A Helpful Hand in Diagnosis: A Case Report of Anti-Synthetase Syndrome with Mechanic’s Hands

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ABSTRACT

Anti-synthetase syndrome is a rare idiopathic inflammatory myopathy that involves a constellation of symptoms including interstitial lung disease, myositis, “mechanic’s hands,” Raynaud’s phenomenon, and polyarthritis. In the appropriate clinical setting diagnosis is confirmed based on the presence of specific auto-antibodies against aminoacyl-tRNA synthetases. Our case is unique in that the patient did not have the typically associated myositis, highlighting the need for a strong clinical acumen for the recognition of this disease. A 37-year-old male presented to his primary care physician with a chief complaint of persistent cough and occasional color change in his hands accompanied by discomfort after exposure to cold for the past 5 months. Lung exam revealed fine bilateral crackles on auscultation. Skin exam revealed hyperkeratosis and fissuring of the skin on the palmar hands. Laboratory results revealed positive anti-Jo-1 antibodies and a diagnosis of anti-synthetase syndrome was made. Our patient was treated with steroids and cyclophosphamide and he improved dramatically. “Mechanic’s hands” are a unique manifestation of anti-synthetase syndrome, occurring in 20% of patients. Careful examination of the hands is a critical component in the workup of anti-synthetase syndrome. This case reinforces the importance of a thorough physical exam to look for the unique diagnostic clues found in patients with anti-synthetase syndrome.

INTRODUCTION

Anti-synthetase syndrome is a rare idiopathic inflammatory myopathy that involves a constellation of symptoms including interstitial lung disease, myositis, “mechanic’s hands,” Raynaud’s phenomenon, fever, and polyarthritis. When these symptoms are present and anti-synthetase syndrome is suspected, the diagnosis can be confirmed based on the presence of specific auto-antibodies against aminoacyl-tRNA synthetases. The most common antibody is anti-histidyl (anti-Jo-1). Patients with progressive interstitial lung disease have a poorer prognosis than those with non-progressive lung disease. Pulmonary involvement is the leading cause of morbidity in patients with anti-synthetase syndrome. The disease typically affects Caucasian...
adult women. Our case is unique in that the patient did not have symptoms of myositis, which occurs in the majority of patients with anti-synthetase syndrome, and also occurs in 90% of patients with positive anti-Jo-1 antibodies. Additionally, our patient had “mechanic’s hands” which only occurs in 20% of patients with anti-synthetase syndrome. This case highlights a unique presentation of anti-synthetase syndrome and highlights the need for a strong clinical acumen for the recognition of this disease.

CASE PRESENTATION

A 37-year-old male presented to his primary care physician with a chief complaint of cough. The patient was in his usual state of good health until 5 months prior when he developed a persistent cough. The cough was dry and non-productive. There were no precipitating factors that the patient was able to recall. The patient had no history of respiratory disease but had a brief occupational exposure to tuberculosis as the patient worked in the healthcare field. A former cross-country runner, the patient had experienced some decrease in exercise tolerance but had attributed this to an overall lack of physical conditioning. The patient did recall occasional color change in his hands accompanied by discomfort with exposure to cold beginning a few months before (Figure 1).

The patient was employed in an office setting. Hobbies included woodworking and home remodeling, but he denied coming into contact with significant adhesives or solvents. This was important to rule out any contact dermatitis, irritant dermatitis, and to note any exposures that may have been damaging to the patient’s health.

Figure 1. Raynaud’s phenomenon occurs during cold exposure.

Figure 2. Hyperkeratosis and fissuring of the skin on the palmar surface of the upper extremity digits.

Figure 3. CT scan of chest. Bilateral lower lobe parenchymal changes consistent with interstitial lung disease.
Family history was significant for drug-induced lupus in a first-degree relative and prostate cancer in a different first-degree relative.

