LIMBAL AND BULBAR INFLAMMATORY NODULES IN A PATIENT WITH PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA

VERHAMME T., ARNAOUT A.** ,*
*AYLIFFE WH.***,*

SUMMARY

Clinical report: We report a case of a 42-year old lady with recurrent bilateral nodular conjunctival inflammation following a diffuse papulo-vesicular rash, mainly over her trunk and scalp. Slitlamp examination revealed limbal and bulbar inflammatory nodules with secondary corneal involvement.
Discussion: Pityriasis lichenoides is considered to be a spectrum of uncommon, acquired maculo-papular skin eruptions. The diagnosis is made by the combination of a typical clinical picture and matching histopathology. In severe cases, there may be associated with mucous membrane involvement.
Conclusion: Although ocular involvement has been reported in pityriasis lichenoides, this is the first report of conjunctival inflammatory nodules with secondary corneal ulceration as a part of the manifestations of the pityriasis lichenoides spectrum. Treatment with topical steroid drops was required to bring this condition under control.

RÉSUMÉ

Cas clinique: nous rapportons l'observation d'une patiente de 42 ans présentant une inflammation nodulaire bilatérale récurrente de la conjonctive apparue dans le décours d'un épisode d'éruption cutanée papulovésiculaire diffuse, intéressant principalement le tronc et la tête. La biomicroscopie antérieure a révélé des nodules inflammatoires de la conjonctive bulbaire limbique avec une participation secondaire de la cornée.
Discussion: le pityriasis lichenoides correspond à un spectre d'éruptions maculo-papulaires rares et acquises de la peau. Le diagnostic se fait lorsque les aspects cliniques typiques sont confirmés par l'examen histopathologique. Une inflammation des membranes muqueuses peut être associée dans les cas sévères.
Conclusion: des manifestations oculaires ont déjà été décrites dans le pityriasis lichenoides. Notre cas clinique qui conjugue une inflammation nodulaire de la conjonctive à des ulcérations cornéennes comme faisant partie des manifestations du pityriasis lichenoides n'a encore été jamais rapporté dans la littérature. Un traitement topique à base de corticostéroïdes a été nécessaire pour contrôler les symptômes.

KEY WORDS

Pityriasis lichenoides et varioliformis acuta, PLEVA, conjunctiva, inflammatory nodules

MOTS-CLÉS

Pityriasis lichenoides et varioliformis acuta, PLEVA, conjonctive, nodules inflammatoires

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* *Department of Ophthalmology*
Mayday University Hospital, London, United Kingdom
University Hospitals of Leuven, Leuven, Belgium
** *Department of Cellular Pathology*
Mayday University Hospital, London, United Kingdom
*** *Department of Ophthalmology*
Mayday University Hospital, London, United Kingdom

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INTRODUCTION

Pityriasis lichenoides encompasses a spectrum of uncommon, acquired maculo-papular skin eruptions (2, 7). The diagnosis is made by the combination of a typical clinical picture and matching histopathology of an active skin lesion. In severe cases, there may be associated mucous membrane involvement. We report a case of recurrent pityriasis lichenoides et varioliformis acuta with associated oral ulceration and bilateral conjunctival inflammatory nodules. To our knowledge, this is the first report of conjunctival nodular inflammation as a part of the manifestations of the pityriasis lichenoides spectrum.



Fig. 2: Limbal inflammatory nodules in the right eye.

CASE REPORT

A 42-year old lady presented to our eye casualty complaining of sticky, sore and photophobic eyes. Prior to the onset of the lesions, she had developed a diffuse papulo-vesicular rash mainly over her trunk and scalp, with a few lesions on her arms (Fig. 1). She also suffered from mouth ulcers and generally felt unwell. Slitlamp examination revealed a bilateral conjunctivitis with limbal inflammatory nodules on both sides, resembling the lesions seen in phlyctenulosis (Fig. 2). One bulbar nodule was present inferotemporally in the right eye (Fig. 3). Central to the limbal nodules, there was corneal involvement, consisting of stromal infiltration with thinning and an overlying epithelial defect. Distinct areas of slight superficial corneal scarring were seen, indicating earlier episodes of peripheral corneal involvement. There were no signs of blepharitis or meibomian gland disease.

