



Case report

Anti-PL-7 antibody-positive dermatomyositis with progressive interstitial pneumonia complicated with tracheal ulcer

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ABSTRACT

Tracheobronchial lesions are rare extramuscular complications for idiopathic inflammatory myopathies including dermatomyositis. We herein report a 65-year-old woman with tracheal ulcer during the progression of dermatomyositis-associated interstitial lung disease. Treatment with corticosteroids combined with immunosuppressive agents resulted in improvement of the tracheal ulcer and pulmonary involvement. We believe that the tracheal ulceration might reflect the disease behaviour of dermatomyositis and dermatomyositis-associated interstitial pneumonia.

1. Background

The idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of diseases in which inflammation of the striated muscles leads to myalgia and weakness. They comprise polymyositis (PM), dermatomyositis (DM), necrotising myopathy, overlap syndrome with myositis including anti-aminoacyl tRNA synthetase (ARS) syndrome, and inclusion body myositis [1,2]. These diseases can affect multiple organs and lead to severe impairment of the quality of life [3]. Although the myositis in most cases responds to immunosuppressive treatments such as corticosteroids, immunosuppressants, intravenous immunoglobulin G, cyclophosphamide, and rituximab, IIMs typically have a limited long-term prognosis due to the development and progression of extramuscular manifestations such as malignancies, cardiac involvement, and interstitial lung diseases (ILD) [2,4–6].

There are few reports of tracheobronchial lesions as extramuscular manifestations of IIMs, and their characteristics and relevance to the IIMs are not clear [7–10]. We report a Case of DM with progressive interstitial pneumonia complicated by a tracheal ulcer.

2. Case presentation

A 65-year-old non-smoking woman was diagnosed as having anti-ARS antibody-positive interstitial pneumonia after a medical check-up in 2007. As there were no symptoms, she was only followed up, and her chest imaging findings remained unchanged for a long period. She developed skin rashes such as Gottron's sign and mechanic's hand and muscle weakness in her thighs and neck in 2017, which led to a definitive diagnosis of DM after examination by a rheumatologist; however, her skin rash and myopathic symptoms spontaneously abated, and no immunosuppressive treatment was initiated.

She visited our hospital in 2020 because of dyspnea and dysphagia over the course of a month. Both normal foods and liquids were difficult to take due to the dysphagia. Her vital signs were blood pressure 124/86 mmHg, pulse 88 bpm with a regular rhythm, body temperature 36.4 °C, and oxygen saturation 97% on pulse oximetry. Chest auscultation revealed fine crackles on inspiration in the bibasilar area. Physical examination revealed Gottron's sign on the extensor side of the knees, mechanic's hand, nail fold bleeding, photosensitivity, and Raynaud's phenomenon. Manual muscle testing showed no obvious findings of muscle weakness in the extremities or trunk.

Chest computed tomography (CT) showed an increase in subpleural

Abbreviations: ARS, anti-aminoacyl tRNA synthetase; DM, dermatomyositis; GGO, ground-glass opacity; IIM, idiopathic inflammatory myopathy; ILD, interstitial lung disease; MDA5, melanoma-differentiation-associated gene 5; PM, polymyositis.

