Current management of dermatomyositis

Dermatomyositis (DM) is a rare chronic autoimmune condition characterized by proximal muscle weakness, characteristic skin lesions and frequently, specific autoantibodies. Involvement of other organ systems, particularly the lungs, is usual and the condition is associated with malignancy in a significant proportion. The morbidity and mortality associated with DM remains high, despite the availability of a large number of therapeutic agents. Over the recent years, considerable progress has been made in the diagnosis and classification of these patients, particularly in the area of myositis-specific antibodies, which has provided further insight into the etiopathogenesis of this complex disease. Advances made in imaging techniques, especially MRI, have enhanced the diagnostic pathway in DM and provided novel means of monitoring disease activity and response to treatment. Although a number of exciting therapeutic trials are underway, the evidence base for the treatment of DM is found wanting. The aim of this review is to give an update on the approach to management of DM.

KEYWORDS: antisynthetase syndrome ▪ cancer-associated myositis ▪ dermatomyositis ▪ idiopathic inflammatory myopathies ▪ myositis

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Release date: 3 April 2012; Expiration date: 3 April 2013

Learning objectives

Upon completion of this activity, participants should be able to:

- Describe the clinical features of dermatomyositis, based on a review
- Describe the diagnostic evaluation of patients with suspected dermatomyositis, based on a review
- Describe the treatment of patients with dermatomyositis, based on a review

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Financial & competing interests disclosure
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Dermatomyositis (DM), one of the idiopathic inflammatory myopathies (IIM), is a chronic autoimmune condition characterized by the subacute onset of symmetrical proximal muscle weakness and muscle inflammation, accompanied by distinctive skin lesions and specific autoantibodies. In some cases, pathognomonic skin changes may exist in the absence of muscle disease – a disease subtype known as clinically amyopathic DM (CADM). As with other autoimmune conditions, DM is more common in females. Estimates of incidence range from 5 to 8.9 cases per million population per year, with onset typically during the 4th to 6th decades and 5-year survival rates of 75–90% [1]. Juvenile DM is recognized as the most prevalent IIM in children [2]; however, his review will focus on the management of adult DM, which should begin with a thorough investigation of the presence and extent of muscle disease, presence of other organ system involvement and the possibility of underlying malignancy [3].

Clinical features

Clinical features at presentation typically include proximal muscle weakness and/or skin rash [4]. Other presenting features may include constitutional symptoms (fever, night sweats, weight loss and fatigue), myalgia, arthralgia or arthritis, Raynaud's phenomenon or respiratory symptoms suggestive of pulmonary involvement. Occasionally, GI tract vasculitis may develop, manifesting as abdominal cramps, pancreatitis, bleeding or perforation, although this is more usual in juvenile DM. Gastrointestinal involvement more commonly manifests as dysphagia and abdominal pain.

Muscle weakness

Muscle weakness affects proximal muscles in a symmetrical fashion, and may develop insidiously, or be absent at the time of diagnosis [1]. Lower limb weakness usually manifests as difficulty climbing stairs and standing from a seated position, while proximal upper limb weakness makes overhead activities, such as combing and washing hair, troublesome. Fatigue and reduced endurance are frequently reported and, in severe cases, weakness of esophageal and respiratory musculature may occur, resulting in dysphagia, dysphonia, dyspnea and rarely, respiratory failure [1]. Recent work investigating hand function in patients with long-standing polymyositis (PM) and DM found that these patients have significantly lower grip force (distal strength) than controls and that this may negatively influence their ability to perform activities of daily living and their health-related quality of life [5].

Cutaneous features

Cutaneous features may include generalized photosensitive erythema in sun-exposed areas, Gottron's papules (raised erythematous papules over extensor surfaces) or a heliotrope rash (violaceous eruption affecting the periorbital region), with the latter two being pathognomonic for the condition. 'Mechanic's hands' (hyperkeratotic, fissured skin on the lateral fingers and palms) may be a feature of a subset of myositis patients with antisynthetase antibodies [1]. Periungual erythema and irregular, thickened cuticles may be obvious clinically, while associated small-vessel inflammation may be indicated by dilated capillary loops seen on nail-fold capillaroscopy [3]. Cutaneous ulcers may develop if vasculitis is more severe. While the cutaneous lesions of DM are photodistributed and frequently photoaggravated, they may also be accompanied by pruritus, a feature that may be of use clinically in distinguishing the skin lesions from those seen in systemic lupus erythematosus (SLE). Other cutaneous manifestations may include panniculitis, erythroderma and alopecia, which may be diffuse or patchy and accompanied by erythema. Cutaneous lesions frequently precede

the onset of muscle weakness, but they may be the only manifestation of disease in a significant proportion of DM patients. CADM, historically referred to as DM siné myositis, is defined as the presence of typical cutaneous features in the absence of evidence of muscle inflammation (normal muscle strength and muscle enzymes) for at least 6 months [6]. It is estimated that 10–20% of DM patients seen in academic centers have amyopathic disease [7]. Furthermore, a substantial number of patients with treated DM will continue to suffer active skin disease even after the myopathic element has stabilized. These patients may be categorized under the term 'postmyopathic DM' and frequently have skin disease that is difficult to manage [8].

Calcinosis is a rare finding in adult DM, but is reported in up to 30% of cases of juvenile DM. Even less common is lipodystrophy, characterized by progressive loss of subcutaneous and visceral fat. Occasionally, patients with biopsy-proven DM present without any cutaneous features (DM siné dermatitis); however, this scenario is rare, and may be because the skin lesions were transient or difficult to recognize (e.g., in dark-skinned people) [3].

Other organ involvement

Pulmonary involvement, in the form of interstitial lung disease (ILD), occurs in a third to half of adults with DM, usually in the context of antisynthetase antibodies such as anti-Jo1, and carries a significant mortality risk. Interestingly, patients with ILD may have little or no muscle or skin disease, and this lack of correlation between pulmonary and other more obvious symptoms may lead to a delay in diagnosis and reduced therapeutic gains [9]. While the prevalence of ILD in PM and DM is similar, it has been suggested that patients with DM and CADM may run a more severe clinical course, and are more likely to have resistant disease with a worse prognosis and higher mortality. Interestingly, lung involvement is rare in juvenile dermatomyositis (JDM) [9]. The spectrum of presentation of ILD in DM is wide, from asymptomatic basal fibrosis to rapidly progressive disease associated with adult respiratory distress syndrome. The most common symptoms are cough and dyspnea, which are often progressive and associated with reduced functional capacity. Chronic respiratory failure, requiring long-term supplemental oxygen, may be the end result. While ILD is an important consideration in these patients, similar symptoms can be due to other related pathologies, including respiratory muscle weakness, infection, aspiration pneumonitis, cardiac involvement, pneumothorax and pneumomediastinum [9].

