Ultrahistopathology of balanitis circinata

LASSE KANERVA,* MERJA KOUSA, KIRSTI-MARIA NIEMI, ALLAN LASSUS, TIMO JUVAKOSKI, AND JORMA LAUHARANTA

From the Departments of *Dermatology, Anatomy, and Electron Microscopy, University of Helsinki, Helsinki, Finland

SUMMARY Penile lesions from six patients with balanitis circinata were examined with the light and electron microscopes. The epithelium showed slight parakeratosis, acanthosis, and elongation of rete ridges. Neutrophil pustules occupied the upper epidermis. Prickle cells formed a spongiform net around the pustules.

The most prominent features detected by the electron microscope were the small-to-medium-sized pustules in the upper epidermis. The thin flattened keratinocytes formed a sponge-like trabecular network. Neutrophils were not found inside the keratinocytes. Chlamydia were not present in the lesions, which indicates that balanitis circinata is due to some reactive mechanism. The fine structure of balanitis circinata resembles that of pustular psoriasis.

Introduction

Balanitis circinata is almost diagnostic of Reiter’s disease and occurs in up to 69% of male patients with this disease.1 Similar lesions (vulvitis circinata) have also been found in the female vulva.2

The spongiform pustules of the skin are the most distinctive histopathological finding of Reiter’s disease detected by a light microscope. These pustules may be seen in cutaneous, oral, and penile circinate lesions.3,5 Hyperkeratosis, parakeratosis, and acanthosis may also be present in cutaneous lesions, which resemble those of psoriasis.

Descriptions of the fine structure of balanitis circinata have not been reported. For this reason we decided to undertake the present study.6

Materials and methods

Six patients with balanitis circinata were included voluntarily in the study. Their clinical and laboratory findings are given in the table. Gonorrhoea was excluded by smear examination and negative culture results for Neisseria gonorrhoeae in all patients. Cultures for Chlamydia trachomatis were performed on urethral specimens in all cases; in two patients the results were positive, in two who had had a previous episode of chlamydial urethritis they were now negative, and in two who had not had chlamydial urethritis previously they were negative.

<table>
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<th>Patient No</th>
<th>Age (years)</th>
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<th>HLA-B27</th>
<th>Chlamydial isolation</th>
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<td>24</td>
<td>Urethritis, arthritis</td>
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<td>Arthritis</td>
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<td>Urethritis</td>
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+ = Positive; − = negative; ND = not done
*Isolation-positive at the time of examination

Samples for conventional light microscopy (one patient) and for light and electron microscopy (all patients) were taken from the circinate lesion of the glans penis with a knife after local anaesthesia with 1% lidocain-adrenaline. For electron microscopy blocks (1 mm³ or smaller) were fixed for two hours or longer in cacodylate or phosphate-buffered (0.1 mmol/l; pH 7.3) 2.5% glutaraldehyde at 4°C, postfixed with 1% osmium tetroxide, dehydrated in a graded series of alcohol, and embedded in Epon 812. Ultrathin sections were cut with a diamond knife on a LKB ultramicrotome, stained with lead citrate, and examined with a Jeol 100S or a Jeol 100CX electron microscope operated at 80 kV.

Results

CLINICAL

The penile lesions in all patients were typical of balanitis circinata. They showed small erythematous...
FIG 1  Histopathology of balanitis circinata by light microscopy. (a) Neutrophil pustules (star) occupy the upper epidermis. (Epon embedment, × 940). (b) Parakeratosis, acanthosis, and elongation of rete ridges and only a few neutrophils are seen, but an extensive mononuclear infiltrate is present. (Paraffin embedment, patient 6, × 210).
areas, which were demarcated from the surrounding normal mucosa by shallow, circinate or serpiginous, slightly raised, greyish white borders.

LIGHT MICROSCOPY
The epithelium showed slight parakeratosis, acanthosis, and elongation of rete ridges. Neutrophil pustules occupied the upper epidermis (fig 1a). Prickle cells formed a spongiform net around the pustules. The basal epidermis was invaded by a moderate number of mononuclear cells. The keratinocytes were moderately oedematous and the intercellular space enlarged.

In the papillary dermis the capillaries were enlarged and increased in number. In one patient, a moderate-to-extensive pericapillary mononuclear infiltrate was present (fig 1b). Some erythrocyte extravasation was present.

ELECTRON MICROSCOPY
In the upper dermis fenestrated (fig 2) or unfenestrated capillaries were widened and surrounded with neutrophils and mononuclear cells of the lymphocytic and macrophagic cell lines. Melanophages were also present. The dermoepidermal junction had a normal appearance with well preserved hemidesmosomes (fig 2), although basal lamina gaps were sometimes found. Leucocytes invaded the epidermis through these gaps.

The keratinocytes showed increased cellular activity with numerous ribosomes, mitochondria, Golgi areas, and endoplasmic reticulum and also

**FIG 2** Electron micrograph of the dermoepidermal junction. (a) Fenestrated (thin arrow) capillary (C) lies close to the basal lamina (thick arrow). Note the flattened basal keratinocytes (K). A proteinous, fine, granular substance is present in the capillary, in the papillary dermis, and in the epidermis (circle) (× 3600). (b) Prominent long band of hemidesmosomes is shown. (BL = basal lamina; D = dermis, × 36 000).
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**FIG 3** Electron micrograph showing prickle cell layer with widened intercellular space (I) invaded by leucocytes (L). Fewer tonofilaments in the keratinocytes (K), some of which are flattened (F), and distended desmosomes (circle) are present. (x 4000).

