Dear Editors,

Mucous membrane pemphigoid (MMP) is a subepidermal autoimmune blistering disease commonly affecting the oral mucosa and conjunctiva. Type XVII collagen (BP180) and laminin 332 are structural proteins of the dermal-epidermal junction and are the main autoantigens in MMP. Binding of autoantibodies leads to local complement activation, influx of inflammatory cells into the upper dermis, and dermal-epidermal separation with blisters and erosion [1]. Here we report on a rare case of MMP with lesions limited to the glans penis.

A 57-year-old Caucasian man was referred to our outpatient clinic with a ten-week history of red plaques on the glans penis that had initially improved spontaneously, but six weeks later, blisters and erosions developed on the glans penis. Mild pruritus was reported. Physical examination revealed two 0.8 × 0.9 cm and 1.2 × 1.7 cm erythematous erosions on the glans penis extending to the corona (Figure 1a). The other mucous membranes and the skin were not involved. The patient was in good general health. The sexual medical history was unremarkable. Long-term medication was clomipramine, prescribed for narcolepsy.

A lesional biopsy showed a mostly missing epithelial layer, intact rete ridges and a lymphocyte-rich inflammatory infiltrate in the upper dermis (histopathology with hematoxylin and eosin staining; Figure 1b). Direct immunofluorescence (IF) microscopy of a perilesional biopsy from the glans penis revealed deposition of complement component 3 (C3) along the dermal-epidermal junction (Figure 1c). Indirect IF microscopy on monkey esophagus, human salt-split skin, and HEK293 cells recombinantly expressing laminin 332 [2] as well as BP180 NC16A-specific ELISA were negative (not shown). Immunoblotting with conditioned concentrated supernatant of cultured human keratinocytes showed IgG antibodies against the soluble ectodomain of BP180 (linear IgA dermatosis antigen, LAD-1) [3] (Figure 1d). In addition, PCR for HSV-1 and HSV-2 DNA of the smear was negative. A Candida albicans infection was excluded by negative cultures of lesional swabs and by negative PAS staining of lesional histopathology sections.

Treatment with oral dapsone 125 mg/day (1.5 mg/kg body weight) for five months accompanied by topical miconazole nitrate (20 mg/g) and fluprednidene-21-acectate (1 mg/g) ointment for the first two weeks led to healing of all lesions after seven weeks. No relapse occurred during a follow-up time of twelve months.

Mucous membrane pemphigoid is a chronic and usually progressive disease with an incidence of about 2.0 per 1 million people per year in Germany [4]. The disease arises at a mean age between 60 and 65 years [5–7]. Mucous membrane pemphigoid can affect one or multiple mucosal sites as well as the skin. The mouth is most frequently involved (85% of patients), followed by conjunctiva (65%), skin (25–30%), nasal cavity (20–40%), anogenital area (20%), pharynx (20%), larynx (5–10%), and esophagus (5–15%) [5, 6], [8]. Most lesions, except the oral cavity, tend to heal with scarring [1]. Except for vulvar MMP in children [9–12], exclusive genital involvement is extremely rare. Only one case of penile MMP has been reported so far [13].

Diagnosis of MMP is based on the predominant mucosal involvement and the deposition of some or all of IgG, IgA, and/or C3 along the dermal-epidermal junction by direct IF microscopy of a perilesional biopsy [8]. Direct IF microscopy of our patient revealed linear C3 deposition at the dermal-epidermal junction, but no immunoglobulin deposition. Histopathology of a lesional biopsy, as in our patient, characteristically shows subepidermal splitting and a moderate inflammatory infiltrate of eosinophils, neutrophils, and lymphocytes in the upper dermis. Sera of MMP patients are usually assessed for circulating autoantibodies with several assays, e.g. indirect IF on monkey esophagus and human salt-split skin, BP180 NC16A, BP230, and type VII collagen-specific ELISA systems, and if still unreactive or if dermal binding is observed on salt-split skin, with indirect IF on human cells expressing recombinant laminin 332. MMP patients with anti-laminin 332 reactivity were shown to be associated with solid malignancies in about 25% of cases [2, 14]. If still unreactive, MMP sera may be subjected to immunoblotting with various cell-derived or recombinant forms of BP180 that are available in specialized laboratories. In our patient, we used one of the latter methods and found IgG reactivity against the soluble keratinocyte-derived ectodomain of BP180; this became negative ten months after initiation of therapy. Reactivity against the ectodomain of BP180 has been reported in about half of MMP patients [15]. In mild MMP (as in our patient) topical corticosteroids in combination with tetracycline or dapsone are usually applied. In unresponsive patients, oral prednisolone can be added and combined with azathioprine or mycophenolic acid [1].