Some form of cardiac involvement, including pericarditis, myocarditis, conduction abnormalities, myocardial infarction and heart failure, is thought to occur in a significant proportion of adults with DM [1]. Although clinically significant cardiac muscle involvement is infrequent, cardiovascular disease is a leading cause of death in myositis. An estimated 10–20% of deaths are directly attributable to cardiac disease, in particular myocardial infarctions, which occur 16-times more frequently than in the general population [10]. It is likely that the development of cardiac disease in DM is multifactorial – related to chronic inflammation and associates, atherosclerosis, inflammation of cardiac muscle itself and possibly the consequence of treatment [1].

Associated malignancy

The link between DM and malignancy is well established. The largest population-based study in this field demonstrated the presence of malignancy in 32% of DM patients, with a standardized incidence ratio of 3.0 compared with the rest of the population [11]. In 58% of cases, the malignancy was discovered after the diagnosis of DM was made, usually within the first year. Ovarian malignancy was the most common, followed by lung, GI tract and breast cancers, and non-Hodgkin's lymphoma. DM patients were found to be at an increased risk of malignancy, even 5 years after the diagnosis was made.

Investigations

Laboratory tests

Elevated muscle enzymes are found in the majority of patients, but these parameters may be normal in those with CADM. Creatine kinase is the most sensitive, but alanine transaminase, aspartate aminotransferase, aldolase and lactate dehydrogenase may also be elevated [12]. It must be remembered that these markers can be elevated in other conditions, including myositis mimics, and that elevated serum creatine kinase may be a normal finding in some population groups (e.g., Afro–Caribbean populations).

Comprehensive autoantibody testing that encompasses recently reported autoantibody specificities yields positive results in approximately 80% of DM cases [13]. A third test positive for antinuclear antibodies, and the presence of other myositis-associated antibodies, such as anti-U1RNP, anti-PM/Scl, anti-Ro, anti-La and anti-Ku, may indicate the existence of an overlapping connective tissue disease. A large

number of myositis-specific autoantibodies have been identified, and are divided into three main groups: antisynthetase antibodies, anti-signal recognition particle (SRP) antibodies and anti-Mi2 antibodies (Table 1). The 'antisynthetase syndrome', characterized by mechanic's hands, Raynaud's syndrome, ILD, arthritis and fevers, is associated with the anti-aminoacyl-tRNA synthetase antibodies including anti-Jo1 (most common), anti-PL12, anti-PL7, anti-EJ, anti-OJ, anti-KS, anti-Ha and anti-Zo [14]. Anti-SRP antibodies, although more frequently associated with severe acquired necrotizing myopathies, have been documented in DM [1]. Anti-Mi-2 antibodies are associated with adult and juvenile DM with classical cutaneous features. Myopathy tends to be less severe, frequency of ILD is lower and response to treatment is typically good in this group [14]. Clinically significant novel autoantibodies including anti-CADM140 (also known as anti-MDA5), anti-p155 (also known as anti-p155/140 or, more correctly, anti-TIF1-γ), anti-p140 (also known as anti-MJ or anti-NXP2) and anti-SAE (small ubiquitin-like modifier activating enzyme) have been described in both adult and juvenile myositis [13]. Anti-CADM140 antibodies have been described in a cohort of Japanese patients with CADM and rapidly progressive ILD [15]. Anti-p155 antibodies have recently been described in DM and are associated with malignancy in this population. A recent meta-analysis determined anti-p155 to have a sensitivity of 78%, specificity of 89% and negative predictive value of 95% for cancer-associated myositis, endorsing its importance as a diagnostic and prognostic tool [16]. Anti-SAE was recently reported in a subset of adult patients with DM who appear to present with CADM initially, but go on to develop myositis with significant systemic features, and have a low risk of ILD [14]. Anti-p140, although more frequently associated with JDM and calcinosis,

Table 1. Myositis-specific antibodies in adult dermatomyositis.

Autoantibody	Frequency in dermatomyositis (%)	Clinical association
Antisynthetase antibodies		
All antisynthetases	30–40	Antisynthetase syndrome
Anti-Jo1	15–20	
Anti-PL12	<5	
Anti-PL7	<5	
Anti-EJ	<5	
Anti-OJ	<5	
Anti-KS	<5	
Anti-Ha	<1	
Anti-Zo	<1	
Other MSAs		
Anti-Mi2	<10	Hallmark cutaneous features, milder myopathy, low risk of ILD, good response to treatment
Anti-SRP	5–10	Necrotizing myopathy
Novel myositis autoantibodies		
Anti-p155 (anti-TIF1-γ)	13–21	Malignancy
Anti-CADM140 (anti-MDA5)	50–73 (Asian cohorts; not found in Caucasian individuals)	CADM and rapidly progressive ILD
Anti-SAE	<5	Initial CADM, later myositis with systemic features, low risk of ILD
Anti-p140 (anti-NXP2)	<5	ILD and hallmark cutaneous features

CADM: Clinically amyopathic dermatomyositis; ILD: Interstitial lung disease; MSA: Myositis-specific antibody; SRP: Signal recognition particle.

has been demonstrated in approximately 5% of European adult DM patients, and appears to be associated with hallmark cutaneous features and ILD [13].

Imaging

MRI is perhaps the most useful imaging modality in the assessment and management of myositis. During the diagnostic work-up, MRI can demonstrate the presence and distribution of muscle inflammation and edema, and may show abnormalities even in clinically amyopathic patients [17]. Establishing sites of maximal involvement enables guided muscle biopsy to be performed, improving the sensitivity of this test [18]. Apart from detecting inflammatory changes, fatty infiltration (a sign of preceding muscle inflammation), subcutaneous reticulation, calcification and signs of steroid myopathy may also be obvious. MRI may also be useful in monitoring disease activity and response to therapy [17]. Ultrasonography of muscles has been suggested, but is not widely practiced. The obvious benefits of this approach are its relatively low cost and accessibility. In some centers, contrast-enhanced ultrasound allows evaluation of muscle vascularization and perfusion, which may aid in differentiating acute from chronic changes in symptomatic patients [19]. PET detects increased muscle metabolism and can accurately localize areas of muscle inflammation. In addition, it can be used to screen for underlying malignancies and localize occult infections in the unwell, immunosuppressed patient [20,21]. Plain radiographs can be useful to demonstrate calcinosis, which usually develops at sites of previous inflammation. In addition, radiographs of the chest may show evidence of overt ILD, infection or an underlying malignancy. While these have limited sensitivity and specificity in the diagnosis and monitoring of ILD, high-resolution computed tomography (HRCT) is highly sensitive and is the modality of choice for detection and characterization of ILD [22]. Nonspecific interstitial pneumonia is the most common histopathological pattern in DM-associated ILD, and typical features of this (or other types of ILD) on HRCT may obviate the need for more invasive diagnostic tests, such as bronchoscopy and lung biopsy [22].

