gous missense mutation, c.6110G>A (p.Gly2037Glu), in exon 73 of the *COL7A1* gene [4, 5]. In the child, who is now 18 months old, spontaneous blisters no longer develop, although milia are still present on extremities (*figure 1B*).
Our patient was diagnosed with SI-DDEB based on laboratory findings and clinical course. In self-improving DEB, colVII cytoplasmic inclusions are regularly observed by IFM and correspond to colVII retention within the RER [2, 3, 6]. Usually, staining for colVII is reduced to such an extent that it is absent at the BMZ. The epidermal inclusions resolve over time, with parallel increase in colVII expression [7, 8]. The concomitant reduction or cessation of skin fragility is thought to be secondary to normalization of colVII secretion from keratinocytes. However, persistence of intraepidermal colVII in the presence of normal BMZ labelling has been observed after resolution of skin fragility [8]. In our patient, the skin biopsy was performed at three months of age, when disease was already markedly attenuated. At that time, IFM for colVII showed granular labelling throughout the epidermis but also linear staining at the BMZ, and ultrastructural examination revealed cytoplasmic inclusions mainly localized within suprabasal keratinocytes, containing few elongated dense structures. We hypothesize that these features capture an intermediate phase in self-improving DEB pathology, corresponding to initial secretion of colVII concomitant with residual retention within keratinocytes.
The dominant colVII glycine substitution, p.Gly2037Glu, identified in our patient has been previously reported. The mutation causes colVII retention within HaCaT keratinocytes and is associated with granular labelling in the basal epidermis [4, 5]. In previous cases, the mutation p.Gly2037Glu resulted in a phenotype of intermediate DDEB; a 12-year-old female had acral and oral blisters together with albopapuloid lesions [4] and a two-year-old child continued to develop blisters on the trunk and lower extremities (*supplementary table 1*). In contrast, in our patient, oral involvement rapidly resolved in infancy and skin blisters were strictly localized to extremities and ceased by the second year of life. However, our relatively short follow-up does not allow to formally exclude that some skin fragility signs recur in the future, a limitation shared by other self-improving DEB cases reported in the literature [6]. In conclusion, comparison of our patient with the other cases carrying the missense p.Gly2037Glu mutation shows that the same mutation may result in a variable phenotype, possibly due to individual genetic backgrounds and environmental factors.

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Table S1: Clinical, immunopathological and ultrastructural findings in dystrophic epidermolysis bullosa (DEB) patients carrying the dominant missense mutation, p.Gly2037Glu, in the COL7A1 gene.

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Herpes zoster following COVID-19: a report of three cases

Milan, its metropolitan area and two close cities, Bergamo and Brescia, in the region of Lombardy, have been severely affected by a dramatic outbreak caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease caused by this virus, named coronavirus disease 2019 (COVID-19), is associated with numerous, different cutaneous manifestations, including erythematous exanthems, erythematous-papulo-vesicular eruptions, urticaria, papular acrodermatitis, pseudo-chilblains and other acral ischaemic lesions [1]. Herpes zoster (HZ) is a manifestation of the reactivation of latent varicella zoster virus (VZV) infection and has been very rarely described in patients with

Table 1. Clinical features and laboratory data of cases reported in the English-speaking literature (including the present study).

	Age (years), sex	Onset of HZ relative to COVID-19	Lymphocyte count (cells/mmc)	CD4+/CD8+ ratio*	Clinical features of HZ
Patient 1	68, F	8 weeks later	1490	0.75	Multi-metameric
Patient 2	44, F	8 weeks later	1700	0.60	Intercostal
Patient 3	64, F	10 weeks later	1800	0.63	Thoraco-abdominal
Shors [2]	49, F	Simultaneous	N/A	N/A	Maxillary with severe neuralgia
Tartari *et al.* [3]	68, F 74, F 71, F 70, M	Simultaneous Simultaneous Simultaneous Simultaneous	530 610 470 620	N/A N/A N/A N/A	Maxillary with necrotic lesions Maxillary with necrotic lesions Maxillary with necrotic lesions Dorsum
Xu *et al.* [4]	73, M	Simultaneous	N/A	N/A	Arm, shoulder and neck; bronchial mucosal involvement
de Freitas Ferreira *et al.* [5]	39, M	Simultaneous	1320	N/A	Orofacial embracing the three trigeminal divisions
Saati *et al.* [6]	57, M	Simultaneous	N/A	N/A	Thoraco-dorsal with residual neuralgia
Elsaie *et al.* [7]	68, M 60, F	2 days earlier Simultaneous	N/A N/A	N/A N/A	Loin Chest and neck
Elsaie *et al.* [8]	44, M	Simultaneous	N/A	N/A	Chest and back

*N/A: not available. *Normal values: 1.0-3.6.*

COVID-19. We report three cases of HZ developing 8-10 weeks after COVID-19 recovery, supporting the hypothesis that persistent impaired immunity may be the key mechanism underlying this association.

