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Correspondence Letter

Dear Editor,

Management of patients with pemphigus vulgaris during the COVID-19 pandemic: Experience of a second level dermatology center

With reference to the interesting article of Wang et al.[1], on the use of immunomodulatory agents for severe cutaneous disease during the COVID-19 pandemic, we would like to share the real experience of a Medium-size Regional Healthcare Dermatological Center treating 72 patients with autoimmune bullous diseases.

In Ancona Regional hospital, a specialist outpatient clinic dealing with the diagnosis and treatment of immunomediated skin disease has been operating since 1985, and 72 patients with pemphigus vulgaris are currently being treated. Since the end of February, when the SARS-CoV-2 pandemic had already spread in most of Italy, a task force composed of 4 dermatologists and 1 immunologist was set up with the aim of addressing problems relating to the specific risk for this class of patients. The main goal was to evaluate risk/benefit in modulating treatment, following a patient-tailored strategy, taking into consideration patients' risk of exposure to SARS-CoV-2 virus, based on the geographical area of residence [coherently with different prevalence of infection between northern (higher prevalence) and southern (lower prevalence) part of the Marche region] and clinical situation. All patients were recommended to observe social isolation.

Treatment details of pemphigus vulgaris patients are summarised in Table 1.

Out of the 72 affected patients, 50 were on monotherapy with systemic corticosteroids, 20 patients were on combined therapy with corticosteroid and steroid sparing agents, 2 patients were not taking any medication because they should have received the next dose of Rituximab 500 mg by the end of April 2020, according to the six-month interval dosing practised in our centre and supported by literature.[2]

Immunosuppression represents an independent risk factor for increasing mortality in COVID-19,[3] however, it is generally accepted that only doses higher than 20 mg/day of prednisone or equivalent are considered immunosuppressive, with the risk of infection at doses of ≤10 mg considered low.[4] Therefore, all patients taking steroids at doses < 20 mg/day were recommended to continue therapy and for patients taking prednisone > 20 mg/day or equivalent (Supplementary Table 1),[5-8] a dose reduction was considered: prednisone 12.5 mg po qd (6 patients), methylprednisolone 16 mg po qd (9 patients) and betamethasone sodium phosphate 2 mg po qd (2 patients). For patients at higher risk for recurrence and/or coming from highly affected geographical areas, the full dosage of steroid was maintained in 11 patients, a reduction of methylprednisolone to 8 mg po qd was established in 4 patients and a reduction of betamethasone sodium phosphate to 1.5 mg po qd in 2 patients.

Table 1 Treatment details of 72 patients with pemphigus vulgaris. per os (po); quaque die (qd); intravenous (iv); bis in die (bid); quater in die (qid)

Treatment performed	N° of patients
Monotherapy	
Betamethasone sodium phosphate 0.5 mg po qd	30
Methylprednisolone 16 mg po qd	9
Prednisone 12.5 mg po qd	6
Methylprednisolone 8 mg po qd	3
Betamethasone sodium phosphate 2 mg po qd	2
Rituximab 500 mg iv qd	2
Association therapy	
Betamethasone sodium phosphate 0,5 mg po qd + mycophenolate mofetil 500 mg po bid	11
Methylprednisolone 8 mg po qd + azathioprine 100 mg po qd	5
Prednisone 10 mg po qd + mycophenolic acid 360 mg po qid	4

For patients under combination therapy, in order to discontinue the conventional immunosuppressant administered as steroid sparing agent,[1] a possible increase of corticosteroid up to an equivalent dose of 20 mg of prednisone has been reported in literature.[9] By aligning with these recommendations, the immunosuppressant was discontinued and the steroid dose was increased. For patients who should have received rituximab therapy, a temporary delay of the drug administration was decided, they were instructed in the self-assessment of their skin and mucosae, and strictly followed by phone, in order to rapidly detect recurrence of the disease.

Two months after, following this strategy, no patient reported a febrile syndrome or respiratory failure or death due to COVID-19. Moreover, only one patient who should have been treated with rituximab, developed a relapse of disease, for which he was treated with betamethasone sodium phosphate 3 mg po qd.

Until official guidelines on pemphigus management in COVID-19 era are available, good clinical practice recommendations, and adoption of behaviours aimed at reducing the risk of infection, such as social distancing and hand washing,[10] would seem to be the best care strategy.

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Supporting Information

Additional Supporting Information may be found online in Supporting Information:

Table S1. Corticosteroid Conversion Table (5–8).

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Correspondence Letter

Dear Editor,

Comedonicus variant of keratinocytic epidermal naevus—Comment on 'An unexpected coexistence of two epidermal naevi on the scalp: Naevus comedonicus and naevus sebaceous'

We have read with great interest the article 'An unexpected coexistence of two epidermal naevi on the scalp: Naevus comedonicus and naevus sebaceous' by Solak et al.[1] Although there are only a few examples in the literature of simultaneous presence of two different epidermal naevi it came up to our attention the fact that two of our patients presented keratinocytic epidermal naevus and naevus comedonicus within the same lesion.

Case 1. A 10-year-old boy was presented for examination with four 1 × 0.3 cm asymptomatic lesions on his back consisting of horizontal hyperkeratotic linear tracts, each one with a comedo on the lateral end (Fig. 1a, b). The first lesion appeared at the age of 8, and the other lesions showed up later.

Case 2. A 13-year-old boy was seen with three lesions between 1 × 0.3 cm and 1 × 0.6 cm on the posterior part of the left thigh formed by verrucous structures and a comedo on the medial end of each one, which caused discomfort due to rubbing with clothing (Fig. 1d, e). Smaller lesions were noticed at birth, which increased in size with time.

None of the family members of any of the cases presented similar lesions.

Dermoscopy demonstrated comedo openings, papillomatous structures and brown circles (Fig. 1c, f).

Ultrasound imaging of the first case showed a hyperechoic superficial line (hyperkeratinisation) with wavy areas in probable relation to the comedo openings and a sharply defined hypoechoic structure at the epidermal level corresponding to the epidermal naevi (Fig. 2a). A mild increase in intralesional flow was seen in the Doppler mode (Fig. 2b).

In both cases, a punch biopsy was performed. Histopathology revealed mild papillomatosis and acanthosis with orthokeratotic hyperkeratosis in the epidermis (Fig. 3a), as well as an infundibular epidermal cyst filled with keratin (Fig. 3b) connected to the epidermis (Fig. 3c). These findings were consistent with keratinocytic epidermal naevus and epidermal cysts.

Epidermal naevi are a group hamartomatous malformations of the epidermis, sometimes involving its appendages, which are the result of cutaneous mosaicism.[2] Large brown circles have been described as characteristic of keratinocytic epidermal naevus when using dermoscopy but can be present in other lesions such as seborrhoeic keratosis or squamous cell carcinoma.[3]

Various mutations have been related to these mosaicisms. Among others, Toll et al.[4] found a postzygotic FGFR2 mutation in some keratinocytic epidermal naevus. This mutation was also described in naevus comedonicus.[2] Both our patients presented a similar pattern in all the lesions; therefore, we suggest that the FGFR2 mutation might be originating this comedonicus variant of epidermal naevi. This same mutation was also thought to be linked to the naevus comedonicus and naevus sebaceous.[1] We consider that our cases support the hypothesis of one mutation being able to express different phenotypes depending on the affected cell and its moment of development.[5]

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