Electromyography

An electromyogram may be helpful in the diagnosis of DM, although normal findings do not exclude a myopathy. Specific abnormalities expected in myopathic illnesses include: a reduction in the duration of action potentials, reduced area:amplitude ratio, increased spontaneous activity with fibrillations, positive sharp waves and early recruitment. Typically, there is evidence of muscle irritability [23]. Electromyogram may also be helpful to distinguish neuropathic and neuromuscular junction causes of weakness from myopathic disease.

Muscle biopsy

Both open and needle muscle biopsies can be helpful in diagnosing DM. As this is a rare condition, and histological features may be subtle, it is recommended that a pathologist experienced in neuromuscular diseases examines the tissue sample. The hallmark histopathological feature of DM is atrophic, degenerating and regenerating muscle fibers in a strongly perifascicular distribution [4]. Perivascular inflammatory infiltrates are also characteristic, although this finding is less specific [4].

Skin biopsy

Skin biopsy may be considered in cases of amyopathic DM. Typically, a paucicellular interface dermatitis is demonstrated, which is difficult to distinguish from that seen in SLE. Other features, such as vacuolar change within columnar epithelium and lymphocytic infiltration at the dermoepidermal junction may be observed, but these are not specific for DM [4].

Other tests

Other investigations may be necessary depending on the patient's presentation. In addition to HRCT, pulmonary function tests (PFTs) are useful to further investigate ILD. A restrictive pattern is typical, with reduction in lung volumes and gas transfer and elevated forced expiratory volume in 1 s:forced vital capacity ratio [9]. Respiratory muscle weakness can also cause perturbations in pulmonary function testing, making the interpretation of these studies challenging. Subtle abnormalities, such as increased residual volume with a normal forced expiratory volume in 1 s:forced vital capacity ratio and reduced maximum voluntary ventilation, may be of use in distinguishing respiratory muscle weakness from ILD [24]. PFTs may be normal in early disease or when coexisting obstructive pathologies exist, such as smoking or asthma.

In some cases, more invasive tests may be required. Bronchoscopy and bronchoalveolar lavage (BAL) is useful to exclude other pathologies such as infection, malignancy and drug hypersensitivity, and in patients with ILD

who deteriorate while on immunosuppressive treatment [9]. Lung biopsy (surgical or transbronchial) may be necessary if the diagnosis remains unclear despite other less invasive investigations. This modality is useful to exclude infection and malignancy and, if ILD is confirmed, may be of use in determining severity and predicting prognosis and responsiveness to treatment [25]. A number of biomarkers of ILD activity and severity have been investigated in research settings, but none are used in routine clinical practice. Krebs von den Lundgen-6, cytokeratin-19 and chemokines such as CXCL9 and CXCL10 are examples [9].

An ECG should be obtained at baseline on all patients to screen for subclinical cardiac involvement, including arrhythmias, conduction defects and ST-T changes [10]. An echocardiogram should be obtained if clinically indicated. Gadolinium-enhanced cardiac MRI can detect areas of myocardial inflammation more reliably than ECG and echocardiogram and is sensitive to change, and therefore useful in monitoring the response to treatment [26]. Endomyocardial biopsy has been used to confirm the presence of myocarditis, but is not routinely used in clinical practice [10].

Barium swallow, esophageal manometry and/or esophagogastroscopy may be indicated if esophageal involvement is suspected.

Nailfold capillaroscopy is a useful adjunct to detect microvascular changes associated with DM and other connective tissue diseases. Pathological changes including enlarged and tortuous capillaries, hemorrhages and capillary loss may be evident. It has recently been suggested that these findings may be associated with disease activity, as reduction in nailfold abnormality scores was noted when the underlying disease was stabilized. This test may therefore have a role in monitoring response to treatment [27].

Screening for malignancy

No consensus guidelines exist directing the use of screening tests for malignancy in DM and the evidence base in this area is mostly anecdotal. Some clinicians may favor a limited approach, based on history, careful examination, routine blood and urine tests, fecal occult blood and chest radiograph, with other tests only if clinically indicated [28]. However, most recommend a more extensive work-up, starting with the basic investigations mentioned above, and progressing to computed tomography (CT) of the chest, abdomen and pelvis, mammography and other tests, including endoscopic examinations (esophagogastroscopy and colonoscopy), bone marrow biopsy and BAL if clinically necessary. A recent comparative study highlighted the potential value of PET in this area. PET/CT was comparable to conventional cancer screening (CT chest and abdomen scanning, mammography, gynecological examination, ultrasonography and tumor marker analysis) with both modalities demonstrating an equal overall predictive value of 92.7% [29]. The obvious benefit of PET/CT is that it is a single, minimally invasive investigation, but its application would be limited in most centers by cost and availability. Serum tumor markers remain a subject of much contention. One study showed elevated CA125 at the time of DM diagnosis to be associated with a significantly increased risk of developing a solid tumor within 5 years; however, significant associations have not been demonstrated with other tumor markers [28]. While oncologists agree that no tumor marker is sufficiently sensitive or specific for screening purposes, proponents of tumor marker testing in DM argue that in a population with a higher probability of malignancy, the usefulness of such tests is greater [30]. Reliable methods of predicting cancer risk would be advantageous in the clinical setting; however, these have not been clearly established. Older age at diagnosis and the presence of a positive anti-p155 antibody are well-recognized risk factors for malignant disease [31].

Diagnostic criteria

Controversy exists surrounding the use of diagnostic criteria for DM and PM. Although a number of classification criteria exist, none has been validated. The most widely used are the Bohan and Peter criteria (**Box 1**), which date back to 1975 and classify PM and DM as either 'definite', 'probable' or 'possible' [12,32]. They have been criticized for being too inclusive, as they may allow patients with myositis mimics, such as muscular dystrophies, to be classified as having an inflammatory myopathy, and inclusion body myositis may be misclassified as polymyositis.