In general, the patient was in no acute distress. Head, eyes, ears, nose, and throat (HEENT) exam was unremarkable. There was no lymphadenopathy. Cardiovascular exam was unremarkable. Lung exam revealed fine bilateral crackles on auscultation greater in the bases than in the upper lung fields. Skin exam revealed hyperkeratosis and fissuring of the skin on the palmar surface of the upper extremity digits (Figure 2). In comparison, the dorsal surfaces of the hands were relatively spared. The nails and nail beds were unaffected. Muscle strength was 5/5 in all muscle groups. The remainder of the physical exam was unremarkable. The patient was initially treated with a respiratory fluoroquinolone for presumed atypical pneumonia (non-productive cough, generalized symptoms) pending lab results. The patient’s symptoms did not change with use of the antibiotic. Chest x-ray revealed bilateral lower lobe parenchymal changes, and chest computed tomography (CT) scan was consistent with interstitial lung disease (Figure 3). Pulmonary function testing was performed and was consistent with restrictive lung disease (Total Lung Capacity (TLC) 76% predicted, Vital Capacity (VC) 78% predicted, Forced Expiratory Volume (FEV₁)/Forced Vital Capacity (FVC) 101% predicted). Lung biopsy revealed nonspecific pulmonary fibrosis.

Laboratory evaluation was remarkable for an elevated Rheumatoid Factor (RF) (27.6), positive antinuclear antibody (ANA) (titer: 2.42) and positive anti-Jo-1 antibodies. There was no leukocytosis. C-reactive protein and erythrocyte sedimentation rate (ESR) were within normal limits. The patient was diagnosed with anti-synthetase syndrome, and started on oral steroids (prednisone 60 mg/day) and oral cyclophosphamide. The patient’s symptoms improved dramatically with the use of the immunosuppressant agents. Cyclophosphamide was discontinued after 6 months and replaced with azathioprine. Prednisone was slowly weaned over the course of 2 years. The patient continues on azathioprine 2.5 years after his initial diagnosis without recurrence or apparent complications. Pulmonary function tests performed after 3 months of treatment revealed normal spirometry. TLC had increased to 80% of predicted.

**DISCUSSION**

The population prevalence of anti-synthetase syndrome is unknown as it is a rare disease and frequently unrecognized. Anti-synthetase syndrome appears to have a female predominance (2:1) and occurs most commonly in Caucasian adult women.¹ Due to its infrequency and variability in presentation, diagnosis may be difficult. Moreover, lung disease may be the predominate factor or may be one of the symptoms in a patient with many nonspecific complaints.¹ Large differences in the distribution and severity of each of these symptoms exist among patients, and also over the course of the disease. Five recognized clinical features may be present at the time of diagnosis or appear as the disease progresses. These characteristics include fever, myositis, interstitial lung disease, inflammatory polyarthritis, and dermatological manifestations. Our patient experienced interstitial lung disease, “mechanic’s hands,” and Raynaud’s phenomenon.

Although the majority of patients with anti-synthetase syndrome have myositis, lung disease can predominate or be the sole manifestation in the absence of clinically apparent myopathy.¹ Most commonly, patients develop proximal muscle weakness and associated muscle pain. Our patient was unique in that he did not have the aforementioned symptoms of myositis, which is
present in 90% of patients with anti-Jo-1 antibodies.¹ Synthetases catalyze tRNA acetylation and play an important role in protein synthesis. There is evidence that suggests these enzymes recruit inflammatory cells to the sites of injury leading to symptomatology.¹ Patients with anti-synthetase syndrome can be misdiagnosed as having idiopathic pulmonary fibrosis if an inflammatory myopathy is not suspected.² This distinction is crucial as the prognosis and treatment of idiopathic pulmonary fibrosis and idiopathic inflammatory myopathy markedly differ. Lung injury in idiopathic pulmonary fibrosis does not respond to immunosuppressive therapy, and ultimately, lung transplantation becomes the only treatment option. However in anti-synthetase syndrome, glucocorticoids are the mainstay of treatment.¹ Our patient’s symptoms were recalcitrant to oral antibiotics, but resolved completely after being treated with glucocorticoids. In addition, studies show that additional immunosuppressive drugs such as azathioprine and methotrexate are often required, both as glucocorticoid-sparing agents and to achieve adequate disease control.³,⁵,⁷ If anti-synthetase syndrome is suspected or diagnosed, a baseline pulmonary function test is indicated, which can often detect occult interstitial lung disease, as it did with our patient. Patients will present with progressive dyspnea and/or persistent nonproductive cough.