Increased numbers of lipid droplets. Giant mitochondria were found frequently in the superficial keratinocytes, some of which were oedematous. There were few tonofilaments. The intercellular space was enlarged and the number of desmosomes decreased (fig 3). The substance in the intercellular space was finely granular as was that inside and around the capillaries, indicating leakage of plasma through the capillaries (fig 4). A coarse granular substance, probably derived from keratinocyte organelles, was also found. Large dark bodies (fig 4) without a visible membrane and with a heterogeneous inner structure were often present in the middle and upper epidermis; these may have been lipid bodies.7

The most prominent feature was the neutrophils, which formed small-to-medium-sized pustules in the interstices (figs 3 and 4); this caused flattening of the keratinocytes. The thin flattened keratinocytes formed a sponge-like trabecular network connected by a few tiny desmosomes. In addition to neutrophils, free lysosomes and other organelles from disrupted neutrophils and possibly keratinocytes were present in the intercellular space in these pustules. Often the surface membrane of contacting keratinocytes and neutrophils was partly absent (fig 5), allowing the passage of lysosomes from the neutrophils into the adjacent keratinocyte. These lysosome-containing keratinocytes were otherwise normal in appearance and did not show prominent features of cytolysis. Neutrophils were not found inside the keratinocytes. Neutrophil pustules were usually present in the superficial layers, corresponding to a "subcorneal" localisation. Lymphocytes occurred rarely in the superficial pustules whereas large numbers of lymphocytes and macrophages were present in the basal layers. Chlamydia were not found in the lesions.

These findings were almost identical in five of the patients. In the sixth patient (patient 6), the invading leucocytes were mostly of the lymphocyte-macrophage series, with only a few neutrophils (fig 1b), and the pericapillary infiltrate of the dermis was dense. The mononuclear cells were in very close contact with the basal lamina and frequently invaded the epidermis through gaps in it (fig 6).
FIG 4  Electron micrograph showing infiltrating neutrophils (L) between keratinocytes (K) containing abundant lipid droplets (I) and dark bodies (D) (× 6000). Left inset: Fine granular intercellular substance at larger magnification (× 60 000). Right inset: Dark body at larger magnification (× 45 000).
Discussion

Reiter's disease has been defined as a disorder of unknown cause consisting of urethritis, arthritis, and conjunctivitis, accompanied in some cases by uveitis, circinate balanitis, and oral lesions, and in rare cases by an eruption simulating rupioid psoriasis (keratodermia blenorrhagica). Reiter's disease has been strongly associated with Reiter's disease, namely enteritis and non-gonococcal urethritis (NGU), which is now the most frequent factor in cases in developed countries. C. trachomatis can be isolated from the urethral tract of about 70% of men with Reiter's disease who show signs of urogenital infection at the time of examination. In Finland, approximately 2% of men with NGU develop signs of polyarthritic Reiter's disease. The histocompatibility antigen HLA-B27 is strongly associated both with Reiter's disease and with balanitis circinata. Thus, balanitis circinata may be an early sign of Reiter's disease, even when it occurs alone.

Keratodermia blenorrhagica of the palms or soles or both has been reported in 1-18% of patients with Reiter's disease and in about one-fifth of patients with other psoriasis-like dermatoses. Our finding of spongiform pustules in the circinate lesions further confirmed the strong relationship between the skin lesions of Reiter's disease and psoriasis. At the fine structural level the spongiform pustules closely resembled those reported in pustular psoriasis and impetigo herpetiformis. Our finding of close interactions between infiltrating neutrophilic leucocytes and keratinocytes has also been reported by Komura et al. The cell membranes of contacting leucocytes and keratinocytes were occasionally partly absent, and the leucocyte granules appeared to move into the adjacent keratinocyte. The cytolytic enzymes of the neutrophil granules probably accounted for the generation of the sponge-like network of keratinocytes. Our study further confirmed that the neutrophils were localised between and not within the keratinocytes, as was believed during the light microscopy era.

Little is known about the pathogenesis of the skin lesions in Reiter's disease. The basic mechanisms may be closely related in several diseases which are characterised by epidermal non-bacterial pustules, such as pustular psoriasis, impetigo herpetiformis, acrodermatitis continua Hallopeau, pustulosis...
palmoplantaris, geographic tongue,\textsuperscript{15} and Reiter's disease. The clinical course and morphological appearance of the circinate lesions which are present in Reiter's disease and psoriasis as well as in leprosy, dermatophytosis, certain varieties of dermatitis, and cutaneous lymphoma indicate an immunological pathogenesis.\textsuperscript{16} Our morphological findings indicated that immunological factors played a part in pustule formation, as previously suggested in pustulosis palmoplantaris\textsuperscript{17} and psoriasis.\textsuperscript{16} We found dilated capillaries with polymorphonuclear leucocytes, basal lamina gaps, basal spongiosis, and pustules of polymorphonuclear leucocytes. Complement-dependent chemotactic factors\textsuperscript{18,19} have been identified in psoriatic lesions and may be present in the skin and mucous lesions of Reiter's disease. These could cause an accumulation of polymorphonuclear leucocytes which release various cytotoxic enzymes\textsuperscript{14} and thus account for the keratinocyte damage. The dilated fenestrated papillary capillaries would discharge the polymorphonuclear leucocytes, which pass through the basal lamina gaps, forming the proximal Kogoj pustules and the more distal Munro microabscesses. Why the penile mucosa is such a characteristic target organ in Reiter's disease is not known, but balanitis circinata seems to occur almost solely in patients with Reiter's disease triggered by a urogenital infection. The absence of chlamydia in the lesions suggests that balanitis circinata is due to some reactive mechanism.
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References