

Efficacy and safety of apremilast in a patient with paraneoplastic dermatomyositis with resistant skin disease

Sirs,
management of cancer-associated dermatomyositis represents a challenge since immunosuppressive agents are often contraindicated in association with chemotherapy for the elevated risk of superimposed infections because of neutropenia or for pharmacological interactions (1, 2).

Apremilast is an oral inhibitor of the phosphodiesterase-4 enzyme (PDE4) currently licensed for psoriasis, psoriatic arthritis, and Behçet's disease aphthosis (3). It works intracellularly to modulate a network of pro-inflammatory and anti-inflammatory mediators by increasing cyclic adenosine monophosphate, and it is not associated with the risk of neutropenia (4).

We report a case of a 79-year-old man suffering from a chronic obstructive pulmonary disease (COPD) and with a history of psoriasis, who was admitted to our Hospital on February 2021 with a progressive worsening of dyspnoea and cough without fever and a recent onset of violaceous skin rash over the extensors, scalp, and chest, and proximal muscle weakness. Laboratory investigations showed a marked elevation of serum creatine kinase (CK) (4126 IU/l, reference range 70-170 IU/l) and the presence of anti-TIF1- γ antibodies.

Muscle biopsy was consistent with an immune-mediated myositis, characterised by CD8+ lymphocyte infiltration and paucity of CD20+ B lymphocytes (Fig. 1 A-D).

The diagnosis of dermatomyositis was made and prednisone was started at the dose of 1 mg/kg/day with rapid normalisation of CK

levels, and improvement of the skin lesions. During the diagnostic work-up, a diagnosis of a poorly-differentiated non-small cell lung cancer (NSCLC), stage cT4-N0-M1a was made, and the patient started Carboplatin and Pemetrexed with a progressive tapering of prednisone.

On December 2021, corticosteroids 0.5 mg/kg/day together with second-line therapy with Gemcitabine 1200 mg/mq for cancer were instituted due to both progression of cancer, and relapse of dermatomyositis skin manifestations.

After one month, skin lesions were persisting with a progressive worsening of generalised pruritus and new onset of finger ulcerations [cutaneous dermatomyositis activity and severity index (CDASI): 42] (2). After the admission to our division, treatment with 1 mg/kg/day of intravenous methylprednisolone combined with high doses of intravenous immunoglobulins (0.4 mg/kg/day for 5 consecutive days) was started, however, with a scarce response on skin disease.

Thus, given that most of the immunosuppressants are contraindicated in the course of chemotherapy, apremilast 30 mg twice daily was introduced while continuing chemotherapy, based on the already published experiences of apremilast in idiopathic, non-cancer related dermatomyositis (5-9).

Starting from 2 months, skin disease significantly improved (CDASI 16 at month +3) and prednisone was tapered to 5 mg/day without relapse (Fig. 1 E-F). Complete recovery from pruritus and finger ulcers was also recorded. Despite the ongoing chemotherapy, the older age, and the comorbidity predisposing to infections (COPD), apremilast was well-tolerated and no infection or adverse events were documented.

This is the first case of cancer-related der-

matomyositis successfully treated with apremilast for severe skin manifestations. Safety was maintained even during the ongoing chemotherapy for cancer. Overall, this report supports the efficacy and safety of apremilast in patients with severe or refractory skin disease in the course of dermatomyositis, as very recently supported even by a controlled study (9). The efficacy of apremilast in dermatomyositis skin lesions may be explained by the local depletion of myeloid dendritic cells, which are highly activated in dermatomyositis skin disease (10), rather than by a systemic effect (6). The efficacy of apremilast in our case that showed the prominence of CD8+ lymphocytes in the affected tissue, is consistent with the possible pivotal role of innate rather than humoral immunity in skin disease associated with cancer-related myositis.

Ethics approval

The patient gave his consent for the images or other clinical information relating to his case.

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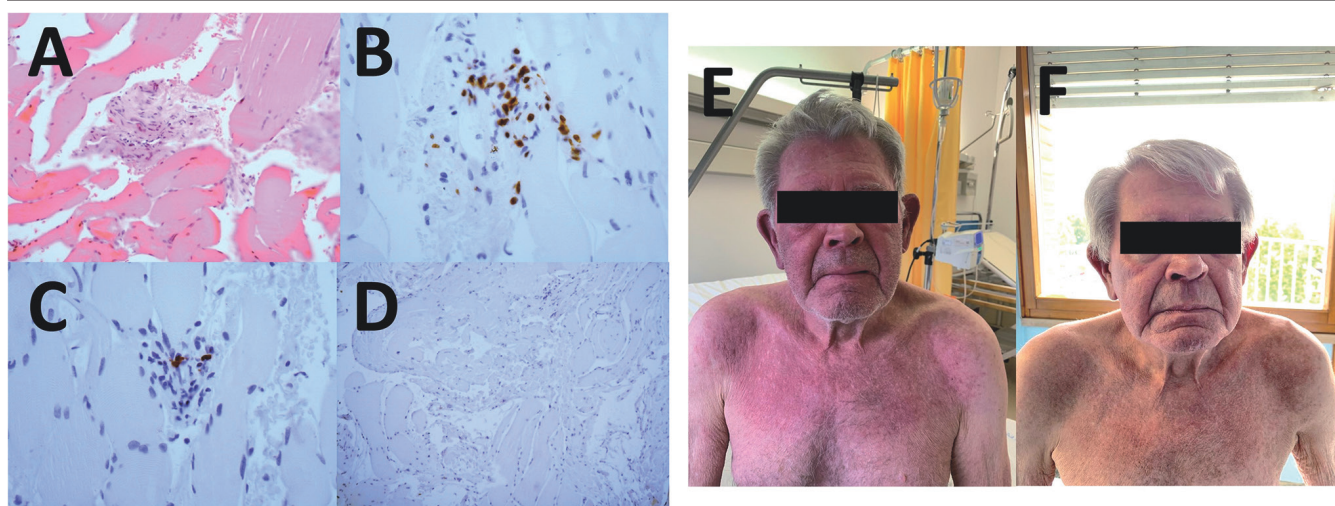


Fig. 1. Histopathological diagnosis.

Panel A shows haematoxylin and eosin-stained muscle-biopsy samples from the right biceps. Arrow indicates the perimysial localisation of lymphocytes.

Lymphocyte infiltrates were confirmed by CD3 immunohistochemistry (**Panel B**) with a prevalence of CD8+ cells (**Panel C**). **Panel D** demonstrates the absence of CD20+ cells. Clinical course: **Panel E** shows the patient before apremilast with a violaceous skin rash on his chest and face; **Panel F** shows the improvement after three months of treatment with apremilast.

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