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CASE REPORT

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Autoimmune pulmonary alveolar proteinosis during the treatment of nonspecific interstitial pneumonia complicated by clinically amyopathic dermatomyositis: A case report

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Abstract

A 46-year-old male was treated with corticosteroids for nonspecific interstitial pneumonia (NSIP). He was referred to our hospital and admitted for worsening dyspnea and diffuse ground-glass opacity on chest computed tomography (CT) during corticosteroid treatment. Gottron's sign was observed, and the patient was diagnosed with clinically amyopathic dermatomyositis on skin biopsy. We increased the corticosteroid dose and added immunosuppressive agents; however, the opacity on the chest CT worsened. Based on periodic-acid-Schiff-positive granular material in the bronchoalveolar lavage fluid and the presence of anti-GM-CSF antibodies, the patient was diagnosed with autoimmune pulmonary alveolar proteinosis (APAP). The concentration of anti-GM-CSF antibodies in preserved serum was also elevated when the patient was diagnosed with NSIP. Thus, we assumed that NSIP and APAP coexisted, and that APAP manifested during immunosuppressive therapy. When exacerbation is observed during the treatment of interstitial pneumonia with immunosuppressive agents, it is necessary to consider APAP.

KEYWORDS

autoimmune pulmonary alveolar proteinosis, clinically amyopathic dermatomyositis, immunosuppressive therapy, nonspecific interstitial pneumonia

INTRODUCTION

Pulmonary alveolar proteinosis (PAP) may have imaging findings similar to interstitial pneumonia (IP) and may be misdiagnosed as IP.[1] Recently, cases of IP with PAP have been reported.[2,3] Here, we describe a case of autoimmune PAP (APAP) treated with corticosteroids and immunosuppressive agents for nonspecific interstitial pneumonia (NSIP) associated with clinically amyopathic dermatomyositis (CADM). APAP manifested during immunosuppressive therapy for IP associated with CADM, and it was speculated that NSIP associated with CADM and subclinical APAP coexisted at the time of NSIP diagnosis.

CASE REPORT

A 46-year-old Japanese male patient was administered abiraterone acetate for stage-4 prostate cancer. Four months after prostate cancer treatment commenced, the patient was admitted to the Brunch Hospital of Tokyo Women's Medical University with fever and dyspnea. Chest computed tomography (CT) revealed diffuse ground-glass opacities. He was initially diagnosed with drug-induced or bacterial pneumonia, and his symptoms slightly improved with antibiotic treatment, and abiraterone acetate was discontinued.

One month after discharge, the patient was readmitted to the hospital because of worsening dyspnea and diffuse ground-glass opacities (Figure 1A). The Drug-Induced