In her history, there had been a similar tender, non-pruritic erythematous papular rash on her back, chest wall and abdomen in February 1999. These papules developed central umbilication and crusting. The skin lesions did not resemble target lesions seen in erythema mul-



Fig. 1: Papulo-vesicular eruption with central umbilication and crusting.

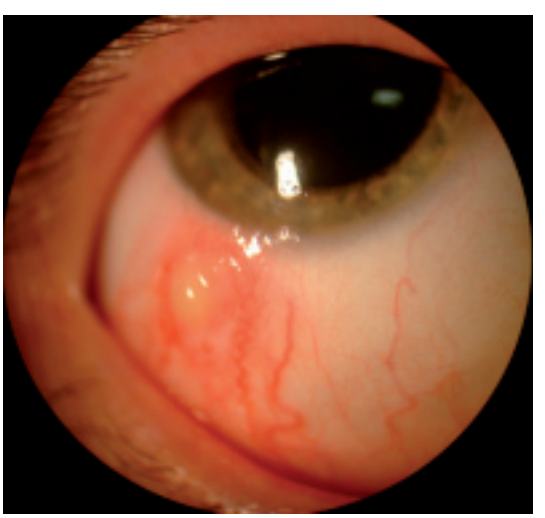


Fig. 3: Bulbar nodule inferotemporally in the right eye.

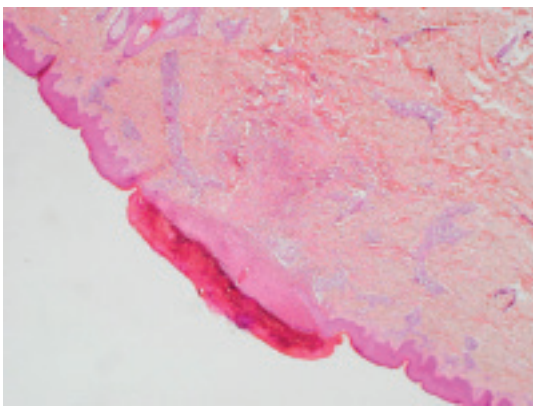


Fig. 4: Skin biopsy of a lesion showing epidermal crusting.

tiforme and there was no dermatomal distribution. The patient had malaise and myalgia. There were accompanying mouth ulcers. There were no signs of internal organ involvement. An initial diagnosis of acute varicellar infection was made at that time, though she reported having had chicken pox in her childhood. Subsequently she developed a bilateral conjunctivitis with limbal nodules. Oral treatment with Aciclovir 500 mg five times a day was initiated. Topically, Prednisolone Sodium Phosphate drops hourly and Aciclovir ointment five times a day were added.

The skin rash slowly resolved over the following 2 weeks, leaving hypopigmented scars. The eye lesions subsided simultaneously. Subsequently, the skin eruption recurred after a few weeks, as did the limbal nodules with peripheral corneal ulceration. By October 1999, she had experienced six similar attacks of skin blistering, occasionally with concomitant oral ulceration and ocular problems. Over these 8 months, she had lost 12 kg in weight.

Investigations by the medical team at that time included a clinical examination, a full blood count, an erythrocyte sedimentation rate (ESR), an auto-antibody screen, renal and liver function tests and a chest X-ray. Except from a raised ESR, all came back negative. Varicella serology showed IgG positivity, but IgM was negative, indicating a previous exposure, but no active infection. An HIV test also was negative. She was referred for a dermatological opinion and for an immunologic work-up to exclude an underlying immunodeficiency. In the differential diagnosis, lymphomatoid papulosis, pityriasis lichenoides et varioliformis acuta and Behçet's disease were considered.

An excisional biopsy of a skin papule was performed for pathologic examination (Fig. 4). This showed epidermal ulceration with crusting, dermal perivascular lymphocytic infiltration, with no signs of malignancy or lymphomatoid papulosis (Fig. 5). The histological features supported the diagnosis of pityriasis lichenoides et varioliformis acuta.

