Papular Purpuric Glove and Socks Syndrome with Evolution into Pemphigus Vulgaris

Dear Editor,

Papular purpuric gloves and socks syndrome (PPGSS) is an uncommon acute dermatosis characterised by symmetrical painful erythematous papules on the hands and feet which evolve to sharply demarcated pruritic lesions at the wrist and ankles.¹ These cutaneous manifestations are often accompanied by fever, lymphadenopathy and oral mucosal lesions. It has also been associated with dysuria, vulvar oedema and erythema.²

A 36-year-old Chinese female—with no significant medical history of note—was seen for itchy rashes over her hands and feet for 2 weeks, associated with painful oral ulcers for 2 days. She was otherwise afebrile and systemically well with no localising signs of infection. No new drugs or traditional medications were started prior to the onset of the rash. Clinical examination revealed confluent erythema on the palms and soles with sharp demarcation at the wrists and ankles (Figs. 1a and 1b). Multiple erosions and ulcers were found on her lips (Fig. 1c), buccal mucosa and hard palate. There were no palpable lymph nodes or conjunctivitis. Laboratory



Fig. 1. Clinical photos of the patient. A) Confluent erythema seen on the palms. B) Confluent erythema present on the soles. C) The lips reveal multiple erosions and ulcers.

tests revealed mild lymphopaenia, suggestive of a viral aetiology, with normal levels of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and liver function test. Syphilis and retroviral screen was negative. Histology of the palmar lesions revealed non-specific changes of spongiotic dermatitis with eosinophils and extravasated red cells (Fig. 2). Parvovirus B19 polymerase chain reaction (PCR) was negative. Her palmoplantar rashes improved with moisturisers and gradually resolved over the next 1-2 weeks. However, her oral erosions persisted despite regular antiseptic mouth gargle and topical steroids. In view of the active progression of oral lesions, an oral mucosa biopsy was performed. Histology of the mucosal epithelium revealed suprabasal acantholysis with basal keratinocytes exhibiting a "tombstone" appearance. They stained positively on AE1/3 stain, and negatively for herpes type 1 (HSV 1) and herpes type (HSV 2). There was a dense upper dermal infiltrate of lymphocytes suggestive of pemphigus vulgaris (PV) (Figs. 3a and 3b). PCR assays for herpes simplex virus, enterovirus, human immunodeficiency virus and parvovirus B19 were negative; serologies for parvovirus B19 and Epstein Barr virus (EBV) were also negative. Her desmoglein 1 antibody levels were 5.7 RU/mL (equivocal range: 14-20 RU/mL) and her desmoglein 3 antibody levels were 50.4 RU/mL (equivocal range: 9-20 RU/mL). Her indirect immunofluorescence (IIF) with monkey oesophagus substrate was positive, showing an intercellular pattern and a 1/20 titre. Her direct immunofluorescence (DIF) was negative. She subsequently developed tiny erosion over her



Fig. 2. Hematoxylin and eosin staining, x100 magnification. Histology of palmar lesions revealing non-specific changes of spongiotic dermatitis with eosinophils and extravasated red cells.



Fig. 3. Histology findings suggestive of pemphigus vulgaris. A) Hematoxylin & eosin staining, x200 magnification. Suprabasal blister with "tombstone" appearance of basal keratinocytes and upper dermal lymphocytic infiltrate suggestive of pemphigus vulgaris. B) Cytokeratin AE1/AE3 staining, x200 magnification. Suprabasal blister with "tombstone" appearance of basal keratinocytes and upper dermal lymphocytic infiltrate suggestive of pemphigus vulgaris.

clitoris with no other cutaneous lesions. Oral prednisolone was started at 30 mg (0.56 mg/kg/day) initially, with the subsequent addition of mycophenolate mofetil (MMF) for control of her condition. She is currently taking prednisolone 17.5 mg/day and MMF 1.5 g BD.

Our patient presented initially with clinical features indicative of PPGSS with acral confluent erythematous plaques clearly demarcated at the wrists and feet. The diagnosis was supported by her blood tests, histology report and the spontaneous resolution of the palmoplantar rashes. The mainstay of treatment in PPGSS is symptomatic, with spontaneous resolution and no long term sequelae.³ The oral mucosal lesions, suggestive of PV in our patient, propose a causal link between PPGSS and PV. It is highly possible that both conditions were triggered by the same virus in our patient. In addition to parvovirus B19 infection identified as a trigger for PPGSS, other viruses such as measles virus, hepatitis B virus, coxsackie B virus, EBV and cytomegalovirus (CMV) have also been identified.⁴ Viral particles were found in vessel endothelium and in basal cell of the epidermis, suggesting that PPGSS might be due to the virus itself or a response to circulating immunocomplexes.³ PV, on the other hand, is an autoimmune bullous disease characterised by acantholysis and blister formation within the epidermis. It involves autoantibodies targeted against desmoglein 1 and desmoglein 3, proteins involved in cell adhesion structure. A viral aetiology has been suggested for PV and it has been hypothesised that mimicry between viral and epidermal proteins causes overactivation of the immune system involving interferons. However, attempts to detect viruses in blood, skin or fluid lesions have yielded inconclusive results.⁵

To our knowledge, this is the first observation of PPGSS evolving into PV and further studies may be performed to investigate a possible causal link between the 2 conditions.

REFERENCES

- Harms M, Feldmann R, Saurat JH. Papular-purpuric 'gloves and socks' syndrome. J Am Acad Dermatol 1990;23:850-4.
- Vassilev TV, Beilke MA, Garcia-Diaz JB. A 35-year-old woman with fever, joint pain and rash. Infect in Med 2001;18:339-43.
- Santonja C, Nieto-Gonzalez G, Santos-Briz A, Gutierrez Zufiaurre Mde L, Cerroni L, Kutzner H, et al. Immunohistochemical detection of parvovirus B19 in "gloves and socks" papular purpuric syndrome: direct evidence for viral endothelial involvement. Report of three cases and review of the literature. Am J Dermatopathol 2011;33:790-5.
- Feldmann R, Harms M, Saurat JH. Papular-purpuric "gloves and socks" syndrome: not only parvovirus B19. Dermatology 1994;188:85-7.
- Sagi L, Sherer Y, Trau H, Shoenfeld Y. Pemphigus and infectious agents. Autoimmun Rev 2008;8:33-5.

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