Case 1 was a 68-year-old woman, who had had symptomatic, swab-confirmed COVID-19 in March 2020, and presented to our department in May with multi-metameric (left scapular and right inguinal) HZ. Laboratory findings showed a mild increase in erythrocyte sedimentation rate (ESR) (28 mm/h; range: 1-20) and lymphopoenia (1,490 lymphocytes/mmc). Immunophenotyping highlighted a reduced CD4+/CD8+ ratio (0.75; range: 1.0-3.6) and a CD3+/CD4-/CD8- population (gamma-delta T lymphocytes), accounting for 10.8% of lymphocytes. The patient was successfully treated with valacyclovir (3 g/day for one week).

Case 2 was a 44-year-old woman who was examined in March 2020 by her general practitioner for fever (<37.8°C), headache, arthralgia, weakness and mild hypogeusia for sweet taste. Laboratory tests revealed lymphopoenia (lymphocytes: 10%, 1,700 lymphocytes/mmc) and elevated ESR. Swab positivity, negative chest CT and 98% oxygen saturation led to the decision of home-treatment with paracetamol only. Complete remission of symptoms occurred four weeks later. Notwithstading the negative pharyngeal swab, ESR elevation persisted, lymphocytes ranged from 13 to 15%, and a significantly reduced CD4+/CD8+ ratio was detected (0.60). Eight weeks after the diagnosis of COVID-19, the patient developed classic intercostal HZ and was successfully treated with valacyclovir at 3 g/day. Anti-VZV IgG and IgM were positive, while an additional pharyngeal swab for SARS-CoV-2 was negative.

Case 3 was a 64-year-old woman who presented to our department in June 2020 because of thoraco-abdominal HZ. Laboratory tests revealed lymphopoenia (lymphocytes: 11%, 1,800 lymphocytes/mmc), and increased ESR and C-reactive protein levels. Furthermore, a slight increase in CD4+ lymphocytes and a marked increase in CD8+ lymphocytes, resulting in a decrease in CD4+/CD8+ ratio, was observed (0.63). The percentage of CD3+ lymphocytes was within normal range. The patient reported a diagnosis of pharyngeal swab-confirmed COVID-19 back in March 2020. At that time, she had developed fever, headache, pharyngitis, dry cough, weakness and arthralgia. Chest CT scan was negative and oxygen saturation was 98%. Hence, the patient was treated only with paracetamol, with complete remission of symptoms and a negative swab five weeks later.

HZ has been rarely observed in patients with COVID-19 [2-8], although its occurrence may be underestimated. At the time of writing, a mere 14 cases - including those described in this paper - have been reported (*table 1*). HZ mostly manifested during COVID-19, approximately one to two weeks after the onset of symptoms [2-8]. According to the available literature, HZ was often characterized by a severe clinical picture [2-4], with necrotic and haemorrhagic features in 21% and 7% of cases, respectively. An unexpectedly high proportion of trigeminal involvement was noted (35%) [2, 3, 5], moreover, in many cases (21%) the course of HZ was complicated with neuralgia [2, 5, 6]. This association was speculated to be the result of impaired immunity [7]. In fact, in some reported cases, as well as in our patients, both lymphopoenia (mean lymphocyte count of available cases: 1,068 cells/mmc) and a decrease in CD4+/CD8+ ratio were observed [3, 5, 7]. In our patients, these findings persisted 8-10 weeks after COVID-19 and may have led to VZV reactivation. Physicians should be aware of this association in the weeks following COVID-19 in order to ensure early diagnosis and prompt treatment of HZ.

