Anti-TIF1-γ antibody-positive dermatomyositis caused by camrelizumab in a patient with oesophageal cancer

Sirs,

Dermatomyositis could be idiopathic, paraneoplastic or caused by certain drugs. Although 15% to 30% of adult-onset dermatomyositis occur as a paraneoplastic (1), there are also some reports of dermatomyositis caused by ICIs, such as pembrolizumab (2), durvalumab (3) and nivolumab (4). Herein, we report a case of a 59-year-old patient who presented a dermatomyositis after seven courses administration of camrelizumab which is an IgG4 monoclonal PD-1 antibody.

In June 2016, a 59-year-old man was diagnosed as middle thoracic oesophageal squamous (T1aN0M0 stage IA) and treated with radical surgery. The chest enhanced compute tomography scan revealed a vertebral body metastasis in May 2020. Because the side effects of first-line chemotherapy were intolerable, he was treated with camrelizumab 200 mg every 2 weeks as the second line therapy, and radiation (30Gy/10F/3Gy) was applied to the bone lesion. After seven doses of camrelizumab, the patient went to our hospital with a swollen face, erythema papules in the cheeks, hands, bilateral hip and both lower extremities, scattered in scales, with pruritus, and was diagnosed as immune-related dermatitis grade G3. The administration of camrelizumab was cut off immediately. After treated with methylprednisolone 40 mg/d for five days, the patient got better and discharged from hospital. However, four months later, the patient went to our centre again for recrudescence of dermatitis and newly developed symptoms of symmetrical weakness in the proximal muscles. Methylprednisolone was useless this time, intravenous immunoglobulin (IVIG) 12.5 g and cyclophosphamide 0.8 g was applied to suppress immune function. From then on, the patient went to our hospital bimonthly for irAEs administration, and treated with methylprednisolone, IVIG and cyclophosphamide every time. In January 2022, the patient's symptom got worser, hence he was moved to the rheumatology department. Physical examination revealed drinking face, heliotrope eruption, V-shape sign, shawl sign, Gottron's sign; scaly erythematous eruption and depigmentation spot scattered on all over the body (Fig. 1A). Laboratory test results revealed an elevated fibrinogen, erythrocyte sedimentation rate and C-reactive protein. Antinuclear antibody, anti-transcriptional intermediary factor-1γ (anti-TIF1-γ) antibody and anti-endothelial cell antibody test were all positive. Histopathology of a skin biopsy found a perivascular infiltrate composed of lymphocytes, scattered neutrophils and eosinophils (Fig. 1B). A magnetic resonance imaging scan of the upper arm demonstrated abnormally high intensity areas in muscle consistent with inflammatory changes (Fig. 1C). Based on these clinical manifestations and findings, the diagnosis of dermatomyositis was apparent. Subsequently, the patient was treated with intravenous methylprednisolone 40 mg/d for one week associated with 10 mg of methotrexate per week, then intravenous methylprednisolone was discharged on oral prednisone. After half a mouth, the patient's cutaneous eruption and facial swelling improved and sore limbs were relieved.

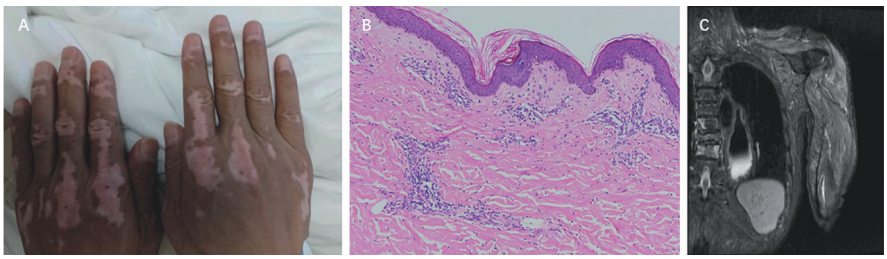

Fig 1. Clinical features of the patient. (**A**) Depigmentation spot on bilateral metacarpophalangeal and interphalangeal joints after recover from Gottron's sign. (**B**) Histological features of skin biopsy, perivascular infiltrates with lymphocytes, scattered neutrophils and eosinophils. (**C**) A magnetic resonance imaging scan of the upper arm showed abnormally high signal intensity in muscles in T2 images.

The rash right after the administration of camrelizumab, the serological transformation of anti-TIF1-γ antibody, and concurrent elevated multiple pituitary hormones levels supported it was triggered by camrelizumab rather than tumour.

On account of T cell activation, triggered by ICIs, increased the interactions between follicular CD4+T cells and B cells (including plasma cells) in germinal centres increased (5). Activation of plasma cells can result in autoantibody production, which could explain the transformation of a series of autoantibodies. It has been reported that anti-TIF1 antibodies are generated during an antitumour immune response (6), which supports our hypothesis.

To the best of our knowledge, this is the first report of dermatomyositis caused by camrelizumab in a patient with oesophageal squamous cell carcinoma. Due to the refinement of clinical subspecialty, oncologists lack the sensitivity to rheumatic diseases resulting the delayed diagnosis of this patient. Therefore, Multi-disciplinary Team could be applied to the management of rare irAE for early diagnosis and treatment to improve the patient's quality of life.

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Competing interests: none declared.

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