Histological Findings of Organizing Pneumonia, Based on Transbronchial Lung Biopsy, May Predict Poor Outcome in Polymyositis and Dermatomyositis: Report of Two Autopsied Cases

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ABSTRACT
Interstitial lung disease in polymyositis and dermatomyositis is a serious complication, associated with poor prognosis. In this article, we describe two cases with histological findings of organizing pneumonia (OP), based on transbronchial lung biopsy (TBB). One is a 66-year-old female patient with clinically amyopathic dermatomyositis (CADM) with anti-melanoma differentiation-associated gene 5 antibody, and another is a 61-year-old female patient with polymyositis with anti-Jo-1 antibody. Both of our cases rapidly deteriorated to death, and autopsy findings showed diffuse alveolar damage. Our experience indicates that TBB findings of OP may be a poor prognostic factor in CADM and polymyositis, in spite of the profile of myositis-specific antibodies.

Keywords: Clinically amyopathic dermatomyositis; dermatomyositis; diffuse alveolar damage; organizing pneumonia; polymyositis.

Interstitial lung disease (ILD) in polymyositis/dermatomyositis (PM/DM) is associated with poor prognosis. Particularly, patients with clinically amyopathic dermatomyositis (CADM),1.2 more recently with anti-melanoma differentiation-associated gene 5 (anti-MDA5) antibody, often have rapidly progressive ILD (RP-ILD).3-5 Autopsy findings frequently reveal diffuse alveolar damage (DAD).6-8 On the other hand, cryptogenic organizing pneumonia (OP) is one of the idiopathic interstitial pneumonias (IIP),9,10 and presents as acute or subacute IIP.10 Chest computed tomography (CT) demonstrates patchy and often migratory consolidation, associated with ground-glass opacity. Cryptogenic OP often responds to corticosteroid treatment, leading to a favorable prognosis.9,11,12 Secondary OP associated with collagen vascular diseases had a poorer prognosis than cryptogenic OP.9,13 In this article, we described two cases with CADM and PM with OP findings, based on transbronchial biopsy (TBB) that subsequently developed DAD.
CASE REPORT

Case 1- A 66-year-old female patient was admitted with a two-week history of dry cough and exertional dyspnea. She also had photosensitivity and rashes on elbows for one year. Medical history included hysterectomy for endometrial cancer 17 years ago. Her oxygen saturation was 93% on room air. There were fine crackles in the lung bases. Manual muscle testing showed normal strength. Erythema was observed on the anterior chest, and the extensor surface of the right elbow (Gottron’s sign). On laboratory test, ferritin level was highly elevated at 2110 ng/mL (≤114), while creatine kinase (CK) level was normal. A level of KL-6 (Krebs von den Lungen 6), a serum marker for interstitial pneumonia, was normal. Antinuclear antibody and anti-Sjögren’s syndrome antigen A (SSA/Ro) antibody were positive at 40-fold dilution (normal, <40-fold dilution) and 12.8 U/mL (<7.0 U/mL), respectively, while anti-aminocyl transfer ribonucleic acid synthetase (ARS) antibodies were not detected. Chest CT showed consolidation and patchy ground-glass opacities, predominantly in the lower lobes (Figure 1a). T2-weighted images of magnetic resonance imaging (MRI) of the thighs revealed high-signal lesions in the vastus lateralis muscles, while electromyogram and muscle biopsy showed no signs of myositis. Skin biopsy from the extensor surface of the right elbow revealed massive subepidermal edema and dermal mucinosis with hyperkeratosis, compatible with DM. TBB showed pathological findings of OP (Figure 1b). Then, a diagnosis of CADM with OP was established. Despite treatment with pulse methylprednisolone
followed by high-dose prednisolone and intravenous cyclophosphamide, her condition deteriorated further. Additional therapy with tacrolimus failed and she subsequently died. Autopsy revealed DAD (Figure 1c). Anti-MDA5 antibody was latterly found in her pre-treatment sera, using immunoprecipitation technique.14

