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Case report

A case of anti-melanoma differentiation-associated gene 5 antibody-positive interstitial lung disease complicated with tracheobronchial ulcers

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ABSTRACT

We herein report the first case, to our knowledge, of tracheobronchial ulcer with anti-melanoma differentiation-associated gene 5 (anti-MDA 5) antibody-positive interstitial lung disease (ILD). A 53-year-old man complained of shoulder and wrist pain and was suspected of having polymyalgia rheumatica at another hospital. Thereafter, treatment with prednisolone was started. Although his arthralgia improved, he suffered from progressive dyspnea on exertion and an abnormal shadow was noted on chest X-ray, so he was transferred to our hospital. Chest computed tomography scan revealed ground-glass opacities and intralobular septal thickening. We diagnosed him as having clinically amyopathic dermatomyositis associated with ILD based on the specific skin findings and elevated anti-MDA 5 antibody titer. Fiberoptic bronchoscopy showed ulcerations of the trachea and bronchus. Treatment with dose increments of prednisolone combined with other immunosuppressive drugs resulted in improvement of his respiratory condition and tracheobronchial lesions. Clinicians should be aware that tracheobronchial ulcers can be associated with anti-MDA 5 antibody-positive interstitial lung disease.

1. Introduction

The trachea and bronchus are affected by a number of primary disorders in adults and are also targets of a variety of systemic diseases [1]. In contrast, anti-melanoma differentiation-associated gene 5 (anti-MDA 5) antibody is specifically detected in patients with dermatomyositis (DM) and is known to be strongly associated with rapidly progressive interstitial lung disease (ILD) [2]. To our knowledge, the complication of tracheal and bronchus ulcers with anti-MDA 5 antibody-positive ILD has not been reported previously. We herein report the case of a patient with anti-MDA 5 antibody-positive ILD and tracheobronchial ulcers whose ILD and tracheobronchial lesions subsequently improved following anti-inflammatory therapy.

2. Case presentation

A 53-year-old non-smoking man complained of shoulder and wrist pain for 1 month and was suspected of having polymyalgia rheumatica at another hospital. Thereafter, treatment with prednisolone at 15 mg/day was started. One month after treatment at this prednisolone dosage, his arthralgia improved. However, he suffered from dyspnea on exertion and an abnormal shadow was noted on chest X-ray, and he was transferred to our hospital. His vital signs on admission were temperature 36.1 °C, blood pressure 97/64 mmHg, pulse 75 bpm with regular rhythm, and oxygen saturation 94% on pulse oximetry. Chest computed tomography (CT) scan revealed bilateral non-septal plate-like opacity, ground-glass opacities, and intralobular septal thickening (Fig. 1A/B). Physical examination revealed erythematous exanthema on discrete areas of the anterior chest (in a V-shaped sign) and posterior aspect of the shoulders (shawl sign) and slight muscle weakness of the neck flexor muscles only. Chest auscultation revealed no abnormal findings, and heart sounds indicated a regular rhythm with no murmur. Elevated levels of C-reactive protein of 0.48 mg/dL, KL-6 of 692 U/mL, and ferritin of 1571 ng/mL were found, but levels of creatine kinase of 74 IU/L and surfactant protein-D of 37.1 ng/mL were normal. Moreover, his rheumatoid factor level was elevated at 76 U/mL, as was his anti-MDA 5 antibody titer at 258 (MESACUP anti-MDA5 ELISA kit; Medical & Biological Laboratories, Nagoya, Japan). Other