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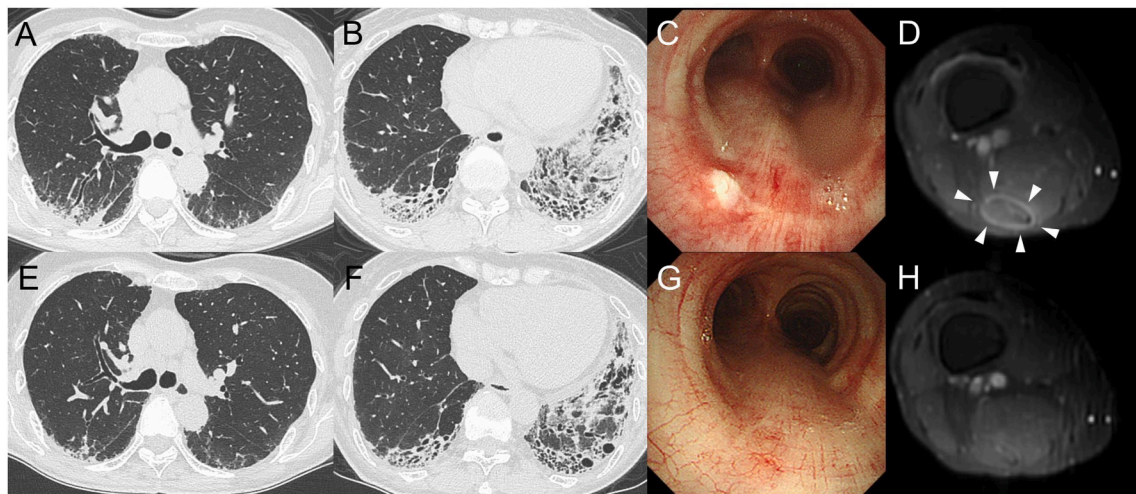


Fig. 1. Radiological and bronchoscopic findings. Chest CT on admission showed subpleural consolidation and GGOs predominantly in the lower lobes accompanying traction bronchiectasis and marked volume loss (A, B). Bronchoscopy showed a white ulcerative lesion on the membranous portion of the trachea (C). Axial short-tau inversion recovery image of the thigh MRI showed a high signal in the fascia of the bilateral femoral flexor muscles (white arrowheads) (D). Three months after the start of treatment, the consolidation, GGOs, tracheal ulcer, and fasciitis improved (E–H).

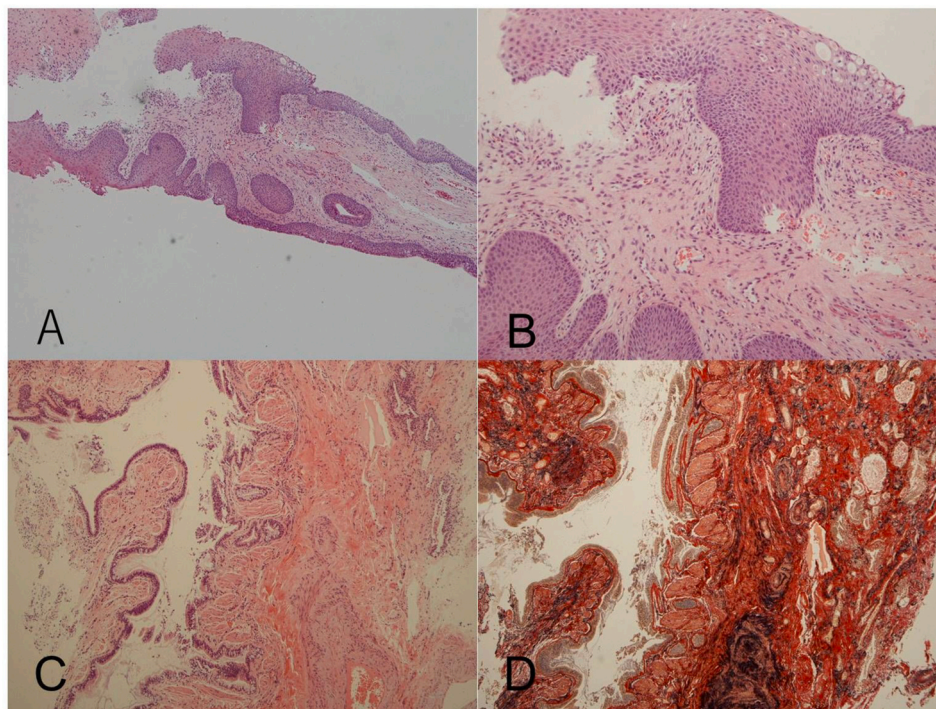


Fig. 2. Pathological findings. The tracheal ulcer showed marked squamous metaplasia without findings of malignancy from granulomatous diseases at low power (A), and mild lymphocytes, plasma cells, and neutrophilic infiltration in the tracheal mucosa at high power (hematoxylin and eosin stain) (B). Transbronchial cryobiopsy specimens obtained from the left lower lobe of the lung showed severe alveolar fibrosis with alveolar collapse (hematoxylin and eosin stain) (C) and elastic fibres with a high degree of contraction from the alveolar region to the interstitial region (Elastica van Gieson stain) (D).

