rose to 13 g/dl, reticulocyte index fell to 1.3% and complement and lactate dehydrogenase levels returned to normal. After six infusions of ofatumumab, complete B cell depletion associated with remission of both AIHA and SLE (SLEDAI = 0) was documented. The patient was gradually taken off steroids and remains on HCQ 400 mg/day.

To our knowledge this is the first case of SLE-associated AIHA refractory to multiple immunosuppressive agents (CYC, rituximab, ciclosporin, IVIG, AZA, MMF) and procedures (splenectomy) that responded to ofatumumab. Thus far the only case report concerning the use of ofatumumab in SLE appeared just recently by Thornton CC *et al*. [6] regarding a patient with persistent systemic (fever, arthritis, rash, weight loss) and serological (hypocomplementaemia and elevated anti-dsDNA titres) activity refractory to multiple immunosuppressive agents (including CYC, MTX, ciclosporin, belimumab and IVIG) and intolerant to rituximab.

Compared with rituximab, ofatumumab binds with higher affinity to a distinct epitope in the CD20 molecule and results in an enhanced complement-dependent cytotoxicity and thus a more effective B cell depletion. These unique features might explain the response of this case to ofatumumab despite previous failure to rituximab. However more data from case-series and clinical trials are warranted in order to support the use of ofatimumab in refractory cases of SLE. In accordance with the Declaration of Helsinki, written informed consent was obtained from our patient for her case to be published.

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Psoriasis and psoriatic arthritis induced by nivolumab in a patient with advanced lung cancer

