

CLINICAL MANAGEMENT RECOMMENDATIONS

Meeting the Challenges of the Dermatomyositis Workup: A Management Paradigm

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Dermatomyositis (DM) is a rare inflammatory myopathy with characteristic skin manifestations. This multisystem disorder is characterized by an increased frequency of pulmonary disease and malignancy. It has a female to male predominance of 2:1, with an average age at diagnosis of 40 years [1]. Diagnosing DM can be challenging due to the heterogeneity of presentations and clinical features that may overlap with other disorders. Although DM has had an established diagnostic criteria by Bohan and Peter since 1975, groups have re-examined the criteria to highlight the importance of skin findings [2-4]. This article will discuss the process of working-up dermatomyositis in an adult from a dermatologist's point of view (Appendix 1).

WHAT ARE THE CUTANEOUS MANIFESTATIONS?

Patients often exhibit skin manifestations first, which emphasizes the importance of dermatologists in recognizing the specific skin findings. In fact, skin manifestations precede myositis in the vast majority of patients. Most of these patients develop symptoms of myositis within 3-6 months, but it may take up to 2 years for these symptoms to appear [5]. In addition, about 10% of DM's

patients exhibit skin limited disease, known as amyopathic dermatomyositis [3].

Gottron's papules/sign are pathognomonic findings of DM [2]. They are defined as erythematous to violaceous papules or macules, maybe with scale, that occur symmetrically over the extensor surfaces of joints, such as the metacarpophalangeal joints, elbows, and knees. This finding is present in two third of DM patients and may mimic the appearance of some papulosquamous diseases, such as psoriasis [1]. Heliotrope eruption is the most specific skin finding but is present in only half the patients [1]. It is defined as an erythematous to a violaceous patch on the upper eyelids that can present with periorbital edema.

Characteristic findings include facial erythema and photo distributed poikiloderma, including the V and shawl sign. These findings may mimic cutaneous lupus erythematosus (CLE), especially earlier in the presentation when poikiloderma appears as erythema. Nasolabial involvement in facial erythema can be helpful in distinguishing DM from CLE's malar rash. Holster sign is poikiloderma that occurs on the photoprotected area of the lateral thighs. Difficulty in detecting erythematous rashes in non-Caucasian patients leads to delayed diagnosis and misrepresentation of disease

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severity [4]. Palpation of the cutaneous findings can help detect the presence of blanchable erythema.

Periungual changes, such as erythema, telangiectasias, and cuticular hypertrophy, are common in DM but can resemble other connective tissue diseases such as scleroderma. Dilated capillary loops can be seen on dermoscopy and may reflect disease activity [4]. Pruritus often is a significant complaint for these patients and can be one of the first symptoms to develop [3]. Scalp erythema and pruritus can be severe and should warrant evaluation for DM. Non-scarring diffuse alopecia of the scalp may occur. Mechanic hands, defined as hyperkeratosis of the lateral fingers and palms, flagellate erythema, and follicular hyperkeratosis are uncommon compatible findings of DM and is associated with antisynthetase syndrome. Flagellate erythema is rare and also can be seen in Still's disease, bleomycin-treatment, and Shiitake mushroom dermatitis. Panniculitis, lipodystrophy, vesiculobullous eruptions and calcinosis cutis are rarely seen in adult DM patient but are strongly associated with juvenile DM.

WHAT TO LOOK FOR WHEN PERFORMING HISTORY AND PHYSICAL EXAM

Patients may present with general complaints such as weakness or fatigue, resulting in an extensive differential. Therefore, a thorough history is essential when it comes to diagnosing DM. The duration, mode of onset, and location need to be identified. Questions regarding daily activities such as climbing stairs, hair grooming, or shaving can be utilized to localize the weakness. A history of recent infections, previous malignancies, travel, and family history can further aid in narrowing the differential. Obtaining a

medication list is crucial as some medication such as d-penicillamine, statins, sulfonamides, isoniazid, tamoxifen, chlorpromazine, antazoline, and phenylbutazone are known to cause a DM-like syndrome [4]. In addition, long-term hydroxyurea use may cause DM-like eruptions [4]. A complete review of systems can detect possible malignancy or one of the systemic features of DM such as dysphagia, arthralgia, or pulmonary involvement.

A general physical exam should emphasize the skin, neurological and musculoskeletal systems. The musculoskeletal exam may identify the pattern of weakness and the extent of muscle involvement. Typically, DM symmetrically affects the proximal muscle groups of the shoulder and pelvic girdle. However, in progressive disease all muscles may become involved. The neurological exam is central to help distinguish between myopathic and neuropathic etiologies, which may present with overlapping clinical features.

WHAT IS THE UTILITY OF AUTOANTIBODIES?

Autoantibodies are classified into two groups: myositis associated autoantibodies (MAA) and myositis-specific autoantibodies (MSA). They are useful in predicting the course of the disease as patients with a particular antibody tend to exhibit homogeneous clinical features [6]. Therefore, it is recommended to obtain autoantibodies, which are available as send-out labs at most institutions. Table 1 discusses the significance of the most common autoantibodies identified in DM patients. There have been strong suggestions to incorporate MSA into the diagnostic criteria as their specificity exceeds 90% and they have a high cumulative sensitivity of 70-80% [6, 7].