In 1991, Dalakas proposed more stringent criteria incorporating specific muscle biopsy features, defining patients as having either 'definite', 'probable' or 'mild/early' DM or PM (**Table 2**) [33]. These criteria have in turn been criticized for being too rigid.

A multicenter project to develop and validate new classification criteria for IIM is currently underway [201]. In the interim, the International Myositis Assessment and Clinical Studies group's (IMACS) consensus guidelines recommend that

'definite' or 'probable' diagnoses of PM or DM, as defined by the Bohan and Peter criteria, are sufficient for enrolling patients in clinical trials, provided that muscle biopsy is consistent with the diagnosis and myositis mimics have been excluded by all available means [34].

Treatment

Treatment will differ for individual patients depending on their disease manifestations and the severity of their illness, but the general approach would be to address the muscle and skin disease, as well as any systemic complications.

Muscle disease

Corticosteroids

Treatment typically begins with high-dose corticosteroids (prednisolone 0.5–1 mg/kg) [1]. Although these are the accepted first-line management, corticosteroids have never been evaluated in the context of a randomized placebo-controlled trial. Recently, pulsed oral dexamethasone was compared with usual therapy with daily prednisolone in patients with PM and DM. There was no treatment advantage in the dexamethasone group, but a more favorable side-effect profile was observed, suggesting that this agent may be a reasonable alternative to prednisolone, especially for patients prone to steroid-related toxicity [35]. Severe disease may warrant the use of pulsed intravenous (iv.) methylprednisolone, 0.5–1 g daily for 3–5 days [36]. After 3–4 weeks, oral steroids are slowly tapered to avoid exacerbating the disease, but this must be balanced against the real risks of steroid-related toxicities, including steroid myopathy, diabetes mellitus and osteoporosis. As treatment with steroids alone is usually insufficient, second-line agents are frequently required.

There is a paucity of evidence regarding immunomodulatory therapies for inflammatory myopathies, and as a result, treatment is typically empirical and dependent on the experience and preference of the treating physician. Commonly used agents include methotrexate (MTX), azathioprine (AZA), mycophenolate mofetil (MMF) and ciclosporin (CsA), although biologics are being prescribed with increasing frequency.

Box 1. Bohan and Peter criteria.

Features

- 1. Symmetrical proximal muscle weakness
- 2. Muscle biopsy evidence of myositis
- 3. Elevation in serum skeletal muscle enzymes
- 4. Characteristic electromyogram pattern of myositis
- 5. Typical rash of dermatomyositis

Polymyositis

- Definite: all of 1–4
- Probable: any 3 of 1–4
- Possible: any 2 of 1–4

Dermatomyositis

- Definite: 5 plus any 3 of 1–4
- Probable: 5 plus any 2 of 1–4
- Possible: 5 plus any 1 of 1–4

Methotrexate

MTX is often considered to be the first-line steroid-sparing agent in DM [1]. Given in doses of up to 25 mg/week, administered orally or subcutaneously, it becomes effective within 6–8 weeks, and therefore is not appropriate for rapid control of fulminant or progressive disease. No clinical trials have compared MTX to placebo, but studies comparing it to AZA and CsA have shown no significant differences in efficacy between the drugs [37,38]. However, MTX was better tolerated than either AZA or CsA, and its acceptable safety profile, familiarity within the fields of rheumatology and dermatology, and low cost

Table 2. Dalakas criteria.

Features	Definite polymyositis	Probable polymyositis	Definite dermatomyositis	Mild/early dermatomyositis
Muscle strength	Myopathic muscle weakness	Myopathic muscle weakness	Myopathic muscle weakness	Normal muscle strength
Electromyogram findings	Myopathic	Myopathic	Myopathic	Myopathic or nonspecific
Muscle enzymes	Elevated (up to 50-fold)	Elevated (up to 50-fold)	Elevated (up to 50-fold)	Elevated (up to tenfold) or normal
Muscle biopsy findings	Diagnostic	Nonspecific myopathy	Diagnostic	Nonspecific or diagnostic
Rash or calcinosis	Absent	Absent	Present	Present

are further advantages. When the combination of oral MTX and AZA was compared with iv. MTX with leucovorin rescue in refractory myositis, a nonsignificant trend towards additional benefit was reported in the combination therapy arm [39]. Although MTX is generally well tolerated, the potential for toxicities must be considered, particularly pulmonary and hepatic. In a series of DM patients treated with MTX, 86% developed side effects, including biopsy-proven mild hepatic fibrosis resulting in discontinuation of the drug. The patients who developed hepatic fibrosis had pre-existing steroid-induced diabetes mellitus, and the authors warn that patients with diabetes should be carefully monitored for hepatic toxicity [40].

Azathioprine

A placebo-controlled trial of AZA in myositis did not show any significant evidence of benefit at 3 months, however, long-term follow-up data suggested that patients treated with AZA were stronger and required less steroid treatment than the group treated with steroids alone [41,42]. AZA is typically administered in doses of 2–3 mg/kg/day depending on thiopurine methyltransferase level, which should be determined prior to commencing treatment in order to identify patients at increased risk of drug toxicity.

Ciclosporin

CsA has been shown to be as effective as MTX in treating the myopathy of IIM, although it is not as well tolerated [37]. Several case reports have highlighted its value in cases of refractory disease [43,44]. CsA has also been used with success in combination with iv. immunoglobulin (IVIg) for patients with resistant or relapsed disease [45]. Commonly reported side effects include renal toxicity, hypertension and infection.

Mycophenolate mofetil

A retrospective review of MMF treatment in IIM patients, resistant to or intolerant of other immunosuppressants, demonstrated its safety and efficacy in this group [46]. This agent has also been evaluated as an add-on treatment together with IVIg in patients with severe myositis. This combination was efficacious and well tolerated, and allowed a significant reduction in steroid dosage [47].

Leflunomide

Anecdotal evidence exists for the use of this agent in recalcitrant DM [48]. Leflunomide (LEF) exerts a broad immunosuppressive effect by inhibiting pyrimidine synthesis, thus impeding DNA and RNA synthesis in activated T and B lymphocytes, and interfering with cell signaling and adhesion. At the recommended dose of 20 mg/day it is well tolerated, but common side effects include hepatic and hematological toxicity, and hypertension.