In June 2006, there was a recurrence of the skin eruption, with concomitant buccal and ocular involvement.

For the ocular part of the current relapse, we started treatment with topical Prednisolone Sodium Phosphate six times daily. Repeated Varicella serology showed an identical result as in 1999 (IgG positive, IgM negative). A biopsy of a limbal nodule was performed and showed a non-granulomatous acute inflammation consisting of lymphocytes, neutrophils and plasma cells. Mild epithelial hyperplasia with spongiosis was noted.

The inflammatory nodules resolved under treatment without scarring. The corneal lesions healed and epithelialized, leaving a grey superficial scar. The steroid drops were gradually tapered according to the clinical response. The patient experienced another relapse after 8 weeks, after which treatment was restarted.

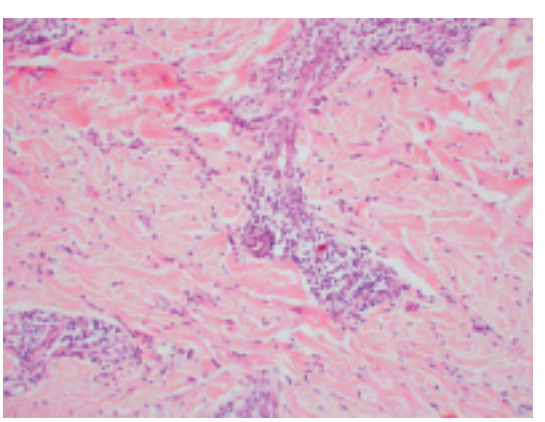


Fig. 5: Perivascular lymphocytic infiltration.

DISCUSSION

Pityriasis lichenoides (PL) is an uncommon, acquired skin condition which is difficult to diagnose, categorize and treat (2, 7). It spans a continuum of similar dermatologic eruptions with different severity. The mildest form, pityriasis lichenoides chronica (PLC) is a gradual manifestation of small red-brown flat maculopapules with mica-like scale. This eruption follows a relapsing course with long periods of remission.

Pityriasis lichenoides et varioliformis acuta (PLEVA), previously known as Mucha-Habermann disease, usually presents as a (sub) acute eruption of multiple small red papules on the trunk, flexural areas and proximal extremities. The papules develop a central vesicle with subsequent crusting and heal within weeks to months, often leaving hypo- or hyperpigmented scars. Constitutional symptoms and mucosal ulceration may be present.

Febrile ulceronecrotic Mucha-Habermann disease (FUMHD) which corresponds to an acute generalized eruption of purpuric and ulceronecrotic plaques with associated systemic involvement, represents the more severe end of the spectrum. Oral and genital mucous ulcers can be associated. Conjunctival ulceration has also been reported in a patient with severe febrile ulceronecrotic Mucha-Habermann disease (12). FUMHD has a mortality rate of 25 % and is considered as a dermatologic emergency.
These three conditions show overlapping features and are considered to indicate disease severity rather than being distinct clinical entities. PL manifests in children and in adults. In adults, the peak prevalence is in the third decade, with most cases diagnosed before the fifth. There is no known racial, geographic or sexual predisposition. The natural tendency of pityriasis lichenoides is to remit spontaneously, though some cases may wax and wane over years.
Typical histopathology shows a dermal wedge-shaped (predominantly CD8+ T-cell) lymphocytic infiltrate, epidermal spongiosis, parakeratosis and variable necrosis of keratinocytes. These features are more subtle in PLC and appear pronounced in FUMHD.

The pathogenesis of pityriasis lichenoides remains unclear. According to a first major theory, it represents an atypical immune response to an infectious or chemical agent in a genetically susceptible individual. Human immunodeficiency virus, Varicella Zoster virus, Epstein-Barr virus, cytomegalovirus, parvovirus B19, adenovirus, several bacteria and drugs have all been implicated as inciting agents (2, 7, 11, 13).