consolidation and ground-glass opacities (GGOs) predominantly in the lower lobes accompanying traction bronchiectasis and marked volume loss (Fig. 1A and B). Laboratory examinations revealed significantly high serum levels of KL-6 (1435 U/mL) and SP-D (76.5 ng/mL). The serum levels of creatine kinase (2559 IU/L), aldolase (49.1 IU/L), and C-reactive protein (1.6 mg/dL) were also high. Anti-PL-7 antibody in ARS antibody was positive, whereas the levels of anti-melanoma differentiation-associated gene 5 antibody (anti-MDA5 Ab) and anti-transcriptional intermediary factor 1-gamma antibody (anti-TIF1- γ Ab) were negative. Respiratory function tests showed evidence of impaired diffusion capacity with a forced vital capacity (FVC) of 1.99 L (83.3%, % predicted), forced expiratory volume in 1 second (FEV1) of 1.76 L (92.6%, % predicted), FEV1/FVC ratio of 88.4%, diffusing capacity of

carbon monoxide (DLCO) of 7.6 mL/min/Torr (49.2%, % predicted), and DLCO/alveolar volume ratio of 71.4% (% predicted). Bronchoscopy was performed to evaluate the degree of inflammatory and fibrotic changes in progressive DM-associated interstitial pneumonia. Bronchoalveolar lavage (BAL) fluid was transparent with a 68% recovery rate. It contained 2.1×10^5 cells/mL consisting of 72.8% macrophages, 6.8% lymphocytes, 19.6% neutrophils, and 0.8% eosinophils, and no microorganisms were cultured. Bronchoscopic observation of the lumen revealed a white ulcerative lesion on the membranous portion of the trachea (Fig. 1C). Pathological evaluation of the tracheal ulcer showed squamous metaplasia suggestive of a post-ulceration occurrence without findings of malignancy from granulomatous diseases (Fig. 2A and B). Neither bacteria nor fungi were found by Gram and Grocott staining.

Table 1

Previously reported cases with tracheal and bronchial ulcer complicated with idiopathic inflammatory myopathies.

No	Age/ Sex	PM/ DM	Auto- antibody	Interstitial pneumonia	Baseline treatment	Position of tracheal or bronchial ulcer	Pathology of transbronchial biopsy	Repeated bronchoscopy
1 ^[7]	30 / M	DM	—	progress within 2 months	PSL15mg + CyA 225mg	carina, membranous portion of lobar and segmental bronchi	subepithelial necrosis	not done
2 ^[8]	41 / F	DM	—	progress	not described	membranous portion of trachea and right main bronchus	inflammatory change with polymorphonuclear infiltrate	not done
3 ^[9]	53 / M	—	MDA-5	progress within 1 month	PSL 15mg	membranous portion of trachea and main right bronchus	necrotizing bronchial inflammation	improved
4 ^[10]	69 / M	—	ARS (EJ)	progress within 1 month	none	membranous portion of trachea	necrotizing tracheal inflammation	improved
5	65 / M	DM	ARS (PL-7)	progress within 1 month	none	membranous portion of trachea	ulcerative change with marked squamous metaplasia	improved

ARS aminoacyl-tRNA synthetase, CyA cyclosporine, DM dermatomyositis, MDA-5 melanoma differentiation-associated gene5, MMT manual muscle test, PM polymyositis, PSL prednisolone.

Transbronchial lung cryobiopsy specimens obtained from the left lower lobe of the lung showed marked alveolar fibrosis with severe alveolar collapse (Fig. 2C and D). Although mild infiltration with lymphocytes and plasma cells were observed in some alveolar areas and non-specific interstitial pneumonia was presumed to be the basal histological pattern, a sufficient evaluation of the overall picture could not be achieved and the pathological diagnosis of unclassifiable interstitial pneumonia was finally made (Fig. 2C and D). Fiberoptic endoscopic evaluation of swallowing (FEES) revealed moderate pharyngeal dysphagia with intradeglutitive aspiration and postdeglutitive residue in the pyriform sinus and vallecula. Thigh magnetic resonance imaging (MRI) showed a high signal in the fascia of the bilateral femoral flexor muscles, but no high signal within the muscle was evident (Fig. 1D).

