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Dermatomyositis: Review and Considerations in Older Adults

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Abstract: Dermatomyositis (DM) is an idiopathic inflammatory myopathy characterized by prominent skin lesions, muscle weakness, and clinically heterogeneous systemic manifestations. Among patients with DM, the male-to-female ratio is 2:1. Juvenile dermatomyositis (JDM) is most prevalent between the ages of 4 and 14 years, while adult-onset dermatomyositis typically occurs between the ages of 40 and 60 years. In a population-based study conducted in Olmsted County, Minnesota, USA, the risk of DM was found to increase with age across different age groups stratified by decade. The incidence rate of DM in individuals aged ≥ 80 years was 3.2 per 100,000 person-years. Dermatomyositis in elderly patients is characterized by unique clinical manifestations, pathogenic mechanisms, and therapeutic approaches. However, discussions regarding geriatric dermatomyositis are currently limited. Therefore, this article aims to review the epidemiology, clinical features, histopathology, and pathogenesis of dermatomyositis, with a particular focus on the unique clinical characteristics of geriatric dermatomyositis.

Keywords: Anti-MDA5 antibodies; Dermatomyositis; Interstitial lung disease; Geriatric; Myositis-specific autoantibodies

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1. Introduction

Dermatomyositis (DM) is an idiopathic inflammatory myopathy marked by distinctive cutaneous eruptions, progressive muscle weakness, and diverse systemic involvement. While the disease can occur at any age, its incidence demonstrates a notable increase with advancing age, particularly among the elderly population [1]. Geriatric dermatomyositis presents distinct clinical phenotypes, pathogenic mechanisms, and therapeutic challenges compared to younger-onset cases. This review aims to summarize the epidemiology, clinical manifestations, histopathology, and pathogenesis of dermatomyositis, with special emphasis on the unique characteristics of geriatric dermatomyositis.

2. Etiology and pathogenesis

The pathogenesis of dermatomyositis is complex and diverse, and it has not yet been fully elucidated. Based on current research, the underlying mechanisms can be broadly categorized into environmental, immunological, and genetic factors.

2.1. Environmental factors

Studies have suggested that various environmental factors may trigger chronic activation of the immune system in individuals. Potential environmental factors include viral infections, pharmacological agents, ultraviolet radiation, environmental pollution, and smoking, among others. In patients with dermatomyositis who are positive for anti-MDA5 antibodies, interstitial lung disease predominantly occurs in the autumn and winter seasons [2], indicating that seasonal respiratory viruses may influence disease pathogenesis. COVID-19 infection has been identified as a potential trigger in patients with anti-MDA5-positive dermatomyositis [2,3].

2.2. Genetic factors

Numerous studies published to date have demonstrated an association between major histocompatibility complex (MHC) polymorphisms and the development of DM. In Asian populations, several HLA alleles (primarily located in HLA-DRB1) have been identified as risk factors for the development of anti-MDA5-positive DM [4–6]. Epigenetic modifications may also play a role in the pathogenesis of DM.

2.3. Immunological factors

Compared to middle-aged and younger individuals, elderly patients exhibit significant features of immune senescence, which are influenced by multiple factors including inflammaging, genetic susceptibility, environmental exposures, and gut microbiota dysbiosis [7]. These factors promote the occurrence and progression of DM in elderly patients through direct or indirect mechanisms. Anti-MDA5 antibodies are common in elderly patients with DM, with a positivity rate of approximately 10%–30%. Other autoantibodies, such as anti-TIF1γ antibodies, are associated with an increased risk of malignancy in elderly patients with DM [8].

3. Clinical manifestations

3.1. Cutaneous manifestations

In elderly patients, cutaneous manifestations can be diverse and variable, may not be exactly consistent with the time course or severity of muscle disease and systemic involvement. For instance:

(1) Pathognomonic lesions: Gottron papules and Gottron's sign are classic. The heliotrope rash, characterized by violaceous periorbital edema and erythema, is another hallmark;

(2) Characteristic lesions: These include the shawl sign, V sign, and mechanic's hands. Nailfold changes, such as periungual telangiectasia and infarcts, are also common;

(3) Other cutaneous features: Patients may exhibit poikiloderma, calcinosis cutis, and panniculitis. It's important to note that the appearance of skin lesions may precede or follow muscle involvement, and their severity is not necessarily correlated with muscle involvement in elderly patients [9].

