CASE REPORT

Progressive Interstitial Lung Disease in a Clinically Quiescent Dermatomyositis

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ABSTRACT

A 60-year-old Filipino woman diagnosed with dermatomyositis was initially on prednisone and methotrexate. She eventually developed interstitial lung disease (ILD) and so methotrexate was shifted to azathioprine; however, azathioprine was discontinued due to cutaneous tuberculosis. Over eight years, the dermatomyositis was controlled by prednisone alone but the ILD worsened. This case demonstrated that the course of ILD may be independent of dermatomyositis.

Keywords: dermatomyositis, interstitial lung disease, immunomodulator

INTRODUCTION

Dermatomyositis is an immune-mediated myopathy characterized by symmetric proximal muscle weakness and distinct cutaneous manifestations that include heliotrope rash (violaceous discoloration of the eyelids with periorbital edema), Gottron sign (erythematous rash over the extensor surfaces of the joints), Gottron papules (raised erythematous rash over the knuckles), V-sign (rash on the sun-exposed anterior neck and chest), and shawl sign over the back of the neck.[1,2] This condition, which occurs in about 9 per 1,000,000 individuals, is more common in women than in men.[3] A variant of dermatomyositis that presents with the characteristic skin findings but lacks muscle weakness, known as amyopathic dermatomyositis has also been described. Similar to other immune-mediated conditions, a significant portion of dermatomyositis patients develop systemic manifestations that include gastroesophageal reflux and dysphagia due to esophageal muscle involvement, arrhythmias, dilated cardiomyopathy, subcutaneous calcification, and respiratory symptoms from thoracic muscle weakness or interstitial lung disease (ILD).[4] ILD, which has been identified in at least 20% of cases, constitutes a significant concern because it is associated with increased morbidity and mortality.[5]

Here, we report the case of a 60-year-old Filipino female with dermatomyositis diagnosed almost a decade ago who eventually developed progressive ILD.

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CASE REPORT

This is the case of a 60-year-old Filipino housewife with no known comorbidities and vices who presented with a 3-month history of generalized myalgia in 2013 associated with difficulty in raising her arms and rising from a sitting position. She also developed a nonpruritic malar rash and erythematous rashes over the back of her fingers and elbows with a 3/5 muscle strength on all proximal muscles of both upper and lower extremities. Initial tests showed a total creatine phosphokinase (CPK) of 1695 u/L (8.8x) and lactate dehydrogenase (LDH) of 574 u/L (2.5x) (Table 1). The nerve conduction study was unremarkable but needle electromyography (EMG) in the deltoid and biceps showed patchy changes suggestive of a myopathic process. The history of proximal muscle weakness, characteristic rashes, and laboratory findings consistent with myopathy led to the diagnosis of dermatomyositis. The patient was then started on prednisone 50 mg/day and methotrexate 10 mg per week with note of clinical and serologic improvement after 5–6 months of treatment. With her steroids tapered to a maintenance dose of 10-15 mg/day plus the weekly methotrexate, the patient eventually went into clinical remission.

In 2014, the patient complained of persistent non-productive cough associated with bibasal reticulonodular densities on chest radiograph (CXR). Shown in Figure 1 are representative CXRs of the patient. She reported no fever, night sweats, or weight loss during this time. She was given courses of azithromycin and levofloxacin with partial improvement. ILD was suspected hence high-resolution chest CT (HRCT) scan was requested showing usual interstitial pneumonia (UIP) pattern (Figure 2). Further workup revealed negative sputum acid-fast bacilli

Table 1. Pertinent laboratory findings at specific time points in the course of the patient's disease