Another leading hypothesis considers pityriasis lichenoides as a self-limited T-cell dyscrasia, arising from a monoclonal lymphocytic population (3, 4, 8, 15). This is based on clonal rearrangement of the T-cell receptor gene, demonstrated in some cases of the three forms of PL and resembling the clonality found in primary cutanous CD8+ epidermotropic cytotoxic T-cell lymphoma (4). Weinberg suggested that pityriasis lichenoides variants represent different grades of immune response to a monoclonal T-cell population (15).

The differential diagnosis of PL is extensive: chickenpox, viral exanthema, Gianotti-Crosti syndrome, erythema multiforme, lichen planus, pityriasis rosea, psoriasis guttata, disseminated zoster, primary HIV infection, drug eruption and arthropod bite. An important entity to recognise and distinguish from pityriasis is lymphomatoid papulosis, a primary cutaneous CD30+ lymphoproliferative disorder with a substantial risk of transformation into cutaneous malignant lymphoma (14). It tends to affect patients in the fourth to seventh decade, a somewhat older population than PL. If clinical features are confounding, the main method of discrimination is histopathology.

At present, there is no standard treatment modality for PL (2, 7). The most successful treatment is phototherapy (psoralen and UVA), particularly for PLC (9). Antibacterial (tetracycline, erythromycin and dapsone) treatment is the mainstay for patients with PLEVA. Topical corticosteroids and immunomodulating drugs (tacrolimus) have also been reported to be beneficial (2, 7, 10). Systemic medications such as corticosteroids, methotrexate, thiobendazole, gold, pentoxifylline, intravenous gamma-globulin and retinoids may be warranted in more

severe cases of PLEVA and in FUMHD. The latter condition may require prolonged hospitalization and burn unit care with skin grafting. Despite anecdotal case reports of malignant transformation, PL generally follows a benign course. However, regular follow-up, with repeated skin biopsies is recommended, especially in patients with atypical, changing skin lesions or frequently recurrent disease.

In our case, the patient presented with a bilateral conjunctivitis with white limbal inflammatory nodules on both sides, resembling the lesions seen in phlyctenulosis. A phlyctenule, derived from the Greek word phyctaena, is a pinkish-white nodule or blister, involving the conjunctiva or the cornea. It is thought to be an aspecific, cell-mediated hypersensitivity response to a foreign antigen. Generally the limbus is primarily affected, though involvement of the bulbar conjunctiva has been described. Corneal phlyctenules are seen as an amorphous infiltrate, which ulcerates and may migrate centrally. Only the corneal component of a phlyctenule heals with scarring. (1). Historically, phlyctenules were seen mostly in association with Mycobacterium Tuberculosis infection. Nowadays, the most common cause of phlyctenulosis is Staphylococcal infection of the eyelid margins. Several parasites, Chlamydia Trachomatis, Candida Albicans, Herpes Simplex virus and adenoviruses have also been implicated in the pathogenesis of phlyctenulosis. Conjunctival inflammatory nodules have also been reported in response to other viral infections, such as Epstein-Barr virus (5, 6). Suarez and others report a case of conjunctival inflammation with conjunctival ulceration in a patient with FUHMD (12).

In this patient, each episode of a skin eruption was followed by a conjunctival reaction with inflammatory nodules and occasionally corneal ulceration. There were no signs of blepharitis or meibomian gland disease. A biopsy of a limbal nodule was performed and showed a nongranulomatous acute inflammation. The lesions resolved slowly after an intensive course of topical steroid drops. Considering the previously discussed infectious theory regarding the aetiology of pityriasis lichenoides, both the dermal and the ocular findings might represent an immunologic response to an undetermined (possible viral) infectious agent in this susceptible host.

CONCLUSION

We present a case of a remitting and relapsing maculo-papular skin eruption with crusting and associated mouth ulcers. A recalcitrant conjunctival reaction with inflammatory nodules was consistently present and developed within weeks after the onset of the skin rash. Histopathologic examination of a skin biopsy confirmed the clinical diagnosis of pityriasis lichenoides et varioliformis acuta. An initial episode lasted for several months and recurred after a remission of seven years. To our knowledge, this is the first report of bulbar and limbal inflammatory nodules as a part of the manifestations of the pityriasis lichenoides spectrum.

