Dermatomyositis – A case based study

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Abstract

Dermatomyositis (DM) is a rare idiopathic inflammatory condition which typically presents in the fourth or fifth decade of life in those affected. Common presenting complaints include proximal muscle weakness, rash, weight loss, and fever. Clinically, the distribution of muscle weakness and the presence or absence of cutaneous manifestations can help differentiate dermatomyositis from other inflammatory myopathies. Diagnostic features including skin biopsy, muscle biopsy, electromyography (EMG) findings, and level of creatinine kinase (CK) elevation in bloodwork can help confirm the diagnosis. In this case, a 55-year-old Caucasian female initially presented to her family doctor with a diffuse erythematous rash. A referral to dermatology prompted further investigations including a skin biopsy and repeat bloodwork. Features suspicious of dermatomyositis on skin biopsy led to further testing including EMG and serial screening of CK levels. Ultimately, a diagnosis of DM was made and the patient was initially managed with topical/oral steroids, and hydroxychloroquine. As the disease progressed, the patient was started on methotrexate and then switched to intravenous immunoglobulin (IVIG) due to intolerance to methotrexate.

Background

Dermatomyositis (DM) is a chronic idiopathic inflammatory condition, typically presenting in individuals in their 40's or 50's (1). Although the mechanism of disease is poorly understood, the disease is recognized as being largely autoimmune in nature. Common signs and symptoms include proximal muscle weakness, myalgia, and muscle atrophy in effected muscles. Frequently affected muscles include the hip flexors, deltoids, and neck flexor muscles (2). Pathognomonic skin features such as Gottron's papules and a heliotrope rash are commonly observed in patients with DM (3). Systemic symptoms such as weight loss and fever may also be present. In some cases, patients may present without signs of muscle weakness or inflammation. In this presentation, DM is more appropriately classified as amyopathic DM, or 'dermatomyositis sine myositis'. The incidence of the disease is approximately 1 in 100,000 persons and is approximately twice as common in females in comparison to males (4).

Dermatomyositis may present in a similar way to other inflammatory myopathies including polymyositis (PM), inclusion body myositis (IBM), and immune-mediated necrotizing myopathy (IMNM). Clinical features such as the distribution of muscle weakness, and presence or absence of skin manifestations can help differentiate DM from other inflammatory myopathies. It is important to recognize that skin manifestation usually precede muscle involvement and thus patients often have normal muscle strength in early stages of the disease. It can take up to one year for patient with DM to develop symptoms of muscle inflammation (1). As mentioned, in cases of dermatomyositis sine myositis, patients may never experience muscle involvement. The presence of skin involvement is a key feature that helps differentiate DM from other inflammatory myopathies. Dermatomyositis is diagnosed using a combination of clinical features and diagnostic testing. The following five criteria are generally used to diagnose DM: (i) muscle weakness in both thighs or both upper arms, (ii) elevated plasma levels of skeletal muscle enzymes including CK, aldolase, glutamate oxaloacetate, pyruvate transaminases, and lactate dehydrogenase, (iii) abnormal electromyogram (EMG) findings, (iv) specific abnormalities visualized from muscle biopsy, and (v) cutaneous manifestations pathognomonic of DM

including a heliotrope rash and Gottron's papules (5). The more criteria that are present, the more likely a patient is to have dermatomyositis. If no dermatologic involvement is present, but the patient fulfills the other criteria, polymyositis is likely. Table 1 summarizes the key differentiating features of dermatomyositis and other inflammatory myopathies with similar clinical presentations.

Table 1. Differentiating features of idiopathic inflammatory myopathies.

