usually results in complete resolution of the symptoms [13]. Relapses are not excluded, as the majority of them predominate during spring–summer months, presented couple of weeks after provocation with sun exposure [13]. The dose can be increased to 6–6.5 mg/kg in more resistant cases or relapses with respect to achievement of clinical remission, but with caution, taking into account the risk for adverse drug reactions such as retinopathy or agranulocytosis with hydroxychloroquine therapy [12, 13].

Modern treatment options include the use of pulsed dye laser, tacrolimus 0.1% ointment, and photophoresis [14, 15]. Although limited, the experience with topical calcineurin inhibitors in LET obtained controversial results [14]. On one hand, topical application of tacrolimus 0.1% ointment is considered as more effective compared with methylprednisolone ointment after 4 weeks of treatment [14]. However, relapses or partial response could also be observed after treatment with tacrolimus [13, 14]. In such a case, a single corticosteroid injection is usually beneficial for improvement, combined with topical application of pimecrolimus [13]. Treatment with topical pimecrolimus 1.0% cream twice daily results in improvement, usually after 3 weeks [14]. General, step-wise approach should be considered, regarding the benefit/risk ratio. Application of topical steroid treatment, antimalarial therapy, followed by systemic steroids, and other immunosuppressants are all reported with controversial results, regarding the clinical improvement [13]. However, complete disease characterization, evidence-based treatment, and a multidisciplinary approach are essential for successful treatment and long-lasting disease-free after-treatment period [13].

Ethical standards

Informed consent was obtained from the patient for whom identifying information is included in this case report.

Conflict of interest

IB, AAC, IK, CT, UW, TL, and GT declare that there are no actual or potential conflicts of interest in relation to this article.

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