Case 2- A 61-year-old female patient was referred for suspected myositis. Eight months previously, she began to have cough and sputum. Three months later, chest CT showed multiple nodules and consolidations in all the lung lobes (Figure 2a), and TBB showed histological findings consistent with OP (Figure 2b). A diagnosis of cryptogenic OP was established, and moderate-dose prednisolone treatment improved her symptoms. A month before admission, she was admitted to the previous hospital for worsening of pneumonia, muscle weakness and elevation of CK (887 U/L). T2-weighted images of MRI showed high-signal lesions in the gluteus maximus muscles. The result of anti-Jo-1 antibody was positive. After methylprednisolone pulse therapy followed by high-dose prednisolone, she was transferred to our hospital. Medical history included appendicitis in her childhood, and hysterectomy for uterine myoma. Her respiratory rate was 21 per minute and oxygen saturation 93% on room air. There were fine crackles in the lung bases. Manual muscles testing showed 3 out of 5 at all the muscle tested. Laboratory testing showed increased levels of CK (514 U/L; <163) and KL-6 (942U/mL; ≤500). Anti-nuclear antibody and anti-SSA/Ro were negative. Although we could not plan electromyogram and muscle biopsy for deteriorating course, she was considered to have OP with PM, as previously reported to often precede PM.15 Despite therapy with tacrolimus, her condition deteriorated. After another course of pulse methylprednisolone, she died of respiratory failure. Autopsy revealed DAD (Figure 2c).

DISCUSSION
In our cases with CADM and PM, TBB showed histological findings of OP. Although the role of TBB in diagnosing OP is limited due to small sample, TBB may be adequate to establish working diagnosis of OP, when clinical and radiological findings are consistent with OP.16–18 Our cases had histological findings of OP, based on TBB, and subsequently died of DAD. Two possibilities may be considered: (i) OP lesions alone at initial presentation that subsequently developed to DAD, (ii) coexistence of OP and DAD at initial presentation, in which TBB specimen only included OP lesions. Nevertheless, our experience suggests that TBB findings of OP may predict respiratory deterioration due to DAD in PM and CADM.

After the proposal of CADM,1,19 an association with RP-ILD gained importance, and thereafter, anti-MDA5 antibody was exclusively discovered in CADM and DM patients.19–21 A retrospective study showed that 20 (74%) of 27 anti-MDA5 positive patients developed RP-ILD, and nine (33%) subsequently died.22 Multiple cutaneous ulcers,23 high titer of the antibody,24 and ferritin elevation3,22 have been advocated as poor prognostic factors. Gono et al.3 reported that all five cases with a ferritin level ≥1,600 subsequently died, as seen in our case (Case 1).

On the other hand, nonspecific interstitial pneumonia (NSIP) or usual interstitial pneumonia, categorized as chronic fibrosing interstitial pneumonia,3,11 is the predominant pattern in anti-ARS antibody-associated IIP.24,25 However, acute or subacute interstitial pneumonia in anti-ARS positive ILD was also reported in 67%,5 and even RP-ILD in 5%-18%.26,27 In an observation of anti-ARS-positive IIP, OP was the second most frequent pattern identified on surgical lung biopsy (52%), after NSIP (67%). Interestingly, OP was found solely in 19%, and concomitantly with NSIP or DAD in 33%.25 Therefore, the histological findings of OP in Case 2 may also be explained by OP alone or concomitant OP.

Out of 29 previously-reported cases with histological findings of OP with PM/DM/CADM,17,28,29 mortality was 21%, which was higher than the pooled mortality (6%) in cryptogenic OP.11 To our knowledge, ours were the first cases with histological findings of OP on TBB, subsequently developing DAD. We propose that TBB findings suggesting OP in PM/DM/CADM may predict poor prognosis, regardless of the profile of myositis-specific antibody.
ORGANIZING PNEUMONIA IN PM/DM

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