Drug-Induced Dermatomyositis

It’s common practice to screen for underlying malignancy in dermatomyositis, but it is also important to look for drug-induced disease.

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A 72-year-old Caucasian woman was referred by her primary care physician for worsening eczema. She complained of fatigue and worsening arthritis that upon further questioning was revealed to be proximal muscle weakness. Her past medical history includes arthritis and hypertension. She had no relevant surgical history. Her medications included Amlodipine-Benazepril 5mg/10mg daily, Metformin 500mg bid, Atorvastatin 10mg at night, and Omeprazole 20mg daily. On physical exam she demonstrated pink fine scaling plaques on her face involving her upper eyelids and a similar eruption on her chest as seen in photos A and B below. She also had periungual telangectasias.

A preliminary diagnosis of dermatomyositis was made. Lesional skin biopsy from the left arm demonstrated interface vacuolization with frequent apoptotic cells, focal pigment incontinence, and mild hyperkeratosis and parakeratosis. There was a mild superficial and deep perivascular infiltrate of lymphocytes and perifollicular chronic inflammation. Direct immunofluorescence from a perilesional skin biopsy revealed patchy granular IgA, IgM, and C3 deposition at the basement membrane zone with no IgG or fibrin deposits identified.

Laboratory evaluation was significant for a positive anti-nuclear antibody (1:640) with a speckled pattern, and a Creatine Kinase within normal limits. Sjogrens Antibody (SSA and SSB) was negative. Aldolase and erythrocyte sedimentation rate (ESR) were within normal limits.

Her complete blood count with differential and comprehensive metabolic panel were unremarkable.

A diagnosis of dermatomyositis was made. The patient was started on prednisone 60mg in the morning with a very slow taper and hydroxychloroquine 200mg twice a day. The patient was referred back to her primary care physician for evaluation of underlying malignancy which was negative. We also asked the physician to discontinue her atorvastatin. She improved gradually. She has been completely free of skin and muscle symptoms for six months.

DISCUSSION

Dermatomyositis is an autoimmune disease that is part of a larger group of inflammatory myopathies including polymyositis and inclusion body myositis. Although many different cutaneous findings have been associated with dermatomyositis, the pathognomonic lesion is violaceous papules or plaques commonly found over the metacarpophalangeal and interphalangeal joints, called Gottron papules. The mechanism driving dermatomyo-
Dermatomyositis is said to be a primarily humoral antibody process where endomysial capillaries are the antigen, leading to the activation of the complement system and the subsequent deposition of the membrane attack complex.\textsuperscript{1-4} Due to the lack of universal diagnostic criteria to differentiate the different disorders that make up idiopathic inflammatory myopathies as a group, epidemiological information is more accurately reported as group data. Recent studies have reported the incidence rates for the group as 4.27 to 7.89 per 100,000 people. Prevalence rates were between 9.54 to 32.74 per 100,000 people.\textsuperscript{7-9} Dermatomyositis is more common in African American women, and it can affect children and adults, which contrasts with polymyositis, which very rarely affects younger individuals.\textsuperscript{10,11} The average diagnosis age of dermatomyositis follows a bimodal distribution with juvenile dermatomyositis occurring most commonly between ages four to 14, and adult dermatomyositis most commonly diagnosed between ages 40-60 years of age.\textsuperscript{12} Juvenile dermatomyositis is the most commonly diagnosed inflammatory myopathy, although still very rare, with an incidence estimated at 3.2 cases per million.\textsuperscript{13} Another recognized subset of patients, called clinically amyopathic dermatomyositis, will have classic dermatomyositis skin manifestations, but do not suffer from myopathy. Based on population-based data, this group makes up at least 20 percent of adults with dermatomyositis.\textsuperscript{14}

A unique characteristic of dermatomyositis that has a large impact clinically is the strong association with malignancy. Specifically, patients diagnosed with dermatomyositis have an increased risk of lung, ovarian, breast, colorectal, cervical, bladder, nasopharyngeal, esophageal, pancreatic, colon, and kidney cancers.\textsuperscript{15} The estimated prevalence of general malignancy in adult patients with dermatomyositis is 20 percent. Furthermore, the patient’s risk of developing cancer is at its peak within a year of diagnosis, and the probability stays elevated up to five years.\textsuperscript{16} Males and patients older than 45 years at diagnosis are at an additional increased risk of developing cancer.\textsuperscript{16,17} Malignancy in association with dermatomyositis is overwhelmingly an adult issue, with no reported cases of juvenile patients in the EuroMyositis registry. Pediatric patients do not require a workup for underlying malignancy upon diagnosis unlike their adult counterparts.\textsuperscript{18}

One tool that physicians can use to risk-stratify patients is myositis-specific antibodies. This was a large focus for the February 2020 continuing medical education (CME) articles in the Journal of the American Academy of Dermatology. In the articles, myositis-specific antibodies were focused on to predict how certain antibody-positivity could predict different systemic manifestations in a highly clinically variable disease such as dermatomyositis. For example, it is known that most malignancy-associated dermatomyositis occurs in patients with either anti-transcription intermediary factor 1, or anti-nuclear matrix protein 2 antibodies.\textsuperscript{18,19} (Another antibody, anti-melanoma differentiation-associated protein 5 (MDA5), is associated with an increased risk of developing interstitial lung disease.\textsuperscript{20} While not yet part of diagnostic criteria, this subject of growing information gives clinicians valuable information that can lead to a cost-effective workup, and more accurate diagnoses by the stratification of dermatomyositis into different subsets.

In the future, myositis-specific antibodies could likely guide treatment plans by personalizing each patient’s treatment based on their specific serology. For example, if a patient was positive for an antibody that was shown to cause more severe disease, it could guide physicians to choose a more robust treatment plan upon diagnosis. The CME successfully outlined the clinically useful applications of myositis-specific antibodies, as well as predicting what the overall treatment of this autoimmune disease could look like in the future. As with all autoimmune disorders, dermatomyositis is thought to develop after an environmental insult triggers a reaction in a genetically predisposed individual. Some of the most common triggers described in literature are ultraviolet radiation, viruses, vaccines, emotional distress, and medications.\textsuperscript{21}

Drug-induced dermatomyositis is not as well described as some other drug-induced autoimmune disease processes, but some of the most commonly cited offending agents are HMG-CoA reductase inhibitors, penicillamine, and hydroxyurea. A 2017 study that aimed to associate common exposures to the likelihood of a dermatomyositis flair found that adult patients that used NSAIDs, blood pressure medications, and psychiatric medications were more likely to flair. Pediatric patients were more likely to suffer from dermatomyositis if they had used NSAIDS or

| TABLE 1. DRUGS COMMONLY ASSOCIATED WITH DERMATOMYOSITIS |  |
| Drug Class | Examples |
| HMG-CoA reductase inhibitors | Atorvastatin, Lovastatin, Pravastatin |
| Chelator | Penicillamine |
| Cytotoxics | Hydroxyurea |
| Local Anesthetic (Amide) | Carticaine |
| Nonsteroidal anti-inflammatory | Niflumic Acid, Phenybutazone |
| Alkylating Agent | Cyclophosphamide |
| Proton pump inhibitor | Omeprazole |
| Vaccine | BCG vaccine |
received the HPV vaccine within six months of disease onset. Numerous other medications have been described in various case reports as seen in Table 1. Treatment of drug-induced dermatomyositis revolves around the prompt removal of the offending agent paired with the current gold standard of idiopathic dermatomyositis care, which is corticosteroids (first line) and other immunosuppressive treatments such as azathioprine, methotrexate, and rituximab (second line).

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