Rapidly progressive lung disease in a patient with signs of clinically amyopathic dermatomyositis

Sirs,

A 25-year-old, previously healthy, Caucasian female patient, presented at our outpatient clinic with painful oral ulcers, arthralgias of the small hand joints and skin lesions on both hands of two weeks' duration. Physical examination revealed an afebrile patient with hyperkeratotic papules, fissured skin of the fingertips and palms (Fig. 1A), erosive ulcers of the buccal mucosa and hard palate, and marginal erythematous gingivitis (Fig. 1B). Symmetric arthritis of the proximal interphalangeal joints was noted and rales of the right lower lobe were audible upon auscultation. Muscle strength was normal and the rest of physical examination unremarkable.

Positive laboratory tests revealed anemia (Hb:11.4mg/dL), a mild elevation of liver enzymes (AST:58U/L, normal range (n.r.):10-40U/L and ALT:66 U/L, n.r:7-56U/l) and lactate dehydrogenase (387U/L, n.r:140-280U/L), elevated creatine phosphokinase (634U/L, n.r:22-198U/L) and hypergammaglobulinemia (γ-globulins:19.7%). Acute phase reactants (CRP/ESR/serum ferritin), serologic testing for hepatitis B/C, HIV, rheumatoid factor, anti-cyclic-citrullinated peptides, antinuclear antibodies, extractable nuclear antigen antibodies, anti-neutrophil cytoplasmic antibodies and serum complement levels were all negative or within normal limits. The myositis-specific autoantibodies panel, including anti-melanoma-differentiation-associated-gene-5 (MDA-5), was negative. Chest high resolution computed tomography (HRCT) illustrated sub-pleural ground-glass opacities in the right posterior lower lobe (Fig. 1C). With the probable diagnosis of clinically amyopathic dermatomyositis (CADM),-on the basis of oral ulcers (1), mechanic's hands (2, 3) and pulmonary involvement (4, 5) in the absence of clinical muscle weakness-, the patient was initiated on oral methylprednisolone (0.5 mg/kg/day) and methotrexate (0.3 mg/kg/week). Within the first two weeks of treatment remarkable improvement of oral ulcers, arthritis and palmar skin rash was noted, while muscle enzymes were normalized. Four weeks later, and while on the same therapeutic regimen, the patient presented with spiking high fevers (39°C), shortness of breath, tachypnea (22/min), tachycardia (ECG:sinus rhythm, 102 pulses/min) and hypoxia (arterial blood gases on air: pO_2:79 mmHg, pCO_2:36mmHg, pH:7.45, HCO_3:26 mmol/L, oxygen saturation: 87%). Anaemia (Hb:9.9g/dL) was deteriorated, thrombocytosis (507K/mm^3) and increased acute phase reactants (ESR:60 mm/1h, CRP:25.4 mg/L, n.r<5 mg/L) were noted. Pulmonary function tests were indicative of a restrictive pattern and impaired gas exchange (TLC:58%, FVC:55%, DLCO:50% of predicted). A new chest HRCT revealed deterioration of the lung parenchymal pathology with extensive ground-glass opacities in the middle and lower lung zones bilaterally, peripheral consolidation in the right lung base and peribronchial and alveolar consolidations in the lower left lung, in the absence of honeycombing (Fig. 1D). Bronchoalveolar lavage or a diagnostic lung biopsy was not feasible due to the patient's critical condition. Thus, after excluding underlying infection with multiple cultures and based on the HRCT findings which suggested bronchiolitis obliterans with organising pneumonia (BOOP), a methylprednisolone pulse (1g/day) was administered. Subsequently, oral methylprednisolone was increased to 1mg/kg/day, oral cyclosporine-A (150 mg/day) was added and intravenous immunoglobulin (IVIg) (0.4 g/kg/day) was given for five consecutive days. On this combination treatment hypoxia, tachycardia and shortness of breath improved drastically. Steroid dose was slowly tapered, while IVIg administration, methotrexate and cyclosporine-A continued. Four months later, the patient (methylprednisolone dose 20 mg/day, while rest of therapeutic regi-