Intravenous immunoglobulin

Two randomized controlled trials have demonstrated the benefit of high-dose IVIg in comparison with placebo in the treatment of refractory myositis [49,50]. The value of this agent for the treatment of severe, steroid-resistant esophageal involvement has been underlined in a retrospective review of IIM patients with life-threatening esophageal complications [51]. IVIg should be considered in the context of corticosteroid failure or rapidly evolving disease with severe weakness [36]. A recent small open-label trial investigating the feasibility and safety of subcutaneous immunoglobulin in patients with severe PM and DM reported encouraging results; however, these findings have yet to be validated in a controlled study [52]. While the clinical response to IVIg may be dramatic, data suggest that the benefit may be short-lived and that ongoing therapy with repeated infusions every 4–6 weeks may be necessary [36]. While the advantages of this treatment are not in doubt, the challenge that remains is its extremely high cost.

Rituximab

A number of case reports and case series have illustrated the efficacy of rituximab in DM, particularly in the context of severe or recalcitrant disease [53]. The RIM study, a randomized placebo-controlled crossover trial of this agent in refractory PM, DM and JDM, was recently completed and has been reported in abstract form [54]. While 83% of patients met the definitions of improvement and rituximab was generally well tolerated, the primary and secondary end points were not reached – possibly owing to weaknesses in trial design, rather than the drug itself. Further investigation of this agent in the treatment of IIM is warranted.

Anti-TNFα

A number of retrospective reports have suggested a possible role for anti-TNF agents in refractory myositis [55,56]. However, further work in the area has not generated particularly promising results. An open study of infliximab in treatment-resistant myopathies demonstrated improvement in only a third of patients, with the remainder deteriorating

both clinically and radiologically [57]. A recently reported randomized controlled trial of etanercept in DM demonstrated the safety of this agent, as well as a steroid-sparing effect, but clinical improvement was less convincing, with just over half of the treated patients meeting the definitions of improvement at 1 year. There was no significant benefit on functional outcomes either [58].

Plasmapheresis & leukapheresis

A placebo-controlled trial of plasmapheresis and leukapheresis in corticosteroid-resistant DM and PM concluded that these treatment approaches are of no benefit [59].

Other treatments

Anecdotal evidence for oral tacrolimus suggests a role for this agent in recalcitrant DM. In addition to beneficial effects on myopathy, improvements in extra-muscular features of the disease have also been shown [60].

A case report of sirolimus (rapamycin) in refractory DM showed improvement in muscle disease, as well as a steroid-sparing effect [61]. Sirolimus is thought to act via inhibition of IL-2 synthesis by autoreactive T lymphocytes, resulting in reduced cell signaling. Side effects include hyperlipidemia and impaired wound healing, but it is generally well tolerated and its antineoplastic potential makes it an interesting proposition in the treatment of DM.

Several case reports suggest chlorambucil may be an effective, steroid-sparing agent in refractory DM [62].

Stem cell transplants are being used increasingly in the treatment of a number of autoimmune conditions [6]. A recently published open-label trial of stem cell therapy in treatment-resistant or severe PM and DM demonstrated the safety and efficacy of this modality, with improvements noted particularly in muscle and lung disease [63].

A small pilot study of the adenine analogue fludarabine in refractory DM and PM demonstrated a clinical benefit in 25% of patients studied [64].

Skin disease

The cutaneous symptoms of DM have a significant impact on quality of life and treatment is often challenging [65]. The evidence base is limited, as most therapeutic trials to date have not directly assessed skin disease as an outcome measure. This may be in part owing to the lack of accepted and validated outcome measures for cutaneous DM, which has recently been addressed [66]. Patients are often already on immunosuppressant treatment for their muscle disease, and are frequently prescribed multiple agents to treat refractory skin disease, thus data on monotherapy, particularly off systemic or topical corticosteroids, is lacking [6].

Photoprotection

Given that the skin manifestations of DM are exacerbated by ultraviolet exposure, sun avoidance and photoprotective measures should be advised in the first instance [6]. The use of sun-protective clothing and wide-brimmed hats, together with behavioral modification, must be emphasized. Year-round daily use of a broad-spectrum sunscreen with a sun-protection factor of at least 30 is recommended, with reapplication every 3–4 h [67]. Even very limited exposure to sunlight may worsen skin lesions, and, similarly to SLE, flares of internal disease have been reported following solar irradiation [68]. Given these strict recommendations, vitamin D status should always be considered, with a view to appropriate replacement if necessary.

Corticosteroids

While systemic corticosteroids are the established first-line treatment for muscle disease, topical corticosteroids are useful for skin lesions, and are particularly helpful in reducing the associated erythema and pruritis. Very potent class 1 corticosteroids are frequently used to treat the scalp, hands and extensor regions, while milder agents are appropriate for facial and periorbital eruptions [6].

Antipruritics

Pruritis may be a prominent feature of DM and have a significant detrimental impact on quality of life [65]. A number of topical agents can be used for symptomatic relief, including menthol, camphor, antihistamines, pramoxine and lidocaine [69]. Oral agents, including antihistamines and amitriptyline, may be more useful.

Antimalarials

Antimalarials are widely used in a number of autoimmune conditions. Numerous potential mechanisms have been described whereby these agents are thought to exert their immunomodulatory effects, including: inhibition of phospholipase A_2, natural killer cell activity, IL-2 and TNF-α production; decreased phagocytosis and chemotaxis; inhibition of antigen–antibody complex formation; stabilization of DNA; decreased peptide presentation due to increased lysosomal

pH; and antioxidant effects [70]. These agents have demonstrated benefit in small open-label trials, and combination therapy has been advocated by some [71]. Hydroxychloroquine in doses of 200–400 mg/day is reported to provide partial control of skin disease in 75% of patients, allowing tapering of steroid dose. Smoking is thought to reduce the efficacy of this agent, so patients should be counseled about smoking cessation, as well as the potential adverse effects, including ocular toxicity, skin rash, gastrointestinal upset and bone marrow suppression [6]. A substantial proportion of these patients go on to develop drug-related eruptions; indeed, patients with DM appear to be at a higher risk of adverse cutaneous reactions than other groups treated with this drug (e.g., those with SLE [72]). Chloroquine, quinacrine and mepacrine are alternatives for patients not tolerating or not responding to hydroxychloroquine. It is important to note that these agents have no benefit on muscle disease.