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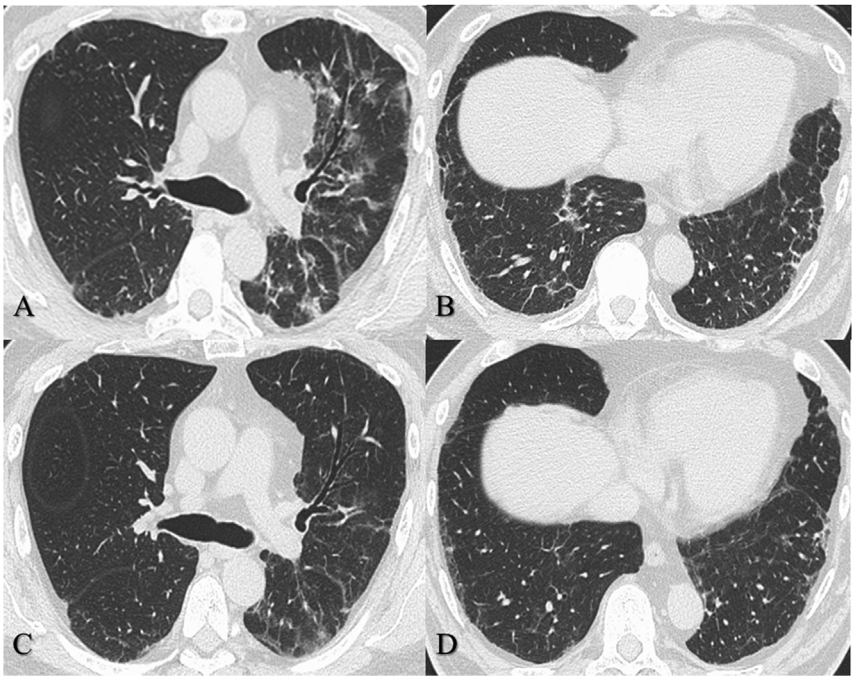

Fig. 1. Radiological course. Chest computed tomographic images showed bilateral peripheral non-septal plate-like opacities, reticulation, intra-lobular septal thickening, and peri-bronchovascular ground-glass opacities at the initial visit (A/B). Afterwards, the lesions had improved at 5 months after starting anti-inflammatory therapy (C/D).

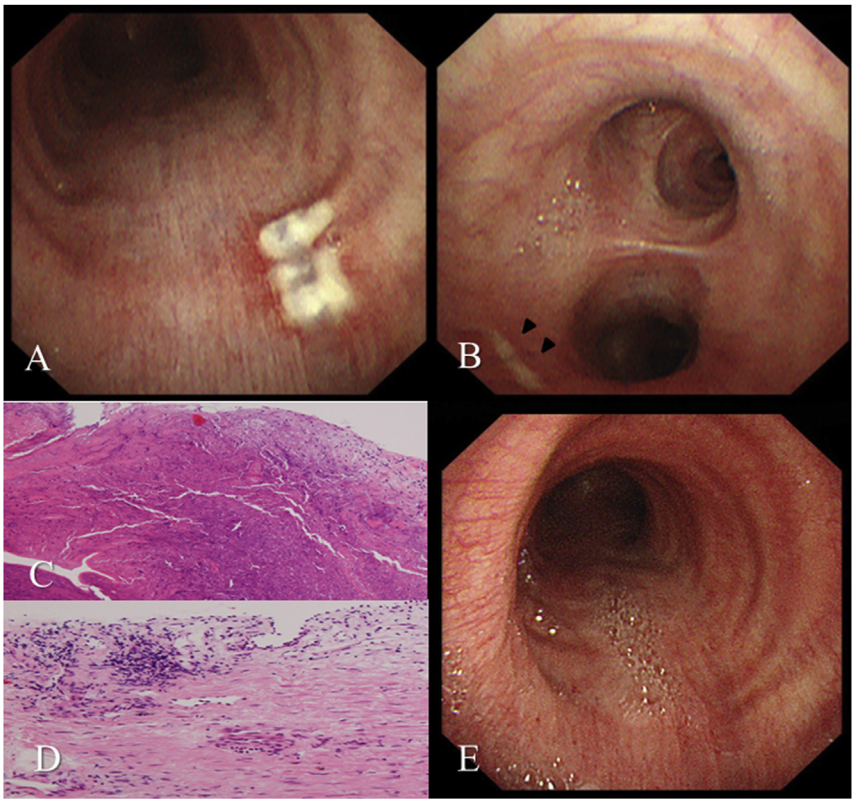

Fig. 2. Fiberoptic bronchoscopy findings showed white plaques on the bronchial mucosa in the trachea (A) and the right main bronchus (arrowhead) (B). Histological findings of plaque from the tracheal ulcer showed necrotizing bronchial inflammation at low-power (C) and high-power magnification (D) (hematoxylin and eosin stain). Bronchoscopy at 6 months after therapy showed disappearance of the tracheobronchial lesions (E).