Laboratory Parameters	July 2013	Jan 2014	Feb 2015	Oct 2015	Feb 2019	Mar 2019	Dec 2019	July 2020	June 2021
Total CPK *(u/L)*	1695	367	16	39	13065	1652	902	721	4
Alanine aminotransferase *(ALT)*	114	50		17	126	85	38	37	
LHD *(u/L)*	570	261		263					
2D Echocardiography									
Ejection Fraction M Mode *(%)*									61 (>55%)
Ejection Fraction Simpsons *(%)*									63 (>55%)
SPAP									10
LVEDD mm									3.0
LVESD mm									2.1
IVS									1.0
									Concentric left ventricular remodeling with adware wall motion and contractility. Normal systolic pulmonary artery pressure

CPK = creatine phosphokinase; u/L = micrograms per liter; SPAP = systolic pulmonary artery pressure; LVEDD = left ventricular end-diastolic diameter; LVESD = left ventricular end-systolic diameter; IVS = interventricular septum

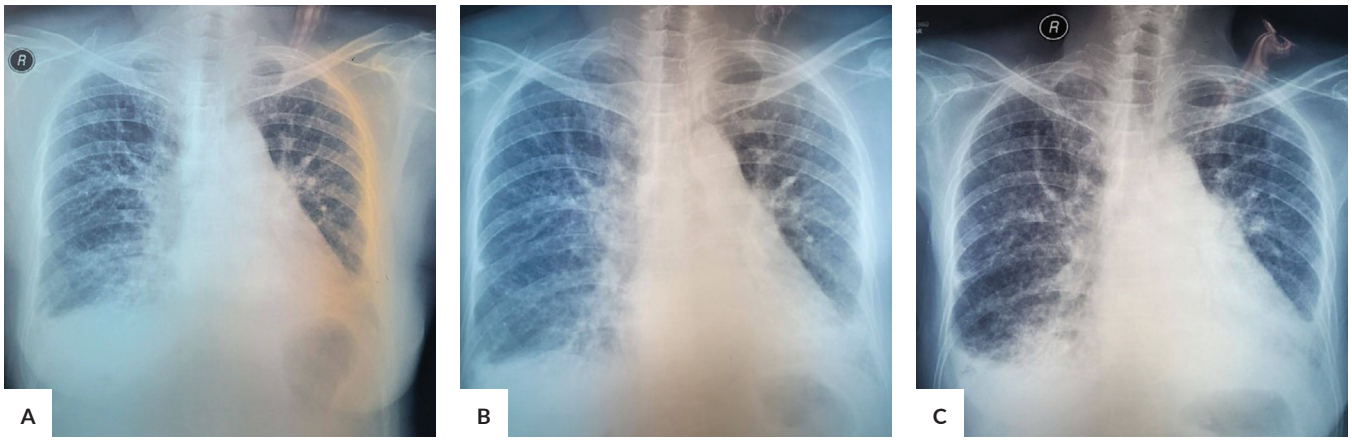

Figure 1. Representative chest radiographs were taken at different time points throughout the patient's course. **(A)** 2018. The interstitial lung markings are thickened. The heart is enlarged. Both costophrenic sulci are blunted obscuring both hemidiaphragms. Images in **(B)** 2019 and **(C)** 2021 are unchanged from 2018.