Table 1: Common myositis specific autoantibodies in DM and their clinical characteristics [6, 7]. Idiopathic inflammatory myopathies (IIM); Juvenile DM(JD); Interstitial lung disease (ILD). Melanoma differentiation-associated gene 5 (MDA5); Nuclear matrix protein-2 (NXP-2); Small ubiquitin-like modifier activating (SAE); Signal recognition particle (SRP); Transcriptional intermediary factor-1 γ (TIF-1 γ).

Autoantibody	Frequency	Clinical characteristic
Antisynthetases: Anti JO-1, PL-7, PL-12, anti EJ, anti OJ, anti KS, anti Zo, anti Ha	Anti JO-1 is present in up to 40% of adults with IIM	-Antisynthetase Syndrome (a constellation of interstitial lung disease, myositis, polyarthritis, Raynaud's phenomenon, fever, and mechanic's hands)
Anti-SRP	4-13%	-Necrotizing myopathy -High risk of cardiac involvement
Anti-TIF-1 γ	Up to 40% of patients with JD	-JD -Increased cancer risk in adults
Anti- NXP-2	Up to 5% of adults Up to 30% of JD patients	-Increased cancer risk in adults - Increased calcinosis in JD
Anti- SAE	Up to 9% of adults	Increased cancer risk in adults
Anti-MDA5	7-48% of adults	Amyopathic DM Rapid ILD

WHAT LAB STUDIES SHOULD BE ORDERED?

Elevation of any of the following muscle enzymes: creatine kinase, aldolase, aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase can be used to support the diagnosis of dermatomyositis [2]. Patients may have at least one elevated muscle

enzyme, though cases of amyopathic DM or significant loss of muscle mass are exceptions [8].

Creatine kinase is very specific to skeletal muscle and is the most common serum marker used to diagnose and monitor the disease progression. Although the levels can vary significantly, they are usually 10 folds higher than the normal level [9]. Aldolase is the most sensitive enzyme and is elevated in more than 60% of patient in various stages of DM [10].

Erythrocyte sedimentation rate (ESR) elevation is not specific and is only present in 50% of DM patients [11]. It cannot be used for diagnosis but might be useful for monitoring the progression of muscle inflammation and response to treatment [11, 12]. Furthermore, recent studies have suggested ESR's potential to screen for pulmonary involvement [12]. A complete blood count may detect a high white blood cell count and a low lymphocyte count, especially in males. Also, low albumin and hematocrit can be found due to the inflammatory process [10]. Antinuclear antibody is found in 2/3 of DM patients, but is not specific and have not shown to influence the prediction of the course of the disease [11].

OTHER DIAGNOSTIC STUDIES

Electromyography (EMG) is particularly useful to differentiate between neuropathic and myopathic etiologies and for selecting the highest yield site for possible muscle biopsy. Abnormal findings consistent with DM include a short, small, polyphasic motor unit potentials; fibrillations, positive sharp waves, and insertional irritability; and bizarre, high-frequency repetitive discharges. These abnormal findings are detected in almost 90% of DM patients with muscle involvement

[8]. EMG may elevate muscle enzymes; therefore, muscle enzymes should be obtained prior to performing EMG.

Magnetic resonance imaging (MRI) can demonstrate the extent of muscle involvement and identify the best site for muscle biopsy if needed. However, the changes seen on MRI are not specific to DM. Skin biopsy is performed when evaluating for

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amyopathic DM or to help differentiate DM from other papulosquamous diseases. However, if the clinical findings are consistent, it is not necessary for diagnosis. Skin biopsy is not reliable in distinguishing DM from CLE. A skin biopsy of DM lesions classically demonstrates vacuolar interface dermatitis with mucin deposition in the dermis.

Muscle biopsy can be obtained but is not always necessary. Infrequently, myositis may precede the cutaneous findings. A closed needle biopsy is preferred as it allows for a larger sample while preserving the orientation of muscle fibers. Abnormal findings consistent with DM include perifascicular atrophy, predominant inflammatory infiltrate of CD4+ cells, and the overexpression of type I interferon-inducible genes.

ADDITIONAL RECOMMENDED SCREENING TESTS

In patients newly diagnosed with DM, further studies are indicated based on the presences of clinical evidence of other organ involvement, such as cardiac, pulmonary, or esophageal disease. However, all patients must undergo screening for malignancy at the time of diagnosis. The evaluation

includes a comprehensive history and physical examination. Diagnostic studies to obtain include: complete blood count, liver function tests, kidney function tests, urinalysis, age and gender appropriate cancer screenings such as mammography, colonoscopy, and pap smear, fecal occult blood if colonoscopy is not indicated, pelvic and breast examination and pelvic ultrasound for women, and prostate examination for men. In addition, most experts recommend pulmonary function tests with diffusion capacity (PFTs with DLCO) and CT with IV contrast of the chest, abdomen, pelvis [13, 14]. Providers should include the request to assess for interstitial lung disease in the CT orders. Further work-up is indicated if any of the above tests yields an abnormal result.

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Appendix 1: An overview of DM work-up.