In summary, we describe a rare manifestation of MMP restricted to the glans penis. Since diagnosis of MMP based...
Correspondence

Clinical Letter

on direct IF microscopy and serology is usually straightforward, it is important to know the clinical spectrum of the disease that includes lesions localized to single mucosal sites such as the glans penis.

Conflict of interest
None.

Katharina Boch1, Ralf J. Ludwig2, Detlef Zillikens1, Enno Schmidt1,2

(1) Department of Dermatology, Allergology and Venerology, University of Lübeck, Lübeck, Germany
(2) Lübeck Institute for Experimental Dermatology (LIED), University of Lübeck, Lübeck, Germany

Correspondence to
Katharina Boch, MD
Department of Dermatology, Allergology and Venerology
University of Lübeck
Ratzeburger Allee 160
23538 Lübeck, Germany
E-mail: katharina.boch@uksh.de

References

1. Schmidt E, Zillikens D. Pemphigoid diseases. Lancet 2013; 381: 320–32.
2. Goletz S, Probst C, Komorowski L et al. A sensitive and specific assay for the serological diagnosis of antilaminin

Figure 1  Erythematous, partly erosive plaque with sharp margins on the glans penis (a). Lesional histopathology with subepidermal splitting, mostly absent epidermis, with infiltration of lymphocytes and neutrophils in the upper dermis (hematoxylin-eosin stain). Direct immunofluorescence microscopy of a perilesional biopsy revealed linear deposits of C3 (arrow) at the dermal-epidermal junction (c). Immunoblotting with conditioned concentrated supernatant of cultured human keratinocytes showed IgG reactivity with the 120 kDa LAD-1 (linear IgA dermatosis antigen-1; arrow), the soluble ectodomain of BP180 (d). NHS, normal human serum; Pat., patient.
332 mucous membrane pemphigoid. Br J Dermatol 2019; 180: 149–56.
3 van Beek N, Zillikens D, Schmidt E. Diagnosis of autoimmune bullous diseases. J Dtsch Dermatol Ges 2018; 16: 1077–91.
4 Bertram F, Bröcker EB, Zillikens D et al. Prospective analysis of the incidence of autoimmune bullous disorders in Lower Franconia, Germany. J Dtsch Dermatol Ges 2009; 7: 434–9.
5 Thorne JE, Anhalt GJ, Jabs DA. Mucous membrane pemphigoid and pseudopemphigoid. Ophthalmology 2004; 111: 45–52.
6 Ahmed AR, Kurgis BS, Rogers III RS. Cicatricial pemphigoid. J Am Acad Dermatol 1991; 24: 987–1001.
7 Hübner F, Recke A, Zillikens D et al. Prevalence and age distribution of pemphigus and pemphigoid diseases in Germany. J Invest Dermatol 2016; 136: 2495.
8 Chan LS, Ahmed AR, Anhalt GJ et al. The first international consensus on mucous membrane pemphigoid: definition, diagnostic criteria, pathogenic factors, medical treatment, and prognostic indicators. Arch Dermatol 2002; 138: 370–9.
9 Hoque S, Patel M, Farrell A. Childhood cicatricial pemphigoid confined to the vulva. Clin Exp Dermatol 2006; 31: 63–4.
10 Belzile E, Funaro D, Powell J. Localized vulvar bullous pemphigoid of childhood: A rare cause of persistent vulvar erosions in children. Pediatr Dermatol 2019; 36: 349–51.
11 Waisboud-Zinman O, Ben-Amitai D, Cohen AD et al. Bullous pemphigoid in infancy: clinical and epidemiologic characteristics. J Am Acad Dermatol 2008; 58: 41–8.
12 Fisler RE, Saeb M, Liang MG et al. Childhood bullous pemphigoid: a clinicopathologic study and review of the literature. Am J Dermatopathol 2003; 25: 183–9.
13 Mirza M, Zamilpa I, Wilson JM. Localized penile bullous pemphigoid of childhood. J Pediatr Urol 2008; 4: 395–7.
14 Egan CA, Lazarova Z, Darling TN et al. Anti-epiligrin cicatricial pemphigoid and relative risk for cancer. Lancet 2001; 357: 1850–1.
15 Schmidt E, Skrobek C, Kromminga A et al. Cicatricial pemphigoid: IgA and IgG autoantibodies target epitopes on both intra-and extracellular domains of bullous pemphigoid antigen 180. Br J Dermatol 2001; 145: 778–83.