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# An Unusual Case of Secondary Pulmonary Alveolar Proteinosis in Recently Diagnosed Anti-MDA5 Positive Amyopathic Dermatomyositis

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**Abstract** Amyopathic dermatomyositis (AMD) is a subtype of dermatomyositis characterized by more prominent involvement of the skin rather than muscle and often positive for melanoma differentiation-associated gene 5 (MDA-5) antibodies. The most frequent pulmonary involvement in MDA-5 positive AMD is nonspecific interstitial pneumonia. However, rare cases of pulmonary alveolar proteinosis (PAP) have also been reported. Here, we present a case of a 28-year-old male who was recently diagnosed with AMD presenting with shortness of breath and dry cough was eventually diagnosed with secondary pulmonary alveolar proteinosis. This case underscores the multidisciplinary approach and diagnostic challenges associated with the diagnosis of PAP secondary to the rarity of the condition.

***Keywords:*** *Amyopathic Dermatomyositis, secondary pulmonary alveolar proteinosis, PAP, MDA-5*

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## 1. Introduction

Dermatomyositis is an idiopathic inflammatory myopathy that is relatively uncommon [1]. A subtype of dermatomyositis referred to as AMD is characterized by the absence of muscle involvement. The presence of MDA-5 antibody in AMD serves as an imperative prognostic marker and enhances the risk for developing lung disease, most commonly interstitial pneumonia, however, in very rare cases secondary pulmonary alveolar proteinosis (PAP) has been reported. PAP is characterized by the accumulation of surfactant protein in terminal bronchioles and alveoli secondary to impaired clearance by pulmonary macrophages [2]. While the majority of the cases of PAP are congenital or have an underlying autoimmune etiology, secondary PAP associated with MDA-5 positive AMD is extremely rare and requires vigilance on the part of clinicians to allow for early recognition and treatment of this progressive disorder.

## 2. Case Presentation

A 28-year-old previously healthy non-smoker male was diagnosed with dermatomyositis after developing proximal muscle weakness and an erythematous, violaceous papular rash on his hands and was being treated with Etanercept and prednisone. Six months following his initial diagnosis, the patient developed a dry cough and worsening shortness of breath and was hospitalized. During the course of his hospitalization, he was found to have bilateral consolidations on computed tomography (CT) scan of the lungs and eventually underwent bronchoscopy with bronchoalveolar lavage which revealed Aspergillus, and the patient was started on Levaquin and Voriconazole. During the same hospitalization, he was found to have MDA-5 antibody positivity. At this point, the patient's medication was changed from Etanercept to Rituximab while prednisone was continued. Despite the change in treatment and addition of antibiotics and antifungal medications, the patient continued to have a worsening dry cough and difficulty breathing. The patient was re-hospitalized with similar complaints two months later. On presentation, the patient complained of dry cough and shortness of breath with occasional chest discomfort. Review of systems was significant for the absence of fever, chills, headaches, vision changes, nasal/sinus congestion, chest pain, palpitations, abdominal pain, muscle weakness, or urinary and/or bowel changes. Physical exam was significant for a violaceous rash on his bilateral fingers and diffuse bilateral crackles on lung exam. Repeat CT performed during his second hospitalization revealed persistent bibasilar consolidation which was thought to be secondary

to organizing pneumonia secondary to dermatomyositis [Figure 1]. However, the patient eventually underwent video-assisted thoracoscopic surgery (VATS) lung biopsy with pathology which revealed pulmonary alveolar proteinosis. PAP was deemed to be secondary to AMD as granulocyte monocyte colony-stimulating factor (GM-CSF) antibody for autoimmune PAP was negative. The patient was tapered off from steroids and was stable without any exacerbations of his pulmonary symptoms on his 3-month follow-up visit after discharge.

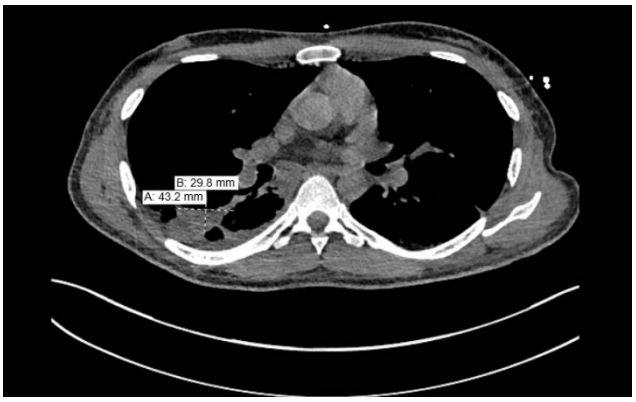


**Figure 1.** Chest tomography (CT) chest showing bibasilar consolidations with the larger consolidation on the right side of approximately 3 x 4cm

## 3. Discussion

Polymyositis and Dermatomyositis are autoimmune inflammatory myopathies with an annual incidence of approximately 1 per 100,000 persons [1]. Amyopathic dermatomyositis (AMD) characterized by more prominent cutaneous rather than muscle involvement is even more infrequently encountered with an annual incidence of only 0.2 per 100,000 persons [1]. It has been observed that cases of AMD which are positive for MDA-5 antibodies have an overall poor survival rate when compared to negative cases [3].

Lung diseases commonly encountered in dermatomyositis include infectious pneumonia, drug-induced pneumonia, aspiration pneumonia, respiratory muscle weakness, and interstitial lung disease [4]. Among these, the most commonly seen pulmonary disease in AMD is nonspecific interstitial pneumonia [5]. An incidence of up to 41% has been reported for interstitial lung disease in dermatomyositis [6]. Pulmonary alveolar proteinosis itself is a rare entity that is defined by the collection of lipoproteinaceous periodic acid-Schiff positive material in alveolar spaces [2]. PAP is mostly congenital, hereditary, or autoimmune with a small number of cases occurring secondary to other hematological, oncological, or rheumatological conditions such as dermatomyositis [7,8]. Given its rarity, this diagnosis was not at the top of our differential when the young 28-year-old man presented with a prominent dry cough and worsening shortness of breath.

PAP usually presents in adults in the fourth to the fifth decade [9] and approximately half of these patients have a history of cigarette smoking [10]. The patient presented in this report developed PAP in his 20's and was a lifetime non-smoker. PAP can be asymptomatic [9] or present with a variety of symptoms, ranging from cough, dyspnea, low-grade fever, chills, fatigue, or weight loss [11]. The physical exam can be normal or reveal inspiratory crackles, similar to our patient and also be remarkable for digital clubbing or cyanosis [9,10]. The presence of anti-granulocyte-macrophage colony-stimulating factor (GM-CSF) antibodies in the serum is very sensitive and specific for an autoimmune variant of PAP [8], while its absence as seen in our patient should entail a comprehensive workup for secondary causes. Investigations include chest x-ray, computed tomography (CT), and pulmonary function tests, although lung biopsy may be required for definitive diagnosis [9]. While the treatment of primary PAP is based upon severity and includes whole lung lavage, rituximab, or GM-CSF [12,13,14], treatment of secondary PAP includes addressing the underlying disorder.

## 4. Conclusion

Although less common than interstitial pneumonia, it is essential to recognize secondary PAP when evaluating patients with AMD presenting with pulmonary symptoms such as dry cough and shortness of breath, as it may otherwise take several admissions and multiple medication trials to reach this diagnosis. Additionally, although our understanding of the pathophysiology of secondary PAP has improved drastically, further research is required to shed light on its treatment and management protocols.

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