Methotrexate

Low-dose oral and subcutaneous MTX has been evaluated in the context of small open-label trials and retrospective reviews in doses ranging from 2.5–40 mg/week [40,73–75]. Improvement in skin disease was noted in the majority, allowing reduction or cessation of other therapies in most cases. Cutaneous lymphocytes have been identified as potential targets of this treatment, with inhibition of peripheral migration of these cells being the suggested mechanism of action [73]. Because both the cutaneous disease and myositis of DM have demonstrated a response to MTX, it is often thought of as the first-line steroid-sparing agent; however, careful patient selection is necessary, as is regular monitoring for hepatic, hematological and pulmonary toxicity.

Mycophenolate mofetil

The effectiveness of MMF for cutaneous lesions of DM has been evaluated by a number of retrospective reviews and open-label studies [76–78]. At doses of 500 mg to 1 g twice daily, MMF has demonstrated benefit for cutaneous lesions recalcitrant to other therapies, including topical agents, antimalarials and MTX. While this agent is generally very well tolerated, regular monitoring for hepatic and hematological toxicity is recommended.

Leflunomide

Usefulness of adjuvant LEF at a dose of 20 mg/day for the treatment of recalcitrant skin lesions of DM was reported in a series of three patients, all of whom responded favorably following addition this drug to their existing immunosuppressive regime [79]. The benefit of LEF has been established in psoriasis, and anecdotal evidence exists for its use in other skin diseases.

Tacrolimus

The usefulness of topical tacrolimus in the treatment of resistant cutaneous manifestations of DM has been demonstrated in a number of case reports and one small open study [80]. The benefit of this agent is that it has minimal systemic absorption and does not impair collagen synthesis, and therefore does not cause skin atrophy [81]. The common side effects of burning, itching and erythema commonly decline as treatment continues owing to improved skin integrity. Pimecrolimus, another a calcineurin inhibitor, has also shown promise as a topical treatment for resistant cutaneous DM [82]. Although there have been several case reports showing improvements in recalcitrant skin disease of JDM with oral tacrolimus, no data exists surrounding its use for skin disease in adult DM patients [6].

Ciclosporin

A single case report has described improvement of refractory skin necrosis in a patient with amyopathic DM previously treated with high-dose steroids and IVIg [83]. Otherwise, data on the efficacy of ciclosporin for cutaneous manifestations of DM is sparse.

Anti-TNFα

Overall, the data on anti-TNF agents in DM are disappointing. In a recent pilot trial comparing etanercept to placebo in DM, five out of 11 patients treated with etanercept developed a worsening rash. However, no major safety concerns were noted and a steroid-sparing effect was observed, prompting the authors to conclude that further investigation of this agent is warranted to fully explore its effect of both the myopathic and dermatological manifestations of DM [58]. Although data are conflicting, the majority of case series and case reports have not demonstrated convincing benefit in cutaneous manifestations of DM treated with anti-TNF agents [84,85]. In addition, there have been numerous reports of the development of DM and DM-like rashes in patients treated with anti-TNF agents for other indications, particularly rheumatoid arthritis [86].

Rituximab

A number of case reports and open-label trials have established the benefit of rituximab

treatment for the myopathic, cutaneous and pulmonary manifestations of refractory DM [87]. It has also been shown to be valuable in the treatment of vasculitic lesions in a case of skin-predominant DM [88]. The typical dose is 2 g, divided into two 1-g infusions given 2 weeks apart.

Intravenous immunoglobulin

Significant improvement in skin disease was demonstrated in a double-blind placebo-controlled study of patients with refractory DM receiving high-dose IVIg (2 g/kg) compared with placebo [50]. It has been suggested that low-dose IVIg (0.1 g/kg) may be sufficient to elicit a clinical response in patients with intractable CADM [89].

Other treatments

Anecdotal evidence suggests that dapsone may be beneficial in recalcitrant cutaneous DM. The anti-inflammatory properties of dapsone have already been exploited in a number of other dermatological conditions, including bullous disorders, erythema nodosum and pyoderma gangrenosum. The literature reports two cases of cutaneous DM, resistant to a number of commonly used immunosuppressants, treated with dapsone with significant and rapid improvement in skin disease. In both cases, withdrawal of the drug precipitated a flare, which settled once it was reintroduced [90].

Possible utility of antiestrogens in treating the cutaneous manifestations of DM has been suggested by the case reports of two female patients with DM who were prescribed these agents (tamoxifen and anastrozole) and experienced improvement in their skin eruptions. The patient taking tamoxifen experienced worsening of her skin rash on withdrawal of the drug and remained resistant to a number of conventional immunosuppressants. Antiestrogens are thought to have anti-TNF properties; however, the exact mechanism by which they exert their immunomodulatory effect in DM is not completely understood, and they are not considered to be mainstream treatment options at this time [91].

Pulsed dye laser is used widely for a number of skin conditions including telangiectasia, rosacea and hemangiomas. Amelioration of the poikilodermatous erythema associated with DM has been described in two Japanese patients given laser treatment [92]. In both cases, the erythema improved significantly following treatment, adverse skin reactions were transient and no recurrence was noted during follow-up.

One case report documents the successful use of oral sirolimus (rapamycin), more commonly used as an immunosuppressant for solid organ transplantation, in a female patient with recalcitrant DM. Striking improvement in skin disease was noted within 4 weeks of treatment and a steroid-sparing effect was evident. Unfortunately, the development of significant hypertriglyceridemia resulted in treatment withdrawal [61].

The effectiveness of efalizumab, a monoclonal antibody against CD11a, has been reported in a single case of resistant DM. A clear reduction in facial and thoracic erythema was noted; however, the periorbital eruption was less responsive [93]. Efalizumab was originally developed for the treatment of psoriasis and is thought to exert its effect by interfering with the recruitment of lymphocytes to the skin. Although it has also shown promise in atopic asthma and renal transplantation, it was removed from the market in 2009 because of the potential increased risk of progressive multifocal leukoencephalopathy [6].

Systemic complications

The treatment of calcinosis is difficult and frequently unsatisfactory. As calcinosis is known to occur in previously inflamed muscle, it is thought that early and aggressive treatment of muscle disease may reduce the development of these lesions, which can be debilitating in some patients [6]. A number of agents have been used with variable success including calcium channel blockers, such as diltiazem, oral and iv. bisphosphonates, IVIg, anti-TNF, warfarin, colchicine and probenecid [6,94–97]. Occasionally, surgical removal of exceptionally troublesome lesions may be warranted, particularly those at risk of recurrent infection, or causing impaired movement or unremitting pain. The risk of recurrence is high [98]. Extra-corporeal shock wave lithotripsy is an old technique, effective for a number of conditions including urolithiasis and calcific tendonitis, which has recently been used in order to treat calcinosis associated with connective tissue diseases. One case report and one case series highlight the analgesic effect of this treatment in recalcitrant calcinosis [99,100].

