Keratoderma blennorrhagica and mucocutaneous manifestations of Reiter's syndrome

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The classical triad of urethritis, arthritis, and conjunctivitis redescribed in 1916 by Reiter²⁵⁴ was originally reported in 1776 by Stoll²⁹⁸ in association with dysentery and in 1818 by Brodie⁴⁵ in association with venereal infection. During the last century other features have been added, resulting in a tetrad or a more complicated set of clinical features. At the other end of the spectrum formes frustes have been clearly defined, and such terms as 'incomplete Reiter's syndrome' have been used.¹⁸

Mucocutaneous manifestations of Reiter's syndrome (RS) have been recognised for several decades. The specific lesions have been included under different names. For example, skin involvement is considered as keratoderma blennorrhagica, mucosal involvement of the mouth as stomatitis, and ulceration of the glans penis as circinate balanitis. Finally, nail disease may occur.

In 1893 Vidal reported the association between keratoderma blennorrhagica and urethral infection.³¹⁹ In 1934 Weidmann clearly described this skin lesion as part of RS.³²⁴ In 1900 Stanislawski reported stomatitis in a patient with gonorrhoea, arthritis, keratoderma blennorrhagica, and shedding of nails.²⁹⁴ Balanitis itself has been recognised since 1897⁶¹ but confusion about the role of gonorrhoea in its causation continued until the late 1930s.

The prevalence and natural history of these skin lesions remain unclear. The primary reason for this is that the mouth ulcers are usually clinically inapparent, causing little or no discomfort and perhaps disappearing within a few days. Moreover, the skin lesions of keratoderma blennorrhagica, usually on the soles of the feet, may go unnoticed by the patient and physician. These too usually cause no symptoms and may disappear within a few weeks with no trace. Balanitis is usually not recognised in uncircumcised patients and even in the circumcised the lesions are often small and symptomless. For obvious reasons, genital lesions in females will often go unnoticed by all concerned.

A further problem results from a lack of consensus on diagnostic criteria. Mouth ulcers are common and

the stomatitis of RS may resemble other non-specific mouth lesions. Keratoderma blennorrhagica looks clinically and histologically like psoriasis. The lesions on the glans penis resemble non-specific infective processes. Nail lesions may mimic those seen following fungal infection or psoriasis.

Keratoderma blennorrhagica

Keratoderma blennorrhagica occurs most often on the soles of the feet, glans penis, and toes. Discrete lesions may be found elsewhere on the limbs, scrotum, trunk, scalp, and palms. In severe cases keratoderma may effect the whole body, resulting in exfoliation and even death.⁵⁶

Macroscopically the lesions begin as discrete vesicles, appearing on the soles of the feet. Within a few days the contents of the vesicles become opaque and the wall thickens, resulting in typical hyperkeratotic nodules. There is little evidence of local inflammation apart from a narrow erythematous base around the lesion. The vesicles may develop in crops, and as they mature further vesicles appear, grow, and sometimes coalesce.

If the initial small vesicular or 'pustular' lesion is opened a keratotic material is found. The hyperkeratotic crust eventually peels from the skin, leaving no scar. Keratoderma blennorrhagica usually develops several weeks after the onset of RS. The lesions may last for days, weeks, or months and often recur.

Histologically the lesions cannot be distinguished from those of psoriasis. Characteristic changes include hyper- and parakeratosis with elongation of the rete pegs. Spongiform pustules are found in the upper malpighian layer with varying degrees of polymorphonuclear leucocyte infiltration through the epidermis. Well-defined microabscesses may be found. The blood vessels are dilated and surrounded by leucocytes. These various changes have been reviewed by Hancock¹⁴⁶ and Csonka.^{68,70}

I have mentioned the difficulty in establishing prevalence and incidence. To try to evaluate the

prevalence and relationship of mucocutaneous lesions to the other manifestations of RS we studied 113 consecutive patients with RS as diagnosed by a seronegative asymmetric arthropathy plus one or more of urethritis/ cervicitis, dysentery, inflammatory eye disease, or mucocutaneous lesions (balanitis, oral ulceration, keratoderma). Patients with primary ankylosing spondylitis, psoriatic arthropathy, or other rheumatic disease were excluded. The mean age at presentation was 33.8 years. The mean duration of disease 6.4 years. HLA-B27 was present in 82% of patients.⁵³

Figures for the prevalence of mucocutaneous lesions, derived from the literature as compared to our own study⁵³ are summarised in the Table. Prevalence figures for keratoderma blennorrhagica have ranged from 1 to 31%. The low figure of Paronen may result from the fact his study was performed during the first world war and other

Table Prevalence of mucocutaneous lesions in Reiter's syndrome

No. of patients	Stomatitis (%)	Balanitis (%)	Keratoderma blennorrhagica	Author
76	11	26	8	Hancock <i>et al.</i>
260	12	23	13	Csonka
16	33	50	31	Weinberg <i>et al.</i>
344	3	33	1	Paronen
113*	27	46	22	Calin <i>et al.</i>
113†	22	29	17	Calin <i>et al.</i>

*At initial visit.