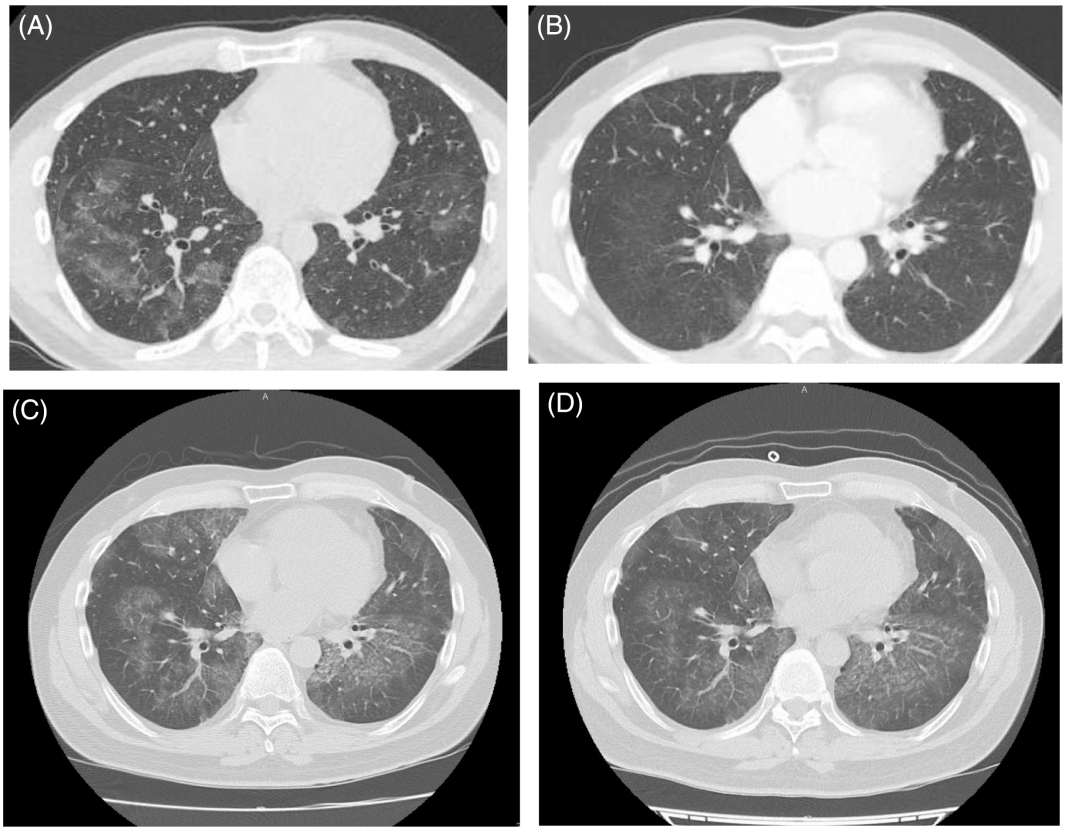

FIGURE 1 (A) Chest computed tomography (CT) showed bilateral diffuse ground-glass opacities. (B) After 12 months of treatment with a corticosteroid, the ground-glass opacity gradually improved. (C) After 16 months of corticosteroid treatment, the ground-glass opacity worsened after reducing the steroid dose. (D) After increasing the corticosteroid dose and adding an immunosuppressive agent, the chest CT scan showed worsening of ground-glass opacity.

Lymphocyte Stimulation Test for abiraterone acetate was negative and the clinical course was not compatible with drug-induced interstitial pneumonia. The bronchoalveolar lavage fluid (BALF) was not milky in appearance and BALF cell analysis showed elevated lymphocyte levels (41.5%). Histopathological evaluation by transbronchial lung biopsy showed lymphocytic infiltration of the alveolar wall without fibrosis (Figure 2A). These results were consistent with those of cellular NSIP. The patient was treated with corticosteroids, and the opacity on CT gradually improved (Figure 1B).

After 16 months of corticosteroid treatment, the opacity worsened after the steroid dose was reduced (Figure 1C), and the patient was referred to our hospital. Physical examination revealed Gottron's sign and mechanic's hands (Figure 2B,C). Laboratory analyses showed a white blood cell count of 12,080/μL (90.1% neutrophils, 7.5% lymphocytes, and 0.7% eosinophils), a C-reactive protein concentration of 0.08 U/mL, and a lactate dehydrogenase concentration of 431 IU/L. The creatine kinase concentration was not elevated (105 U/L), but the Krebs von den Lungen 6 (KL-6) concentration was elevated at 2069 U/mL. The patient tested negative for autoantibodies. Pathological examination of the skin revealed excessive keratinization and lymphocytic infiltration of the dermis. These findings were consistent with Gottron's sign, and the patient was diagnosed with CADM. After the diagnosis of CADM, the corticosteroid dose was increased and an immunosuppressive agent was added.

After increasing the corticosteroid dose and adding an immunosuppressive agent, his chest CT scan showed worsening ground-glass opacity (Figure 1D), and the KL-6 concentration was elevated to 6517 U/mL. Despite the immunosuppressive therapy, no improvement was observed. BAL was performed again, and the BALF appeared white and cloudy with a white sediment (Figure 2D). Based on the periodic-acid-Schiff-positive granular material in the BALF (Figure 2E) and the presence of anti-GM-CSF antibodies, the patient was diagnosed with APAP. We also tested for anti-GM-CSF antibodies in preserved serum from when the patient was initially diagnosed with NSIP, and the anti-GM-CSF antibody concentration was also elevated at this time. We assumed that NSIP associated with CADM and subclinical APAP coexisted. Following the diagnosis of APAP, tacrolimus was discontinued and the corticosteroid dose was reduced. Segmental/lobar bronchoscopic lavage was performed three times, and oxygenation and chest CT findings slightly improved.