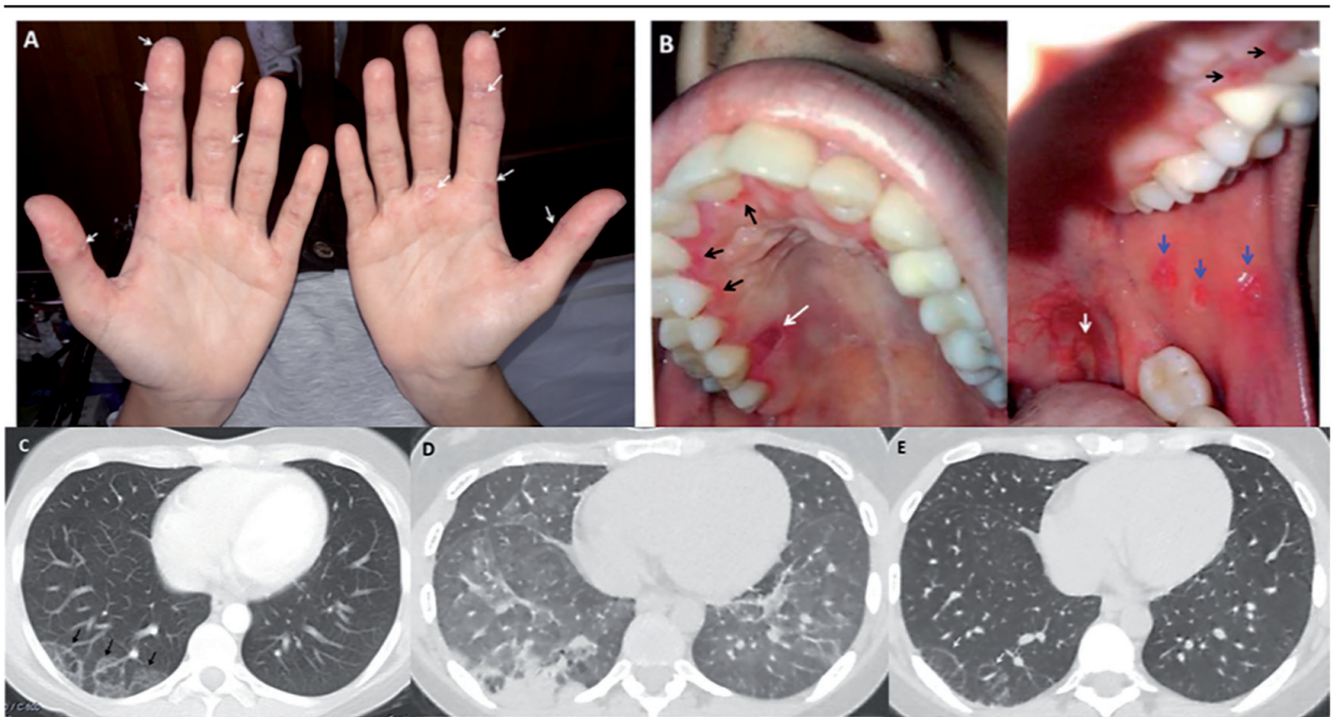

Fig. 1. **(A)** Palmar skin at presentation: hyperkeratotic eruptions with desquamation and rhagades mainly on the tips and sides of the fingers (arrows). Oedematous proximal interphalangeal joints (2nd, 3rd) due to arthritis can be noted on both hands. **(B)** Painful oral ulcers of the buccal mucosa and the hard palate (deep ulcers: white arrows, superficial ulcers: blue arrows) and marginal erythematous gingivitis (black arrows). **(C)** Chest high resolution CT (lung windows, level of lung bases) at presentation: ground glass opacities are noted peripherally in the right lung base (arrows) with associated interstitial thickening. **(D)** Chest high resolution CT with symptoms of fever, rapidly progressing shortness of breath, tachypnea, tachycardia and hypoxia. Extensive bilateral ground glass opacities are noted in the mid and lower lung zones. Peripheral consolidation in the right lung base and peribronchial consolidation in the left lower lung lobe are seen, without traction bronchiectasis or interlobular septal thickening. **(E)** Chest high resolution CT four months after initiation of combination immunosuppressive therapy. Complete regression of the ground glass opacities and consolidations is evident. There remains interstitial thickening and fibrotic changes peripherally in the right lung base.

men remained the same) was clinically well, laboratory tests were unremarkable and a new chest HRCT revealed regression of the ground glass opacities and consolidations with remaining limited interstitial thickening and fibrotic changes peripherally in the right lung base (Fig. 1E). Taking into account the patient's improvement, cyclosporine-A was discontinued.

The case of this young, otherwise healthy, woman is reported a) for its insidious presenting clinical features and the very infrequent initial manifestation of oral ulcers b) for the development of early and severe lung involvement despite treatment and in the absence of anti-MDA-5-positivity, present only in 0–13% Caucasian adult patients and more frequent (10–48%) in Asian patients with CADM-associated rapidly progressive interstitial lung disease (6-8) and c) to stress the importance of timely introduction of combination immunosuppressive treatment.

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