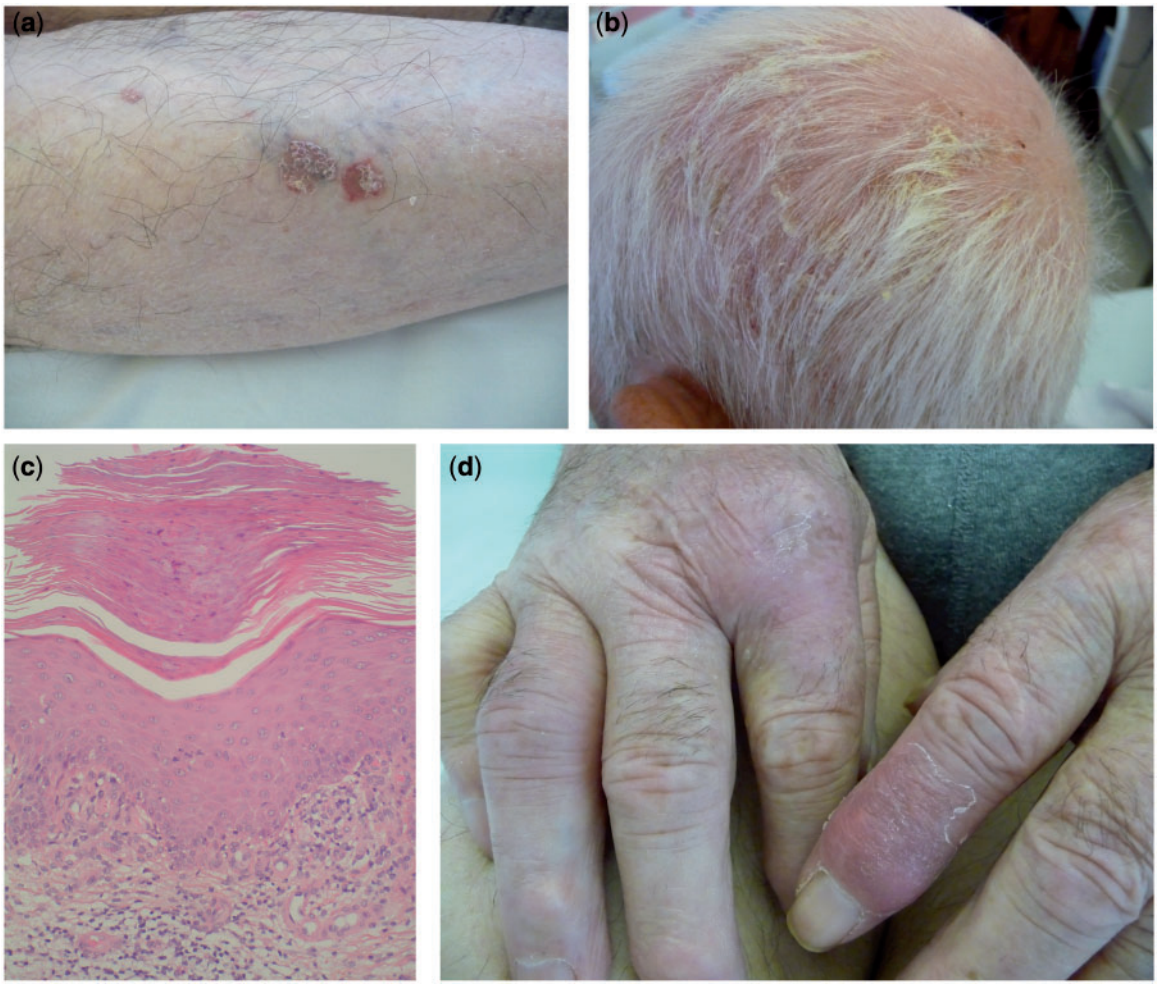
Rheumatology key message

- Nivolumab-induced psoriasis may correlate with nivolumab anti-tumour activity.

SIR, The programmed death 1 protein (PD-1) is an immune checkpoint receptor expressed by activated T cells. PD-1 binds to its ligands PD-L1 and PD-L2, which are expressed on tumour cells, thereby causing immunosuppression and preventing the immune system from rejecting the tumour [1]. mAbs targeting both PD-1 and PD-L1 have demonstrated significant clinical activity in patients with advanced cancers. Nivolumab is a mAb that targets PD-1 and has been recently approved by the National Institute for Health and Care Excellence for advanced melanoma patients [2]. In addition to the treatment of melanoma, the European Medicines Agency approved nivolumab for the treatment of advanced non-small cell lung cancer after prior chemotherapy [3]. Here, we present a patient with no personal or family history of psoriasis who developed psoriatic skin lesions associated with peripheral inflammatory arthritis during nivolumab therapy for metastatic lung cancer. The occurrence of nivolumab-induced psoriasis temporally coincided with regression of the lung cancer lesions.

An 80-year-old man was referred to our hospital for treatment of stage IV (T4, N3, M1) squamous non–small cell lung cancer. The patient had no personal or family history of psoriasis. Initial CT revealed a left upper lobe mass with a left lower lobe nodule. A PET/CT scan also revealed cervical, mediastinal and retroperitoneal lymphadenopathy. A bronchoscopic lung biopsy revealed squamous cell carcinoma, and the molecular studies were all negative, including *BRAF, EGFR, KRAS* and *PIK3CA* mutations, *ALK* rearrangement and *FGFR1* amplification. The

FIG. 1 Psoriasis and PsA in a patient with advanced lung cancer treated with nivolumab



(**A**) Psoriatic skin lesions on the leg and (**B**) the scalp. (**C**) Skin biopsy of a lesion showing typical psoriasiform epidermal hyperplasia with parakeratotic hyperkeratosis, acanthosis, dilated superficial dermal capillaries and a moderate lymphocytic infiltrate in the upper dermis (haematoxylin and eosin stain; ×200). (**D**) Painful swelling of the left index DIP joint and right index MCP joint.