There is a paucity of evidence for the treatment of interstitial lung disease in DM. As with other chronic respiratory illnesses, supportive strategies, including supplemental oxygen therapy, prophylaxis against opportunistic infections, appropriate vaccinations, control of exacerbating conditions and pulmonary rehabilitation are important [9]. High-dose

corticosteroids are the mainstay of treatment in early disease, but steroid-sparing agents should be considered from the outset in order to limit steroid-related toxicity and because a significant proportion of patients have steroid-resistant disease [9]. Cyclophosphamide (CYC) has been evaluated in a small open-label trial that demonstrated significant improvements in PFTs, symptoms and HRCT findings in patients treated with monthly pulsed iv. CYC for at least 6 months [101]. Its established safety record, route of administration and fast onset of action as compared with other steroid-sparing agents makes iv. CYC an attractive choice for acute or progressive ILD. This agent has also been used successfully to treat refractory disease in combination with other steroid-sparing agents including azathioprine and ciclosporin [9]. The use of T-cell targeted therapies, such as the calcineurin inhibitors tacrolimus and ciclosporin, is logical given the predominance of this cell type on BAL and lung biopsy specimens. Anecdotal evidence of benefit exists for both agents, but tacrolimus, which is 100-times more potent, seems more suitable for severe, diffuse disease, while ciclosporin is appropriate for early, slowly progressive ILD [9]. A recent case report highlighted the value of tacrolimus in progressive ILD refractory to other immunosuppressants including ciclosporin, and several reports have demonstrated its benefit in ILD associated with antisynthetase antibodies [102,103]. Several small retrospective analyses have reported the successful use of MMF in ILD associated with connective tissue diseases; however, only one case series has assessed this drug in DM-associated ILD specifically [104]. Normalization of PFTs, reduction of dyspnea and a steroid-sparing effect were observed in three patients who were given MMF for at least a year. An increasing body of evidence is emerging for B-cell targeted therapies in connective tissue diseases. A recent study demonstrated elevated levels of B-cell activating factor, also known as B-lymphocyte stimulator, in myositis patients with ILD and antisynthetase antibodies, further strengthening the rationale for the use of anti-B-cell therapy in such patients [105]. Although data to support the use of rituximab in IIM-associated ILD is anecdotal, several case reports and retrospective reviews have highlighted its potential value in recalcitrant ILD and as a rescue therapy in rapidly progressive disease [106,107]. While there is clear evidence of benefit for IVIg in muscle and skin disease, its role in ILD is unclear. A single, small retrospective study of IVIg in IIM-associated ILD resistant to corticosteroids and other immunosuppressants suggested its potential role as salvage therapy in severe, intractable cases [108]. Both MTX and AZA are widely used in the treatment of myositis, including associated ILD, and are probably beneficial; however, little data exists to support their use [109]. Fibrotic disease is permanent and is not responsive to immunosuppressive therapy. Patients with advanced, progressive ILD may be considered for lung transplantation, although they are often denied this on the basis of extrapulmonary manifestations [9,110]. Ventilatory insufficiency can also be caused by respiratory muscle weakness, which may not respond to immunosuppressives and can be life-threatening in some cases. Noninvasive mechanical ventilation has been shown to reduce chronic hypoventilation and improve quality of life in these patients. Furthermore, it can be operated in the home environment and may be useful to 'buy time' while immunosuppressive therapy achieves efficacy [111].

Diet & exercise

Creatine supplements are used widely for a number of neuromuscular conditions including inflammatory myopathies. A recent placebo-controlled trial of creatine supplements with home exercise versus exercise alone in patients with established DM and PM showed a substantial functional improvement in the group receiving creatine. No significant adverse events were noted in either group [112]. The safety of creatine supplementation has been demonstrated in other studies [113] and there is little evidence that toxicity (particularly renal) is a clinical problem, provided that purified creatine from an approved manufacturer is administered, and there is no pre-existing renal disease or serious underlying medical condition [112].

For reasons that are not entirely clear, the majority of myositis patients, including those responding to treatment, will go on to develop sustained disability [114]. Therefore, a structured and monitored exercise regime is recommended for all patients. In the acute phase, exercises to maintain range of motion and reduce complications of immobility (e.g., pressure sores and hypostatic pneumonia) are required. The safety of exercise in active myositis has been established. In stable patients, exercises to maintain and improve muscle function and endurance are advised and patients and physicians should be reassured that there is no evidence that exercise hastens or exacerbates muscle disease [115].

While the clinical benefits of exercise are well recognized, the molecular basis underlying these improvements remains elusive. A recent longitudinal study of a group of myositis patients undergoing an intensive resistance training program documented marked reductions in their expression of proinflammatory and profibrotic genes, accompanied by reduced tissue fibrosis and a shift toward oxidative metabolism, suggesting that exercise may induce a reduction in inflammation and fibrosis in skeletal muscle [116].

Monitoring

Multidisciplinary team input is vital in a complex disease such as DM, and in many cases, the involvement of a number of healthcare professionals will be required. Regular monitoring of disease activity and review of medications should be carried out in order to supervise a slow taper of medications and recognize and treat any relapses or flares. In addition, patients should be assessed for the development of treatment-related toxicity and malignancy.

Patients with ILD should be under the care of a respiratory physician for regular review of clinical signs and symptoms and functional status. The 6-min walk test, frequently used in the evaluation of chronic respiratory illnesses, may not be appropriate in patients with a myopathy. Serial HRCTs and PFTs are useful objective measures of disease progression and response to therapy [9]. Rigorous investigation for underlying malignancy should be undertaken at the time of diagnosis, but it has been suggested that this should be revisited annually for at least the first 3 years after diagnosis.