Diagnostic features	**Dermatomyositis (DM)**	**Polymyositis (PM)**	**Inclusion body myositis (IBM)**	**Immune-mediated necrotizing myopathy (IMNM)**
Age at onset	40's, 50's	>18 years	>50 years	Adult/ Elderly
Pattern of muscle weakness	Proximal > distal	Proximal > distal	Finger flexors, knee extensors, dysphagia	Proximal > distal
Cutaneous involvement	Heliotrope rash, Gottron's papules	None	None	None
Lab investigations	CK[a] normal or ↑ up 50x	CK ↑ up to 50x	CK normal or ↑ up 10x	CK ↑ >10
EMG findings	Myopathic	Myopathic	Myopathic with mixed potentials	Myopathic
Muscle biopsy findings	Perimysial and perivascular inflammation	Endomysial inflammation	Rimmed vacuoles, endomysial inflammation	Necrotic muscle fibers, mild or absent inflammatory infiltrate

Data adapted from references (1–6)
[a] Creatinine kinase

Once a diagnosis of dermatomyositis is made, initial investigations, if not already conducted, should include pulmonary function tests (PFT's), electrocardiogram (ECG), Chest X-ray, Barium swallow studies, and muscle MRI or ultrasound of the deltoid to quantitate muscle destruction (1). Bloodwork including complete blood counts (CBC), creatinine kinase (CK), aldolase, aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH), creatinine, anti-nuclear antibody (ANA), extractable nuclear antigen (ENA), rheumatoid factor (RF), thyroid stimulating hormone (TSH), and tumour markers, including CA-125, should be followed throughout treatment (1).

Dermatomyositis is managed with oral/topical steroids for acute flares, and immunomodulation agents including methotrexate and azathioprine for long-term therapy (2). Generally, a regimen of 1 mg/kg/day x 1-3 months with a slow taper or methylprednisolone 500-

1000mg IV/day x 3-4 days followed by oral prednisone is recommended to treat acute flares for patients with DM with muscle weakness (2). Second line therapies include methotrexate 7.5 mg PO weekly, increasing by 2.5 mg weekly to 20 mg PO weekly as needed; with folic acid 1 mg daily except on day of methotrexate (2). Other second line therapies include intravenous immunoglobulin (IVIG) 0.4 grams/kg/day x 5 days each month or 1 gram/kg/day every 2 weeks (2). Azathioprine 1-3mg/kg/day can also be used. In patients with skin involvement lacking muscle involvement, topical agents such as hydroxychloroquine are recommended (2).

Case presentation

Overview

A 55-year-old Caucasian female with a history of hypertension and hypothyroidism, presented to her family physician with a diffuse erythematous rash that had been present for one month. Initial bloodwork was unremarkable. A referral to dermatology prompted a skin biopsy which exhibited characteristics suspicious of dermatomyositis. EMG test results were suggestive of a myopathy consistent with an inflammatory muscle disease such as dermatomyositis. The patient was ultimately diagnosed with dermatomyositis and treated for acute cutaneous flares with topica/oral prednisone and hydroxychloroquine. Serial CK measurements began to show signs of myositis, at which point the patient was prescribed methotrexate. After failure with methotrexate, symptoms were ultimately managed on IVIG.

History

The patient's history was gathered from the patient's chart.

This 55- year old mother of four, lives at home with her husband and children with no pets in the home. She works as a nurse at a personal care home. At initial presentation, the patient reports a one month history of a rash present on her arms, legs, and abdomen. She describes the rash as painful and burning, however, there is no discharge or bleeding from the rash. The patient has no allergies to foods, molds, pollen, or other known allergens. She does not report contact with any new exposures including cosmetics, detergents, etc. The patient's only medications are levothyroxine for hypothyroidism and hydrochlorothiazide and amlodipine for hypertension.