REFERENCES

(1) ARFFA R.C. – Grayson's diseases of the cornea. 4th ed. Mosby-Year Book, St.-Louis, 1997; 512-15.

(2) BOWERS S., WARSHAW E.M. – Pityriasis lichenoides and its subtypes. J Am Acad Dermatol 2006; 55: 557-72.

(3) COZZIO A., HAFNER J., KEMPF W., HAFFNER W., PALMEDO G., MICHAELIS S., GILLET M., ZIMMERMAN D., BURG G. – Febrile ulceronecrotic Mucha-Habermann disease with clonality: a cutaneous T-cell lymphoma entity? J Am Acad Dermatol 2004; 51: 1014-7.

(4) DEREURE O., LEVI E., KADIN M.E. – T-cell clonality in pityriasis lichenoides et varioliformis acuta: A heteroduplex analysis of 20 cases. Arch Dermatol 2000; 136:1483-6.

(5) FEINBERG A.S., SPRAUL C.W., HOLDEN J.T., GROSSNIKLAUS H.E. – Conjunctival lymphocytic infiltrates associated with the Epstein-Barr virus. Ophthalmology 2000; 107:159-63.

(6) GARDNER B.P., MARGOLIS T.P., MONDINO B.J. – Conjunctival lymphocytic nodule associated with the Epstein-Barr virus. Am J Ophthalmol 1991; 112: 567-71.

(7) KHACHEMOUNE A., BLYUMIN M.L. – Pityriasis lichenoides. Pathophysiology, classification and treatment. Am J Clin Dermatol 2007; 8: 29-36

(8) MAGRO C., CROWSON A.N., KOVATOVICH A., BURNS F. – Pityriasis lichenoides: a clonal T-cell lymphoproliferative disorder. Hum Pathol 2002 33: 788-95.
(9) PINTON P.C., CAPEZZERA R., ZANE C., DE PANFILIS G. – Medium-dose ultraviolet A1 therapy for pityriasis lichenoides et varioliformis acuta and pityriasis lichenoides chronica. J Am Acad Dermatol 2002; 47: 410-4.
(10) SIMON D., BOUDNY C., NIEVERGELT H., SIMON H.U., BRAATHEN L.R. – Succesful treatment of pityriasis lichenoides with topical tacrolimus. Br J Dermatol 2004; 150: 1033-5.
(11) SMITH K.J., NELSON A., SKELTON H., YAEGER J., WAGNER K.F. – Pityriasis lichenoides et varioliformis et acuta in HIV-1+ patient: a marker of early stage disease. Int J Dermatol 1997; 36: 104-9.
(12) SUAREZ J., LOPEZ B., VILLALBA R., PERERA A. – Febrile ulceronecrotic Mucha-Habermann disease: a case report and review of the literature. Dermatology 1996; 192: 277-9.
(13) TOMASINI D., TOMASINI C.F., CERRI A., SANGALLI G., PALMEDO G., HANTSCHKE M., KUTZNER H. et al. – Pityriasis lichenoides: a cytotoxic T-cell mediated skin disorder. Evidence of human parvovirus B19 DNA in nine cases J Cutan Pathol 2004; 31: 531-8.
(14) VARGA F.J., VONDERHEID E.C., OLBRICHT S.M., KADIN M.E. – Immunohistochemical distinction of lymphomatoid papulosis and pityriasis lichenoides et varioliformis acuta. Am J Pathol 1990; 136: 979-87.
(15) WEINBERG J.M., KRISTAL L., CHOOBAK L., HONIG P.J., KRAMER E.M., LESSIN S.R. – The clonal nature of pityriasis lichenoides. Arch Dermatol 2002; 138: 1063-7.

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Address for correspondence and reprints:
Dr. Thibault VERHAMME
Dienst Oogziekten
Universitair Ziekenhuis St Rafaël
Kapucijnenvoer 33
B-3000 LEUVEN
Belgium
Email: thibault.verhamme@gmail.com