patient began first-line carboplatin/paclitaxel combination therapy. After six cycles of chemotherapy, the lung lesions progressed, and the patient underwent second-line treatment with nivolumab alone (3 mg/kg every 2 weeks). After the eighth infusion, erythaematous and scaly skin lesions appeared on both legs (Fig. 1A) and the scalp (Fig. 1B). Psoriasis vulgaris was clinically diagnosed and confirmed via a skin biopsy (Fig. 1C). The skin lesions were simultaneously accompanied by swelling and tenderness of the left index DIP joint and right index MCP joint as well as by pain and joint stiffness in both knees (Fig. 1D). Radiographic evaluation revealed no evidence of established erosive disease. Serum antibody tests for RF, anti-CCP and ANA were negative, and the serum urate level was normal. The patient fulfilled the Classification of Psoriatic Arthritis (CASPAR) criteria and was diagnosed with PsA. A restaging scan was performed and revealed a marked regression of the left upper lobe mass and mediastinal lymphadenopathy, with a dramatic clinical improvement (weight gain and improved performance status). Nivolumab was discontinued for 4 weeks. Therapy with oral MTX at a dose of 10 mg/week in combination with a low dose of oral prednisone (15 mg/day) and topical corticosteroids was introduced. After 1 month of therapy, both psoriatic skin lesions and joint symptoms gradually resolved, allowing gradual tapering of MTX and prednisone. Thereafter, nivolumab was restarted with continued response and without recurrence of the psoriasis.

Accumulating evidence suggests that IL-17, the principal effector cytokine of Th17 cells, plays a key role in the pathogenesis of both psoriasis and PsA and therefore has provided the rationale for development of IL-17 inhibitors as therapeutic agents in these autoimmune diseases [4]. PD-1 and its ligands are key regulators of T cell activation and play crucial roles in the regulation of autoimmunity, infectious immunity and tumour immunity [5]. Previous

studies have demonstrated that the blockade of the immune checkpoint receptors, such as PD-1, by its antibodies augmented the Th1 and Th17 responses in patients with advanced cancer, resulting in an increased production of IFNγ, TNF-α, IL-2, IL-6 and IL-17. In addition, these effects are associated with improved patient survival [6]. Consistent with these observations, growing evidence is emerging that Th17 cells harbour anti-tumour activity, suggesting that PD-1 blockade may promote anti-tumour activity through stimulation of Th17 cells [6].

In our patient, we hypothesize that nivolumab-induced Th17 upregulation resulted in the overproduction of pro-inflammatory cytokines, which may have contributed to the onset of the psoriasis and PsA. In addition, the occurrence of the psoriatic skin lesions as well as joint symptoms temporally coincided with the regression of lung cancer lesions, suggesting that the induction of psoriasis may correlate with the anti-tumour activity of nivolumab. Interestingly, a recent study has demonstrated that PD-1 expression levels are inversely correlated with the DAS28 in patients with PsA [7]. These findings suggest that the PsA in our patient might have been exacerbated by inhibition of the PD-1 pathway induced by nivolumab.

A case of *de novo* psoriasiform eruption during anti–PD-1 therapy has recently been reported [8]. In this case, an 80-year-old man with unresectable melanoma of the oral cavity received nivolumab therapy. The patient had no personal or family history of psoriasis, and the occurrence of the patient's psoriasiform eruption after the fourth dose of nivolumab coincided with a regression of the melanoma lesions.

PD-1 inhibitors are generally well tolerated. The most frequent cutaneous adverse events reported include maculopapular rash, pruritus and vitiligo-like depigmentation [1]. Further studies are needed to clarify the relationship between the induction of psoriasis and the anti-tumour activity of PD-1 inhibitors.

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Successful outcome using bortezomib in adult refractory IgA vasculitis: a case report

Rheumatology key message

- Proteasome inhibition is a potential treatment for IgA vasculitis and other autoimmune diseases.

Sir, Proteasome inhibition is a potential treatment for autoantibody-associated autoimmunity. We describe a patient with adult refractory IgA vasculitis (IgAV/Henoch–Schönlein purpura), successfully treated with the proteasome inhibitor bortezomib.

A 49-year-old Caucasian female was diagnosed with progressive IgA vasculitis, comprising renal insufficiency (creatinine 130 μmol/l), polyarthritis, painful lower leg vasculitic rash (Fig. 1A), gastrointestinal symptoms and fatigue, causing severe morbidity and incapacity. The IgA level at diagnosis was 2 g/l. Renal histology showed a mesangial proliferative glomerulonephritis, without crescents or endocapillary proliferation (Fig. 1B). There was dominant IgA deposition in the mesangium (Fig. 1C). She was resistant to or intolerant of a variety of therapeutic options, including oral and intravenous corticosteroids, high dose intravenous immunoglobulin, alemtuzumab, rituximab (three doses of 1 g in