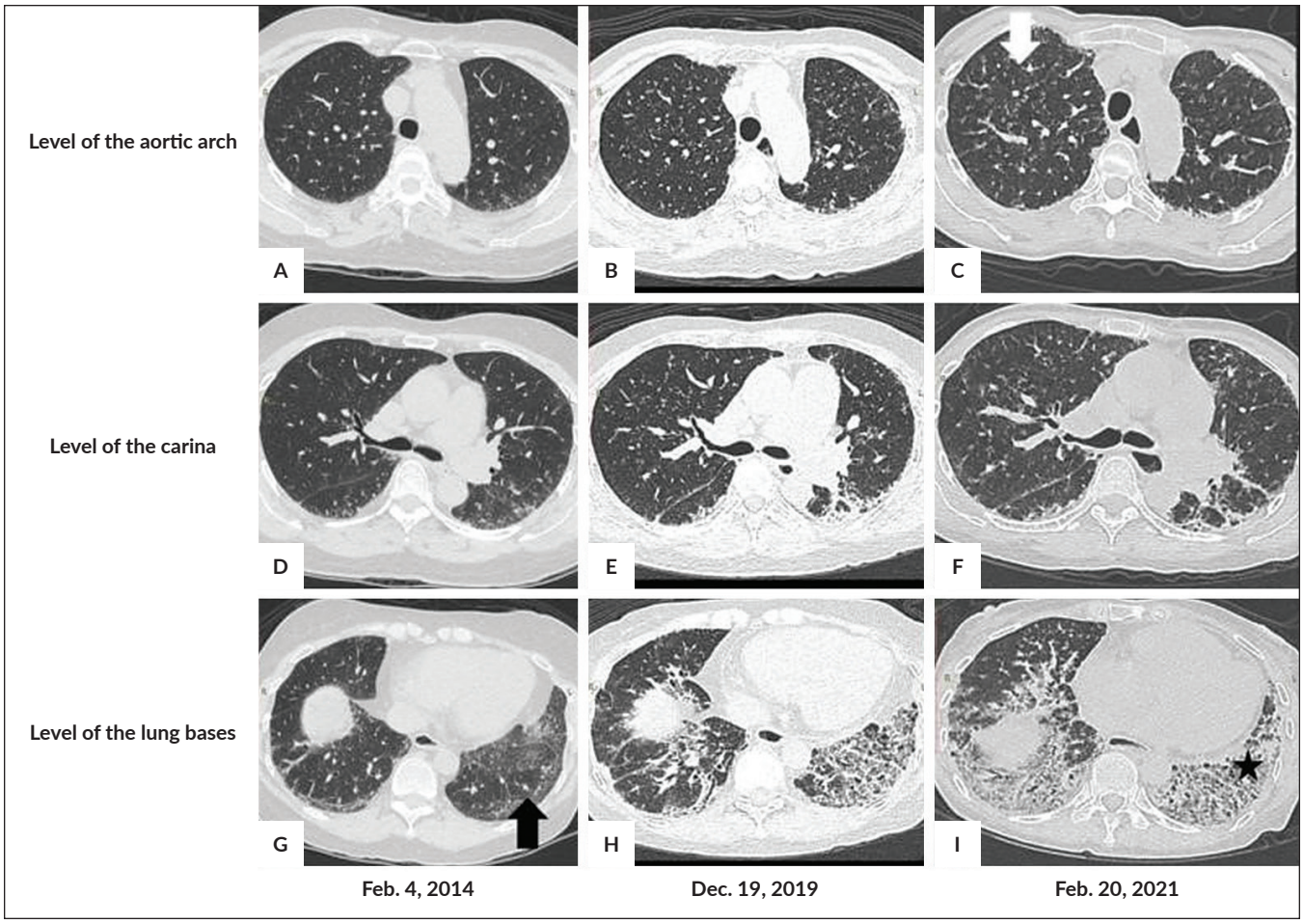

Figure 2. Axial sections of HRCT scans dated February 4, 2014, December 19, 2019, and February 20, 2021, were taken at the levels of the aortic arch **(A-C)**, carinal bifurcation **(D-F)**, and lung bases **(G-I)**. These images show interval progression of reticulonodular opacities *(white arrow)* in both lungs. Septal thickening, predominantly in the lung bases *(black arrow)*, is observed in the first imaging study, with progression in both lungs and assuming a "honeycomb" appearance *(black star)*, in the succeeding studies. Traction bronchiectasis, subpleural bands, and multiple fibrosis are likewise noted.

(AFB) and GeneXpert but TB Quantiferon Assay returned positive. The patient was given isoniazid for nine months for consideration of latent TB infection but she still complained of residual cough. Due to the development of ILD, methotrexate was shifted to azathioprine, still in combination with steroids.