Physical exam

The dermatologic exam revealed the following as presented by the consulted dermatologist: Confluent erythema over the face with fine white scale on the surface predominant in the per auricular area and at the anterior hairline. The facial rash is strikingly photo-distributed, extending onto the neck in a V shape. There is also marked poikiloderma present over the cheeks and nose. The extensor of the arms reveals 2 mm erythematous, scaly papules coalescing into reticulate plaques. There is a large plaque of linear coalescing papules over the left lateral hip covering an area of approximately 10 cm squared. Examination of the periungual area reveals dilated and tortuous capillaries at the proximal nail folds with increased erythema in these areas. The DIPs and PIPs also reveal areas of violaceous papules coalescing into plaques with extension on the interdigital web spaces. There are no oral lesions. The clinical findings of the

Shawl sign, Holster sign, poikiloderma along with changes on the dorsal hands consistent with Gottrons papules and periungal telangiectasia support a diagnosis of dermatomyositis.

On initial presentation, an MSK exam did not demonstrate any muscular weakness in the upper arms or legs.

Laboratory investigation
Bloodwork at initial presentation was unremarkable.

Bloodwork at onset of muscle weakness:
WBC – 5 (normal)
HgB – 155 (normal)
Ferritin: 137 (normal)
TIBC – 51 (normal)
Iron saturation – 48% (normal)
ESR elevated - 30 (normal)
C reactive protein – 7 (high)
ANA – slightly elevated
ALT - 55 (high)
AST – 23 (normal)
GGT – 30 (normal)
ALP - 77 (normal)
LD: 235 (high)
Albumin – 48 (normal)
CK: 255 (high)

Skin biopsy report:

3 skin biopsies were ordered:

1) Left lateral hip for hematoxylin and eosin stain (H and E): The specimen consists of a 0.4 cm tan punch biopsy with underlying tissue to a depth of 0.4 cm. Complete specimen put through – 1 cassette (1 piece).
2) Left lateral elbow: The specimen consists of a 0.4 cm tan punch biopsy with underlying tissue to a depth of 0.4 cm. Complete specimen put through – 1 cassette (1 piece).
3) Left lateral hip for DIF: forwarded to Dynacare, Dept of Pathology.

Microscopic description:

1) Sections of skin show a mild perivascular lymphocytic infiltrate within the superficial and mid dermis. Very rare eosinophils are noted. Scattered telangiectatic blood vessels are observed. Very focally a few lymphocytes are noted at the dermal-epidermal interface, however, associated basal layer degenerative changes are not evident. Thickening of the epidermal basement membrane is not observed. The epidermis is of approximate normal thickness with compact hyperostosis. Minimal follicular plugging is noted. Special stains for fungal organisms are negative. There may be a very slight increase in connective tissue mucin. Although some features suggest a connective tissue

disease resembling dermatomyositis, the lack of established interface inflammation precludes a definite diagnosis. Correlation with clinical finding and other investigations required.

2) Sections of skin show similar findings to that of specimen 1. Additionally, a hint of perifollicular inflammation is noted and there appears to be more convincing increase in connective tissue mucin. The interpretation is same as specimen 1. Findings suspicious but not diagnostic of dermatomyositis
3) IgG Negative, IgA negative, IgM negative, C3 Negative
No fluorescence pattern characteristic of any particular cutaneous immunologic disorder is identified.

EMG report:

The EMG findings recorded indicate unequivocally that this patient is subject to a structural myopathy, and although positive evidence of inflammation is not recorded, this is commonly the case with inflammatory muscle pathologies that are not exuberantly active, so that the absence of positive evidence of muscle inflammation only dictates that exuberantly active inflammation is not present. Conversely, the EMG findings recorded might reflect any of a range of structural muscular pathologies, so that they are best regarded as consistent with, but not diagnostic of an acquired myopathy, and particularly an inflammatory muscular pathology such as dermatomyositis.

Discussion

Dermatomyositis can be an elusive diagnosis for a variety of reasons. In early stages of the disease, muscle weakness and systemic symptoms may be quiescent. Patient often present solely with, what appears to be, a diffuse maculopapular rash. To add to the difficulty, patients often have normal bloodwork at the onset of the disease. These features make misdiagnosis in the early stages of this condition quite common. In this case, the patient presented initially with skin involvement and absence of muscle pain or weakness. Bloodwork taken at this time was unremarkable. The patient was prescribed topical corticosteroids for which she reported temporary relief. When the rash recurred, the patient was given a consult to a dermatologist for further assessment.