†At mean follow-up 6.4 years.

features of the disease may have been more relevant. The true figure seems to lie in the region of 20%.

The natural history of this skin lesion has seldom been clearly defined, but there is a consensus that the lesions are usually self-limiting, lasting from one to several weeks or even months. Since the lesions heal without residual scarring the precise duration is

Fig. 1 Reiter's syndrome: keratoderma blennorrhagica. Early hyperkeratotic lesions on soles and feet.

Fig. 2 Keratoderma blennorrhagica: later stage with crusted lesions.

difficult to ascertain. Some representative lesions are shown in the figures provided. Early lesions on the sole of a foot are shown in Fig. 1. Later these lesions spread (Fig. 2). Fig. 3 shows this same foot six weeks later completely healed with no residual scarring. Minimal nail lesions are still seen. Figs. 4, 5, and 6 show, respectively, examples of keratoderma of the sole, the palm and, the lower limbs.

The relationship between skin lesions and overall severity and prognosis of RS has not been defined. In our study⁵³ there appears to be no correlation between keratoderma blennorrhagica at any time during the course of the disease and overall functional status at follow-up of 6.4 years. Balanitis (present in 46% of individuals at outset) was still present in 29% of patients after a mean follow-up of 6.4 years. Likewise keratoderma present in 22% of patients at the beginning of the study was present in 17% at

Fig. 3 Same foot as in Figs. 2 showing disappearance of lesions during remission.

Fig. 4 *Reiter's syndrome: keratoderma blennorrhagica of sole.*

follow-up. Oral lesions were also prevalent: 27 of the patients had evidence of buccal ulceration at the outset and 22% at 6.4 years.

There is no specific treatment for the skin lesions. Various keratolytic agents may be used with a varying degree of success. Topical glucocorticoids may give some help but, in view of location, occlusive dressings are required with the danger of atrophy. The responses to methotrexate or azathioprine seem favourable but, again, no formal double-blind control studies have been performed. There have been controlled studies with psoriasis and psoriatic arthropathy, but clearly extrapolation to RS is not necessarily valid.

Stomatitis

Oral lesions are often symptomless. Even a careful search may fail to find the small, painless ulcers. That the superficial mucosal lesions are so rarely secondarily infected is surprising considering the location. The recorded prevalence of mucosal

Fig. 5 *Reiter's syndrome: keratoderma of palm with peeling of skin.*

Fig. 6 *Reiter's syndrome: hyperkeratotic lesions of keratoderma on lower limbs.*

lesions varied from 3 to 33% (Table). Almost certainly these figures are an underestimate since stomatitis may appear and disappear at different times during the course of the disease.

The lesions occur on the palate, tongue, buccal mucosa, and lips. They appear as shallow ulcers, sometimes with an irregular erythematous base or opaque vesicles. The histopathology of the oral lesions has been described by Epstein.¹⁰⁰ Changes are similar to those found in the skin. Parakeratosis, elongation of the rete pegs, acanthosis, micro-abscesses, and mixed dermal infiltrate are found.

The painless lesions require no treatment.

Circinate balanitis

Painless and superficial erosions of the glans penis commonly occur. Prevalence figures range from 23 to 50% (Table). Again, these figures may well be an underestimate since the lesions reappear at different times and cause no symptoms.

Balanitis may present with a small opaque vesicle of 2 mm to 3 mm in diameter, but may rupture to

form a painless superficial erosion with little surrounding erythema. Several lesions may coalesce to form a circinate pattern (Fig. 7). The coronal margin of prepuce and nearby glans are the areas most often affected. The lesions appear different in circumcised and non-circumcised patients. In the former a hard crust overlying the lesion may form. In the latter the lesion remains moist and may develop a secondary infection. The lesion may last a few days, months, or indefinitely. We have several patients who have had these lesions for over a decade.

Of great interest, the lesions may predate other manifestations of RS. Lassus¹⁹⁶ has described a group of patients with persistent circinate erosive balanitis and no other stigmata of RS. Most of them were HLA-B27 positive. Thus, circinate balanitis may occur as a forme fruste of RS. Four of our 113 patients had balanitis for a mean of four years before the onset of urethritis, arthritis, and conjunctivitis.⁵³

Fig. 7 *Reiter's syndrome: circinate balanitis. Note superficial ulceration of glans penis.*

Nail involvement

Nail involvement may be associated with keratoderma blennorrhagica or may occur as a separate entity. Early changes consist of a red, rolled edge of the nail fold. Subungual corny material accumulates and lifts the nail plate, which becomes yellow, opaque, ridged, and thickened. The nail is brittle and may eventually shed. The nail bed may show papular keratonised excrescences. The nail

changes may persist indefinitely or clear. Occasionally inflammatory areas in the skin adjacent to the subungual keratotic material may be mistaken for paronychia. The yellowish waxy hyperkeratotic substance that accumulates under the distal end of the nail plate may discharge at intervals (Fig. 8).

One striking aspect of the mucocutaneous lesions seen in RS is that none of them are seen in association with ankylosing spondylitis, a disease closely related to RS.

Fig. 8 *Reiter's syndrome: typical nail lesions with subungual accumulation of hyperkeratotic material.*