Our patient presented with the clinical manifestations of “mechanic’s hands,” which are a well-recognized manifestation of anti-synthetase syndrome, occurring in about 20% of patients.¹ This manifestation is closely associated with anti-Jo-1 antibodies.⁴ The term describes the well-demarcated, hyperkeratotic, thickened, erythematous, and fissured skin of the tips and margins of the lateral and palmar hands and fingers. The hands are said to resemble the calloused hands of manual laborers.

Dermatomyositis (DM) is another inflammatory myopathy that has unique dermatological manifestations that when present can help differentiate DM from anti-synthetase syndrome. These signs include Gottron’s papules, heliotrope rash, and the “shawl” sign. Gottron’s papules are a hallmark sign of DM, and appear as erythematous to violaceous papules and plaques over the extensor surfaces of the metacarpophalangeal and interphalangeal joints.⁸ Another dermatological sign of DM is the heliotrope rash, which presents as violaceous erythema of the upper eyelids often with associated edema and telangiectasia.⁹ The “shawl sign” refers to erythema over the upper back, posterior neck, and shoulders, sometimes with extension to the lateral arms that often appears in patients with DM. Our patient did not present with any of these cutaneous manifestations. It is important to note that “mechanic's hands” are a cutaneous marker for anti-synthetase syndrome, but can also be seen in patients who do not have anti-synthetase antibodies. Although myositis-specific, these antibodies are not commonly seen in DM.⁸ These cutaneous signs can help differentiate these two inflammatory myopathies.

One study found that when “mechanic’s hands” was associated with idiopathic inflammatory myopathy, it never appeared as an isolated skin sign.⁴ Those authors suggest that when “mechanic’s hands” appears later in the course of anti-synthetase syndrome, it is associated with deep tissue involvement and could indicate a flare-up of the disease, suggesting why it is almost always accompanied by multiple other symptoms.⁴ “Mechanic’s hands” and Raynaud’s phenomenon were the two cutaneous clues that led the primary care physician to suspect anti-synthetase syndrome, even though myositis was not present. Careful examination of the hands is a critical component in the workup of anti-synthetase syndrome.

Anti-synthetase syndrome is a rare inflammatory idiopathic myopathy that is characterized by
the presence of specific antibodies against various aminoacyl-tRNA-synthetases. Our patient presented with interstitial lung disease, Raynaud’s phenomenon, and “mechanic’s hands.” Large variations in the distribution and the severity of each of these symptoms are reported from one patient to another, and also over the course of the disease. The heterogeneity of this autoimmune connective tissue disease has led to difficulties in its diagnosis. Our case is unique in that the patient did not have the typically associated anti-synthetase syndrome myositis, highlighting the need for strong clinical acumen and thorough physical exam, including a detailed skin exam, for the recognition and diagnosis of this disease.

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**LEARNING POINTS**

- Anti-synthetase syndrome is a rare idiopathic inflammatory myopathy that involves a constellation of symptoms including interstitial lung disease, myositis, “mechanic’s hands,” Raynaud’s phenomenon, and polyarthritis.
- In the appropriate clinical setting a diagnosis of Anti-synthetase syndrome is confirmed based on the presence of specific auto-antibodies against aminoacyl-tRNA synthetases.

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The heterogeneity of this autoimmune connective tissue disease reinforces the importance of a thorough physical exam to look for the unique diagnostic clues found in patients with anti-synthetase syndrome.

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**REFERENCES**