In 2015, azathioprine was eventually discontinued due to the development of recurrent skin infections on the bilateral popliteal areas not improved with multiple antibiotics. Tissue AFB turned out to be positive for which she completed six months of isoniazid / rifampicin / pyrazinamide / ethambutol (HRZE) with resolution of the skin lesions. No adverse drug reactions were reported while she was on anti-TB treatment. Although subsequent bouts of myositis would be controlled by escalating the doses of prednisone without additional immunomodulators, her nonproductive cough persisted. From 2016 to 2018, the patient was lost to follow-up.

The patient resumed her clinic visits in 2019. She had occasional muscle pains which would resolve with titrating prednisone doses. However, her lingering cough was now associated with exertional dyspnea. A repeat HRCT was done which showed interval progression of her ILD. The plan was to start mycophenolate mofetil but the patient was again lost to follow-up.

The patient sought consult in 2021, this time for recurrence of her cutaneous TB on the right popliteal area. Surveillance CT scan demonstrated progression of the septal thickening and traction bronchiectasis in the bilateral lower lobes compared to imaging done in 2019. Repeat sputum GeneXpert had negative results. Two-dimensional echocardiography indicated left ventricular hypertrophy, LV diastolic dysfunction, and the absence of pulmonary hypertension. The patient is currently undergoing HRZE treatment. The plan is to start antifibrotic agents once TB treatment is completed.

DISCUSSION

Dermatomyositis is a chronic inflammatory muscle disease associated with distinct skin involvement.[6] It is one of the idiopathic inflammatory myopathies along with polymyositis, inclusion body myositis, and immune-mediated necrotizing myopathy.[6] Apart from malignancy, vasculitis, esophageal, and cardiac manifestations, dermatomyositis is also associated with increased risk of ILD, the presence of which causes significant morbidity and mortality.[5] A study by Huh et al. (2006) revealed that the 3-year survival rate of dermatomyositis patients with ILD was significantly lower (62%) compared to patients without ILD (89%) ($p < 0.05$).[7]

The diagnosis of dermatomyositis was initially outlined by Bohan and Peter in a two-part paper published in 1975.[8] The classic dermatomyositis is defined by the presence of proximal muscle weakness, characteristic dermatologic manifestations, elevated muscle enzymes such as creatine kinase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), LDH and aldolase, abnormal electromyogram, and abnormal muscle biopsy which may show necrosis, phagocytosis, regenerative activity, and atrophy.[8] Although muscle biopsy was not done in this case, the rest of the manifestations were exhibited by the patient, making the diagnosis possible.

Dermatomyositis is complicated by ILD in at least 20% of cases, usually presenting with exertional dyspnea, persistent nonproductive cough, and poor exercise function.[4,5] Local data on the incidence of dermatomyositis-related ILD is however lacking. The temporal association between ILD and dermatomyositis varies.[9] A literature review by Dellaripa et al. (2021) indicated that ILD may manifest before the diagnosis of dermatomyositis by months, present concurrently with myositis at the outset, or may appear after the onset of weakness.[10,11] Interestingly, ILD has also been documented among dermatomyositis patients who lack muscle weakness i.e., amyopathic dermatomyositis.[12] The evaluation of a suspected dermatomyositis-associated ILD usually begins when a patient with known dermatomyositis develops symptoms or imaging findings suspicious for ILD. The combination of history, clinical presentation, laboratory tests confirming the underlying connective tissue disease (CTD), high-resolution CT scan, and pulmonary function test is sufficient to make a diagnosis of dermatomyositis-induced ILD[10,13] Experts agree that lung biopsy among those with systemic rheumatic diseases adds little diagnostic and prognostic information.[14] In general, the appearance of the HRCT is enough to determine the type of ILD and predicts the underlying histologic pattern. One such case is a definite usual interstitial pneumonia pattern (i.e., subpleural, basal predominance, reticular abnormality, honeycombing with or without traction bronchiectasis) in the absence of peribronchovascular predominance, extensive ground-glass abnormality, profuse micronodules, discrete cysts, diffuse mosaic attenuation or air-trapping. When a UIP pattern is seen on HRCT, it has 90–100% specificity for UIP on histopathology and precludes the need for invasive procedures.[15-17] Our patient exhibited a UIP pattern on her chest CT scan, making lung biopsy unnecessary. In addition, unlike the idiopathic forms of ILD, the histopathologic pattern in CTD-related ILD does not significantly affect treatment decisions since steroids and immunosuppressive drugs are still the primary therapeutic options. Some exceptions to doing lung biopsy in the context of CTD include cases in which neoplastic conditions cannot be ruled out noninvasively, unusual features at imaging, or when the CTD is very poorly characterized due to limited systemic manifestations.[18]