Moreover, since HZ is a cause of considerable morbidity, especially in elderly or critically ill patients, one may propose VZV vaccination for fragile patients, in order to boost cell-mediated immunity [9]. Theoretically, this may prevent the reactivation of latent VZV infection following COVID-19.

In conclusion, we report three cases of HZ that appeared 8-10 weeks after COVID-19 recovery. Persisting COVID-

19-related lymphopoenia [10] and a significant decrease in CD4+/CD8+ ratio appear to be the most likely predisposing factors underlying this association. ■

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Good syndrome associated with lichen planus: a case report and review

Good syndrome (GS) is an adult-onset immunodeficiency syndrome, in which thymoma is associated with hypogammaglobulinaemia. It can also be associated with autoimmune diseases such as lichen planus (LP), myasthenia gravis or erythroblastopenia.

We report a 65-year-old woman who was diagnosed based on her cutaneous lesions. She had developed haemorrhagic lingual erosions and soft palate purpuric erosions since 2013. Some months later, lesions of LP (confirmed histologically) appeared on her legs, hands, back, and genitalia. Her past medical history included idiopathic erythroblastopenia associated with anaemia since 2008. She was initially treated with corticosteroids (1 mg/kg) for three months, then by cyclosporine for two years, which had to be discontinued because of kidney dysfunction. Finally, she received multiple blood transfusions with no significant improvement. Physical examination revealed multiple haemorrhagic erosions of the tongue (*figure 1A*), associated with genital erosions (*figure 1B*) and lesions of LP on the legs, hands (*figure 1C*), and back. Laboratory workup showed anaemia (8.3 g/dL), thrombocytopenia (7,000/mm^3), and leukopenia (4,750/mm^3). She had IgA, IgG, and IgM deficiency. Lymphocyte immunophenotyping showed T-cell lymphopenia CD4 (20%). Bone marrow examination also showed significant erythroblastopenia without megakaryocytes.

Serological tests were negative for hepatitis B, hepatitis C, HIV, CMV, and EBV. Computed tomography revealed a voluminous thymoma (*figure 1D*). Surgical thymomectomy was performed, and thymoma was confirmed by histology. The patient was treated with local and systemic steroids (1 mg/kg). Her LP lesions improved significantly, but the oral and genital erosions persisted. The patient died two years later from digestive bleeding because of severe thrombocytopenia.

GS is a rare syndrome characterized by B- and T-cell immunodeficiency associated with hypogammaglobulinaemia and thymoma [1]. This syndrome has been associated with LP, most commonly oral erosive LP [2]. Reportedly, oral LP (OLP) is present in 12.4% of patients with GS [3].

OLP is a chronic inflammatory disease characterized by reticular white lesions with mucosal atrophy and erosions. It results from the destruction of basal cells by Langerhans cells, macrophages, and T lymphocytes.

A literature search was performed on Pubmed using the terms "thymoma," "hypogammaglobulinemia," "immunodeficiency," and "Good's syndrome". The search revealed 15 cases of LP in GS patients (*supplementary table 1*). All cases were associated with hypogammaglobulinaemia, thymoma, and LP with oral involvement, and six patients had extra-OLP. In addition to LP, other autoimmune diseases were observed, including myasthenia gravis, vitiligo, alopecia areata, Addison's disease, and erythroblastopenia (our patient). In 10 of the previously reported cases, LP presented before thymoma, and in six patients it improved or resolved after thymomectomy, in addition to local and systemic steroids in the case of our patient. IV immunoglobulins were given to some patients, but proved less efficacious than thymomectomy. Thirteen of the 16 cases were associated with an erosive LP. LP seems to be more frequent in the setting of GS than in the general population. The majority of cases presented with erosive OLP, suggesting that this association is not fortuitous [4].

The pathogenesis of GS in the oral mucosa remains unknown. Maehara *et al*. investigated the expression of infiltrating lymphocytes, T-helper cells, cytokines, and interleukins in buccal mucosa specimens from GS patients compared with OLP patients, and suggested that the pathogenesis of the two conditions is different [5]. Genetic factors, stress, trauma, and infection can be predisposing factors for OLP. Epithelial barrier dysfunction may precede infection of basal epithelial cells by bacteria, viruses or possibly fungi, as suggested by the histopathological involvement of T cells in OLP [6].

Our patient represents another case of GS associated with OLP, but the relationship between the two conditions is still unclear. Cytokines and infectious agents could be involved;