A case of severe pityriasis rubra pilaris with a dramatic response to apremilast

Pityriasis rubra pilaris (PRP) is characterized by hyperkeratotic follicular papules and widespread erythema with areas of spared skin, which may evolve towards erythroderma with palmoplantar keratoderma. Whereas the disease may spontaneously heal, many patients experience long periods during which the condition is disabling. Treatments used for psoriasis are given with variable results. Apremilast, a phosphodiesterase 4 (PDE4) inhibitor, which increases cyclic adenosine monophosphate levels leading to suppression of tumour necrosis factor (TNF) alpha production [1], has recently been available for moderate-to-severe psoriasis. We report a case of refractory PRP successfully treated with apremilast.

A 47-year-old, overweight man presented with a one-month history of PRP, without arthritis (figure 1A, B, E). He first received ointments, then acitretin at 25 mg/day, with progressive rise to 40 mg, associated with UVB. Seven months later, the disease was not controlled, and erythema spread with severe palmoplantar keratoderma and dystrophy of all 20 nails (figure 1A, B). As a second line, methotrexate was excluded due to the possibility of liver toxicity in overweight men, and in November 2016, oral apremilast was started at a dose of 10 mg/day and was raised over five days to the recommended maintenance dose of 30 mg, twice daily. One month later, there was a significant improvement in erythema with a dramatic response regarding keratoderma and nails. Complete healing was obtained after two months, and in June 2017, seven months later, while still under apremilast 30 mg twice daily, complete remission was maintained (figure 1C, D). Treatment was well tolerated without side effects.

PRP is rare, no large trials have been performed, and treatments are empirical, in contrast to psoriasis [2, 3]. In a recent series of 50 patients with PRP, 64% received retinoids, 42% methotrexate, and 20% TNF blockers, resulting in a favourable outcome in 59%, 52%, and 40%, respectively [4].

Phosphodiesterases are enzymes that hydrolyse and degrade cyclic adenosine monophosphate (cAMP), leading to an increase in cellular synthesis. One of these, PDE4, regulates immune and inflammatory processes through the control of intracellular cAMP levels, protein kinase A pathways, and TNF production. This mechanism accounts for the therapeutic effect by inhibitors of PDE4, such as apremilast, on psoriasis and, in theory, other skin inflammatory diseases. The orally available form of apremilast has a few, transient, mild-to-moderate side effects, mainly gastrointestinal symptoms and headaches [5]. No biological toxicity has been reported to date. Our patient dramatically responded to apremilast with maintenance of response over a long period. In PRP, spontaneous periods of remission may occur. However, in our case, disease improvement started within a few days after apremilast introduction, despite a worsening of disease over six months previously using different treatments.

Only one case of remission of PRP under apremilast has been previously reported [6], this was a 70-year-old man with PRP resistant to acitretin, methotrexate, cyclosporine, and infliximab. As in our patient, PRP healing started four weeks after apremilast was initiated and complete remission was obtained after eight months. In this case and in ours, the rapid improvement after treatment introduction strongly argues in favour of a therapeutic role for apremilast. Clearly, no consensus presently exists regarding the duration of apremilast intake. In our case, we decided to continue apremilast treatment for six additional months, mainly because the patient feared the occurrence of a relapse.

Based on our case and the previously reported case, it is not possible to draw any definitive conclusions concerning the use of apremilast for PRP, and a prospective controlled trial is mandatory. Moreover, there is no reliable efficient treatment for PRP, and some treatments, such as methotrexate, may lead to severe toxicity, while others, as TNF blockers, are very expensive, and none are legally authorized as a treatment for PRP. Based on these two clinical cases, the observations suggest that oral apremilast, which does not require pre or per treatment investigations and is associated with few contraindications and low toxicity, should be considered as an option for PRP treatment.

Third-line pembrolizumab-induced immune-related interstitial pneumonitis after ipilimumab and nivolumab failure

Pembrolizumab is a humanized monoclonal antibody that blocks programmed cell death 1 (PD-1) and results in continuous T-cell activation [1]. However, this T-cell activation is not tumor-specific and causes immune-related adverse events (irAEs) [2]. Here, we report a patient who developed autoimmune interstitial pneumonitis (IP) induced by pembrolizumab as the third-line treatment after nivolumab and ipilimumab failure.

A 44-year-old man was admitted to our hospital because of progressive dyspnoea and a dry cough, three weeks after receiving his first dose of pembrolizumab. Three years previously, he was diagnosed with metastatic malignant melanoma in the retroperitoneal cavity, and nivolumab was initiated. Although he achieved a partial response with only minor irAEs, the tumour became resistant to pembrolizumab. Ten days after the second pembrolizumab administration, the treatment had to be stopped because the patient developed Grade 3 irAEs (hepatitis and colitis), for which he was given 1 mg/kg prednisolone. Three months later, after complete termination of the prednisolone treatment, pembrolizumab was started. Although the patient had no serious adverse events during the 28 months of nivolumab treat-