Being mindful of certain distinct cutaneous features of dermatomyositis can benefit general practitioners and specialists in making an early diagnosis. One key feature is that of photo-distributed poikiloderma (1). This feature is characterized by telangiectasias, hyper/hypopigmentation, and atrophy of skin in areas which are exposed to sunlight; commonly the upper back and chest (1). These signs are colloquially referred to as the Shawl sign (present on the upper back), and the V-neck sign (present on the chest). Skin lesions are also prominent on extensor surfaces including elbows, knees, MCP, PIP, and DIP surfaces (1). Other cutaneous features include changes in the nail folds including cuticle dystrophy (i.e. ragged cuticles), nail fold telangiectasias, and dilated capillary loops (1). Gottrons papules which are red or violet papules observed over the MCP, PIP, and DIP joints are also typical (1). Eyelid edema, a rash

around the eyelids (known as a heliotrope rash), and a violaceous rash over the upper hips (known as Holsters sign) can also be observed (1). In this case, the patient presented with several of these features including Shawl sign, Holster sign, Gottrons papules, prominent poikiloderma on the dorsal aspect of the hands, and cuticle changes including telangiectasias on both hands.

Initial workup of the patient as ordered by the dermatologist included a skin biopsy. The results of the skin biopsy were highly suggestive but not diagnostic of dermatomyositis. The clinical features of the skin rash coupled with the results of the skin biopsy were sufficient to treat the patient for amyopathic dermatomyositis. The patient was managed with hydroxychloroquine and oral prednisone in cases of acute flares. An EMG and serial CK measurements were advised to screen for myositis. About one year after the onset of the disease, the patient began to present with some proximal muscle weakness in her hip flexors. She described this as a difficulty getting up from a seated position. At this time, an EMG was ordered. EMG results indicated myopathic features which were consistent with an inflammatory myopathy including dermatomyositis. The patient was initially managed on methotrexate, however, due to concerns of aminotransferase elevation in her bloodwork she was switched to intravenous immunoglobulin (IVIG). She was advised to undergo a thorough malignancy screen and cardiac/pulmonary testing.

Literature suggests that patients with DM are at increased risk of malignancy, cardiovascular disease, and respiratory disease (1). Multiple studies report the incidence of malignancy in patients with dermatomyositis to be 15-25% (1). Patients with classic DM or amyopathic DM are both at increased risk of malignancy (1). Polymyositis and juvenile onset forms of DM do not carry an increased risk of malignancy (1). Common cancers affecting those with DM include ovarian, colon, breast, lung, gastric, pancreatic, and lymphomas (1). Guidelines suggests that patients have CT scans of the chest, abdomen and pelvis as part of initial malignancy screening in patients with DM (6). Transvaginal pelvic ultrasound is also recommended in women as part of initial screening (6). The value of repeat cancer screening in patients with DM is not well established (6). Literature suggests that the risk of malignancy gradually declines five years after the onset of the disease (6). Thus, continued imaging for malignancy is generally not advised unless symptoms develop (6). Cardiovascular disease in patients with DM typically presents with conduction defects including arrhythmias (1). 15-20% of patients with DM will develop interstitial pulmonary fibrosis (1). Routine ECG's, chest X-rays, and PFTs are recommended in patients with a diagnosis of DM (1).

Recommendations

Early detection and diagnosis of dermatomyositis is crucial. Awareness of the various cutaneous manifestation of the disease can be helpful in early diagnosis. Laboratory investigations may be normal at onset of the disease. A skin biopsy, muscle biopsy, and EMG results can be used to help confirm a diagnosis. Once diagnosis is confirmed, corticosteroids and immune-modulating agents are the cornerstone of therapy. Screening for malignancy, cardiovascular disease, and pulmonary disease is recommended once diagnosis is made.

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