Standardization of monitoring within the context of clinical trials and long-term observational studies has recently been addressed by the IMACS group. A core set of disease activity measures has been developed to assess the manifestations of myositis thought to be a direct result of the inflammatory process, and therefore reversible. These include physician and patient global activity scores (measured using a 10-cm visual analogue scale and 5-point Likert scale), manual muscle testing, assessment of physical function using the Health Assessment Questionnaire, laboratory evaluation of muscle enzymes and assessment of extra-muscular disease activity using the Myositis Disease Activity Assessment Tool [117]. This tool, incorporating both the myositis disease activity visual analogue scale (MYOACT) and myositis intention to treat index (MITAX) instruments, each of which has been independently tested and partially validated for use in adult patients with myositis, has now also been validated for use in this group [118,119]. IMACS has also developed and partially validated 13 preliminary definitions of improvement for myositis patients that define clinically meaningful changes in each of the core set activity measures [120]. The concept of disease damage relates to those persistent changes in anatomy, physiology, pathology or function resulting from previously active disease, complications of treatment or other factors, which are often postinflammatory, cumulative and irreversible. A preliminary core set of measures to assess damage has been developed to include assessment of physical function, muscle strength, physician and patient global damage scores (using a 10-cm visual analogue scale and 5-point Likert scale) and the Myositis Damage Index, which has been tested and partially validated together with the MITAX and MYOACT instruments [117,118]. While these instruments have not been formulated for use in the everyday clinical setting, they are easily available and may guide the treating physician in their assessment and monitoring of these patients.

Future perspective

More well-designed randomized controlled trials investigating the various available therapeutic options are needed in order to develop a rational, evidence-based approach to treatment of all aspects of DM. On searching the US, UK and European research registers, a promising selection of ongoing randomized controlled trials is discovered, investigating both traditional immunosuppressants and the newer biologics. Phase II trials investigating agents such as methimazole, eculizumab, abatacept, BAF312 and MEDI-545 (sifalimumab, an anti-IFNα antibody) are underway, and it is hoped that the results of these studies will further develop our understanding of the etiopathogenesis of DM, and aid the development of rational treatment approaches. It is likely that new immunotherapeutics, designed for autoimmune diseases other than idiopathic myopathies and targeting novel molecular pathways, may be amenable to investigation in myositis. Anakinra (IL-1 receptor antagonist), fingolimod (anti-T lymphocyte migration) and natalizumab (inhibitor of cellular adhesion) are examples of such applications [36]. Further work on autoantibody subsets in IIM is underway, and it is anticipated that this will enable better categorization of patients, prediction of natural history and prognosis, and enhanced medical treatment.

Executive summary

General considerations

- Although dermatomyositis (DM) is rare, morbidity and mortality rates are high and management is complex.
- Approach to management should begin with assessment of muscle disease and other organ system involvement, and investigation for underlying malignancy.

Clinical aspects

- Key features are proximal muscle weakness and skin rash.
- The antisynthetase syndrome is characterized by myositis, pyrexia, nonerosive arthritis, mechanic's hands, Raynaud's phenomenon and interstitial lung disease.

Diagnostic work-up

- Serum muscle enzymes are usually raised, but may be normal in amyopathic DM.
- Comprehensive autoantibody testing yields positive results in 80% of cases, but most centers only offer a limited selection of tests routinely. Autoantibodies have a role in distinguishing subtypes of DM and predicting natural history, prognosis and response to treatment.
- MRI accurately demonstrates acute and chronic changes of myositis, and has a role in diagnosis and monitoring of disease activity and response to treatment.
- Nailfold capillaroscopy is a useful adjunct and may have a role in monitoring disease activity.

Systemic involvement

- Investigations for suspected pulmonary involvement may include high-resolution computed tomography, pulmonary function tests, bronchoscopy and bronchoalveolar lavage, and lung biopsy.
- All patients should have an ECG at baseline. Echocardiogram and cardiac MRI are of use if cardiac involvement is suspected.

Malignancy

- Malignancy is diagnosed in approximately 30% of DM patients, and is particularly associated with anti-p155 (anti-TIF1-γ) antibody positivity and older age at diagnosis.
- The risk of malignancy is greatest within the first 3 years of diagnosis.

Treatment of muscle disease

- Treatment begins with high-dose corticosteroids, which should be gradually tapered over time.
- Methotrexate and azathioprine are the most widely used second-line agents, followed by mycophenolate mofetil and ciclosporin.
- IVIg, rituximab, other biologics and stem cell transplant may be considered in resistant disease.

Treatment of skin disease

- Photoprotection is vital; and topical agents (steroids, antipruritics and tacrolimus) are of use.
- Hydroxychloroquine improves skin disease in most cases. Other beneficial systemic treatments include corticosteroids, methotrexate, mycophenolate mofetil, leflunomide and tacrolimus.
- Recalcitrant disease may respond to rituximab or IVIg.
- Calcinosis is notoriously difficult to treat.

Treatment of interstitial lung disease

- High-dose corticosteroids are of use in early disease, but steroid-sparing agents should be introduced early.
- Intravenous cyclophosphamide has a definite role.
- Rituximab and IVIg may be of use as salvage therapy in severe or intractable disease.

Other management considerations

- Exercise in DM is a safe and valuable adjunct to medical treatment.
- Creatine supplements may be of benefit in established disease.
- Monitoring of all aspects of disease activity is vital and multidisciplinary team involvement is a fundamental aspect of management.

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1. On the basis of the review by Drs. Vermaak and McHugh, which of the following statements about the clinical features of dermatomyositis is **most likely** correct?

- ☐ **A** Key features are distal muscle weakness and skin rash
- ☐ **B** The antisynthetase syndrome is characterized by myositis, fever, nonerosive arthritis, mechanic's hands, Raynaud' phenomenon and interstitial lung disease
- ☐ **C** Malignancy is diagnosed in about 10% of patients with dermatomyositis
- ☐ **D** Lung involvement is rare

2. Your patient is a 52-year-old woman with proximal muscle weakness and skin rash suggestive of dermatomyositis. On the basis of the review by Drs. Vermaak and McHugh, which of the following statements about diagnostic evaluation of this patient is **most likely** correct?

- ☐ **A** Serum muscle enzymes are usually normal
- ☐ **B** Testing for autoantibodies is not helpful
- ☐ **C** Investigations for suspected lung involvement may include high-resolution CT, pulmonary function testing, bronchoscopy and bronchoalveolar lavage, and/or lung biopsy
- ☐ **D** MRI and nail-fold capillaroscopy play no role in diagnostic evaluation of dermatomyositis

3. The patient described in question 2 is diagnosed with dermatomyositis without ILD. On the basis of the review by Drs. Vermaak and McHugh, which of the following statements about treatment is **most likely** correct?

- ☐ **A** First-line therapy is high-dose corticosteroids, which should be gradually tapered over time
- ☐ **B** Second-line therapy is IVIG, rituximab, or other biologic agents
- ☐ **C** Calcinosis is highly responsive to steroid therapy
- ☐ **D** The best treatment regimen is supported by conclusive evidence