On the basis of these findings, we diagnosed anti-PL-7 antibody-positive DM complicated by a tracheal ulcer, progressive interstitial pneumonia with severe fibrosis, and moderate dysphagia. No obvious malignancy or cardiac involvement was found. Although the pulmonary pathology findings made it reasonable to choose anti-fibrotic therapy over anti-inflammatory therapy, we chose to introduce treatment with anti-inflammatory therapy first, expecting an improvement of the dysphagia, which had the greatest impact on the patient's quality of life. We started treatment with tacrolimus plus intravenous (i.v.) methylprednisolone (500 mg i.v. 3 days/week for 2 weeks) followed by prednisolone (1.0 mg/kg/day). Her dyspnea and dysphagia gradually improved, and her serum levels of KL-6 (715 IU/L) and creatinine kinase (485 IU/L) decreased after 1 month of treatment. Although FEES was not reperformed, she was able to ingest normal food and liquids without any apparent aspiration. Evaluation by CT, MRI, and bronchoscopy performed 3 months after the start of treatment showed that consolidation, GGOs, fasciitis, and tracheal ulcer had all improved (Fig. 2E–G).

3. Discussion and conclusions

We experienced a Case of tracheal ulceration during the progression of DM-associated interstitial pneumonia. Tracheobronchial ulcers are rare extramuscular manifestations in IIM. We recently reported two cases of ARS antibody-positive interstitial pneumonia and MDA5 antibody-positive interstitial pneumonia associated with tracheobronchial ulcers [9,10]. Here, we present 5 cases of tracheobronchial ulcers in IIM together with other previously reported cases (Table 1) [7–10]. All cases were associated with interstitial pneumonia, and 4 showed the subacute progressive course of interstitial pneumonia except for 1 case in which there was no detailed description of the clinical course. In cases 3–5 shown in Table 1, improvement of the tracheobronchial ulcers was confirmed by repeat bronchoscopy after anti-inflammatory treatment, as were the chest CT findings associated with interstitial pneumonia. These results suggest that tracheobronchial ulcers in IIMs may be related to the progression of interstitial pneumonia, and a thorough observation of central airway lesions with bronchoscopy is important in progressive

cases of IIM-ILD.

Non-traumatic tracheal ulcers are rare findings on bronchoscopy. They are thought to be caused by airway invasion from solid tumors or lymphoma, airway lesions from antimicrobial or fungal infections, or radiation therapy or endotracheal intubation [11,12]. In this Case, there were no malignancy, granulomatous lesion, or pathological findings suggestive of infection at the ulcer site, and the luminal findings improved with anti-inflammatory treatment, and we diagnosed the ulcer to be a DM-associated tracheal ulcer. As shown in Table 1, there are no specific findings in DM-associated tracheal ulcers, although pathological findings such as necrosis, inflammatory changes, and squamous metaplasia have been reported. We believe that it is common to determine whether a tracheal ulcer is related to DM by examining the relationship with disease behaviour of DM and excluding other diseases. Since perivascular inflammatory cell infiltration and fibrin deposition in vascular wall are often observed in muscle and skin lesions of DM, it is assumed that a similar vasculopathy exists in the background of tracheal ulcers [7,9,13,14]. However, there have been no reports demonstrating vasculitis in the tracheal ulceration by pathological evaluation, and further accumulation of cases is needed in the future.

In conclusion, we experienced a Case of tracheal ulcer during the progression of dermatomyositis and dermatomyositis-associated interstitial lung disease. Treatment with corticosteroids combined with immunosuppressive agents resulted in improvement of the tracheal ulcer and pulmonary involvement. We believe that the tracheal ulceration might reflect the disease behaviour of dermatomyositis and dermatomyositis-associated interstitial pneumonia.

Declaration of competing for interest

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

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