The initial course of ILD among dermatomyositis patients follows three patterns: asymptomatic type, chronic form with slow progression, and progressive form with acute onset.[19,20] Regardless of the presenting clinical behavior, ILD generally improves or at least stabilizes with successful treatment of the autoimmune disease. In a study by Marie et al. (2011) on 107 patients with dermatomyositis / polymyositis-associated ILD, 51% presented with progressive lung manifestations, 18.7% demonstrated acute onset ILD, and 29.9% were asymptomatic. Among these patients, 33% had complete resolution of respiratory symptoms with a return to baseline of pulmonary function and CT scan appearance; 51% exhibited improvement of symptoms but with residual abnormalities in the PFT and CT scan; and 16% developed ILD deterioration despite giving appropriate treatment.[20] Although concomitant symptoms related to dermatomyositis were not reported among those who had ILD deterioration, serologic parameters including ESR, CRP, creatine kinase, and liver function tests were all within normal limits for this subgroup of patients after receiving steroids and/or immunomodulators.[20] In our patient, the muscle weakness, rashes, and biomarkers improved with steroids but her ILD continued to worsen.

Dermatomyositis-induced ILD is associated with several major histopathologic types.[9,21,22] The specific subtype dictates therapy and impacts prognosis.[21] Non-specific interstitial pneumonia (NSIP) seems to be the most common in dermatomyositis and polymyositis.[22] Organizing pneumonia (OP), usual interstitial pneumonia (UIP), and diffuse alveolar damage (DAD) have also been described. NSIP and organizing pneumonia are associated with a good prognosis while UIP and DAD have a poorer prognosis with only a 33% survival rate at 5 years.[23]

The choice of therapy for dermatomyositis-related ILD is similar to the medications used for the treatment of myopathy. Systemic steroids are still the mainstay of treatment for dermatomyositis-related ILD. A second immunomodulator is added if the ILD is progressive, unable to taper glucocorticoids, or the patient is intolerant to its side effects, with impending respiratory failure, and in ILD associated with melanoma differentiation-associated gene5 (MDA5).[10] These immunosuppressive agents include

methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, intravenous immunoglobulin, calcineurin inhibitors, and biologics.[24] However, the response of the muscle and skin involvement is not associated with nor does it predict the response of the lungs.[25] An earlier case report by Schwarz et al. (1976) documented a patient with dermatomyositis whose cutaneous and muscle symptoms responded well to steroids but the ILD progressed.[9] As illustrated in this case, the muscle and skin involvement of our patient decreased after corticosteroid, methotrexate, and subsequent azathioprine but with progressive lung disease as exhibited in the serial HRCT scans. It is not clear whether this poor response was from the interruption of the second-line agents due to recurrent skin infection or because of the histologic subtype of the patent's ILD. Dellaripa et al. (2021) reported that the UIP pattern is less responsive to steroids and immunomodulators and may require anti-fibrotic agents as an alternative treatment.[10]

CONCLUSION

This report documented the occurrence of ILD in a Filipino patient with dermatomyositis. The course of ILD may be independent of the clinical activity of dermatomyositis.

Statement of Authorship

All authors contributed in the conceptualization of work, acquisition and analysis of data, drafting and revising and approved the final version submitted.

Author Disclosure

All authors declared no conflicts of interest.

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