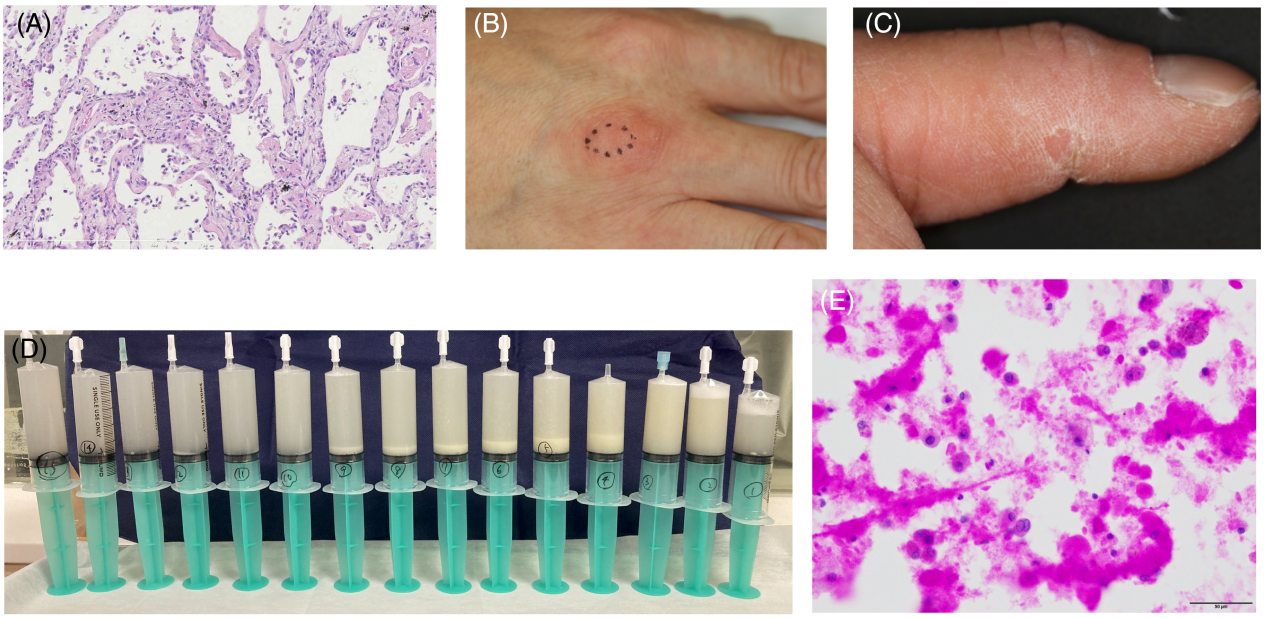

FIGURE 2 (A) Histology of a lung specimen obtained by transbronchial lung biopsy showed lymphocytic infiltration in the alveolar wall without any fibrosis of the interstitium (haematoxylin–eosin staining) (B) Gottron's sign and (C) mechanic's hands were observed. (D) The bronchoalveolar lavage fluid (BALF) appeared white and cloudy, and a white sediment was observed. (E) Periodic acid Schiff (PAS)-positive granular materials were observed in the BALF (PAS staining).

DISCUSSION

This patient was diagnosed with APAP during treatment for NSIP associated with CADM, although there were no findings suggestive of APAP in the histological examination or BAL findings at the time of diagnosis of NSIP. However, preserved serum from the time of the NSIP diagnosis tested positive for anti-GM-CSF, indicating that potential APAP already existed at the time of NSIP diagnosis. Steroid treatment for APAP enhances alveolar macrophage dysfunction and exacerbates the condition.[1,3] In this case, steroid treatment for NSIP improved the shadows on the CT scan; however, after prolonged steroid treatment, the disease gradually worsened, and increasing the steroid dosage and concomitant use of immunosuppressive agents caused further worsening of the disease. In this case, the administration of steroids and immunosuppressive agents was thought to have caused macrophage dysfunction and the manifestation of APAP.

PAP is associated with markedly elevated KL-6 concentrations.[4] In this case, the KL-6 concentration markedly elevated as the disease worsened, and it was necessary to suspect a complication of PAP when the KL-6 concentration was markedly elevated during IP treatment.

The frequency of complications associated with APAP and autoimmune diseases is low. In a cohort study in Japan, the combination of collagen disease and APAP occurred in 3 of 223 cases (1.3%).[5] Only two cases of APAP were associated with dermatomyositis or polymyositis, as seen in the present case.[2] Whether such complications of APAP and collagen disease are merely incidental or have some kind of causal relationship needs to be investigated in the future, but in all cases of dermatomyositis and polymyositis reported thus far, worsening of PAP occurred during steroid treatment,[2] therefore, when IP worsens during steroid treatment, the possibility of the coexistence of APAP should be considered.

Herein, we report a case of APAP diagnosed during the course of IP associated with CADM. It has been reported that PAP is often misdiagnosed as IP because they present similar clinical features.[1] However, as in this case, IP and potential APAP may occur together, and it was concluded that PAP complications should be suspected when the disease worsens or when KL-6 concentrations are markedly elevated during immunosuppressive therapy for IP.

AUTHOR CONTRIBUTIONS

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and the accompanying images.

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