autoantibodies were negative. Bronchoalveolar lavage (BAL) was performed using sterile saline solution at the left lingula (B5) of the left lung. BAL fluid analysis revealed a marked increase in lymphocytes (54.4%), and other cells included neutrophils (1.8%), eosinophils (1.2%), and macrophages (42.6%). The *Pneumocystis jiroveci* PCR result was negative, and no microorganisms were cultured in the BAL fluid. In addition, multiple lesions of white plaques on the bronchial mucosa were found in the trachea and bilateral main bronchi (Fig. 2A/B). The histopathology of these lesions revealed a necrotizing bronchial inflammation (Fig. 2C/D). We then diagnosed him as having clinically amyopathic dermatomyositis (CADM) associated with ILD [3] that was also complicated with tracheobronchial ulcers. Intensive immunosuppressive therapy, including high-dose corticosteroids (prednisolone at 60 mg/day), calcineurin inhibitor (tacrolimus at 4 mg/day), and intravenous cyclophosphamide (IVCY) pulse therapy at a dose of 500 mg/m^2, was administered. The prednisolone dosage was gradually tapered with the tacrolimus and IVCY repeated in 6 monthly cycles. We confirmed improvement of his respiratory symptoms and

reduction of the disease extent of the ILD (Fig. 1C/D) and bronchial lesions (Fig. 2E) at 6 months after the start of the medical intervention.

3. Discussion

We experienced a case of tracheobronchial ulcerations in a patient with anti-MDA 5 antibody-positive ILD. Anti-MDA 5 antibody is a useful prognostic marker for this disease, which is associated with rapidly progressive ILD, a condition with a high mortality rate [2]. Chest CT findings in our patient revealed peripheral non-septal plate-like opacities and intra-lobular reticular opacities that were compatible findings in patients with anti-MDA 5 antibody-positive ILD [4]. As the initial treatment of ILD patients with anti-MDA 5 antibody, a combination of corticosteroids, cyclophosphamide, and calcineurin inhibitor is recommended [5]. Our patient was also immediately started on these therapies and then recovered in good condition.

Ulcers of the trachea and bronchus are caused by a variety of conditions such as infection, malignancy, vasculitis, and stimulation by foreign matter [1,6]. Among these, only two cases of reported DM were associated with tracheobronchial ulceration [7,8]. From another perspective, it is interesting that presentation with ulcerations of trachea and bronchus in patients with anti-MDA 5 antibody-positive ILD has not been reported previously, other than our case. Patients positive for anti-MDA 5 antibody have characteristics of a high frequency of skin lesion such as skin ulcerations and tender palmar papules because of vascular disorders [9]. In fact, biopsy specimens of skin lesions show a vasculopathy characterized by vascular fibrin deposition with variable perivascular inflammation [9]. Kono et al. reported a case of DM complicated with pneumomediastinum and tracheobronchial ulcerations, which indicated that necrosis of the bronchial wall might be considered as being caused by focal ischemia with vasculopathy that could then cause an air leak resulting in pneumomediastinum [7]. Although we could not perform a biopsy of the skin lesion in our patient, we confirmed the improvement of his multiple tracheobronchial ulcerations following anti-inflammatory therapy. Therefore, we thought that the tracheobronchial ulcerations were associated with the vasculopathy. In addition, because the results of myositis-associated autoantibodies such as anti-aminoacyl-tRNA synthetase antibodies and anti-MDA 5 antibody were unclear in the two previously reported patients, we hypothesized that these patients might also have positive results of anti-MDA 5 antibody as did our patient.

There is one thing to note in our case. Arthritis and arthralgia occur frequently in anti-MDA 5 positive CADM [10]. The arthritis is typically symmetric and affects the small joints of the hands, resembling rheumatoid arthritis (RA). Regarding arthralgia as the initial symptom (i.e., shoulder and wrist pain), we could not deny that our patient was complicated with RA. Because CADM-RA overlapping may make tracheobronchial ulcer, further studies are needed to clarify in the future.

In conclusion, we herein described the first known case, to our knowledge, of tracheobronchial ulcerations in a patient with anti-MDA 5 antibody-positive ILD. Because this disorder is unusual and the prognosis is poor, clinicians might fail to notice tracheobronchial lesions that are present along with the skin and muscle lesions or ILD. Case reports on CADM or DM presenting with tracheobronchial ulceration are rare, and thus, the educational value of the present case is high.

Conflicts of interest

The authors declare no Conflicts of Interest (COI) in association with this article.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.rmcr.2018.08.020.

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