3.2. Muscular involvement

Muscle involvement is a defining feature of DM, with approximately 80% of elderly patients experiencing

myopathy [10]. For example:

(1) Proximal muscle weakness: The classic presentation is symmetric, proximal muscle weakness, affecting the limbs and trunk;

(2) Dysphagia and dysphonia: These symptoms indicate possible involvement of pharyngeal and esophageal muscles, which are associated with a poor prognosis [9,11].

3.3. Systemic involvement

DM can involve multiple organ systems, with significant systemic manifestations in elderly patients as outlined below:

(1) Interstitial lung disease (ILD) is the most common systemic manifestation, affecting up to 78.9% of patients, and this proportion is even higher in elderly patients. Its characteristic feature is the rapid progression of pulmonary function deterioration within a short period (typically within 4 weeks);

(2) Cardiac manifestations include arrhythmias, conduction defects, pericarditis, and cardiomyopathies;

(3) Joint pain or arthritis, particularly involving the small joints of the hands and wrists, is common.

Elderly patients with DM are at risk for several complications due to the chronic nature of the disease and the use of immunosuppressive therapies:

(1) The use of immunosuppressive agents increases the risk of infections, particularly viral and fungal infections;

(2) Older age and immunosuppressive therapy for DM have been linked to an increased incidence of malignancy [12]. Regular screening and monitoring are essential;

(3) The risk of cardiovascular events, including myocardial infarction and heart failure, is elevated in DM patients;

(4) Long-term use of corticosteroids for elderly patients can lead to complications such as osteoporosis, hypertension, and diabetes.

In summary, dermatomyositis in the elderly is a complex and multifaceted disease with significant cutaneous, muscular, and systemic manifestations. Early diagnosis and targeted treatment are crucial for managing the disease and mitigating complications.

4. Diagnosis and assessment

4.1. Laboratory investigations

4.1.1. Muscle Enzymes

Serum creatine kinase (CK) levels in patients vary widely. Therefore, there is no clear correlation between CK levels and the severity of muscle weakness. In elderly patients with reduced muscle mass or in those with advanced disease who have lost a substantial amount of muscle tissue, significant muscle weakness may occur with persistently low serum muscle enzyme levels.

CK-MB elevation can occur in the absence of myocarditis, typically due to increased enzyme expression in regenerating skeletal muscle affected by inflammatory disease, although in rare cases it may indicate cardiac involvement. Aldolase may be elevated in myositis patients with normal CK levels, particularly those with significant perifascicular atrophy. Elevated levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are common in myositis patients and often indicate a poorer prognosis and higher

mortality risk.

4.1.2. Inflammatory markers

Changes in C-Reactive protein (CRP) levels can be used to monitor disease activity and response to treatment. A marked increase in erythrocyte sedimentation rate (ESR) is closely associated with disease activity, particularly during acute inflammatory phases.

4.1.3. Autoantibodies

Extensive research has demonstrated that myositis-specific autoantibodies (MSAs) function as serum biomarkers in DM, aiding in clinical classification, diagnosis, and disease activity assessment. Autoantibodies include as follows:

(1) Anti-Mi-2 antibodies occur in 4–20% of DM patients exhibiting classic skin manifestations like Gottron's sign and heliotrope rash;
(2) Anti-NXP-2 antibodies are found in 3–24% of DM patients. These patients exhibit a distinct clinical phenotype, and in elderly patients, malignancy is more likely;
(3) Anti-MDA5 antibodies are detected in approximately 13–30% of DM patients, and highly associated with ILD;
(4) Consistent studies have identified anti-TIF1-γ as the strongest predictor of malignancy in adult DM patients;
(5) Only a few cases have explored the relationship between anti-SAE serum levels and disease activity.

4.2. Imaging studies

High-Resolution Computed Tomography (HRCT) is particularly useful for the early diagnosis of dyspnea or chronic cough caused by ILD in elderly patients with DM. It allows for the early detection of pulmonary lesions and assessment of disease progression.

In MRI imaging, short tau inversion recovery (STIR) sequences exhibit a sensitivity of 89–100% for detecting inflammatory changes, outperforming muscle biopsy, which has a sensitivity of 66%. In the context of IIM, 18F-FDG PET/CT emerges as a valuable tool with multifaceted applications. Electromyography (EMG) is most helpful in differentiating myopathic weakness from myasthenia gravis and neurogenic weakness, such as in amyotrophic lateral sclerosis (ALS) and polyneuropathies. If physical examination is inconclusive regarding the presence of muscle weakness, EMG can be used to identify suitable muscles for biopsy [13].

4.3. Muscle biopsy

The primary histological manifestations of dermatomyositis are perifascicular atrophy, reduced number of capillaries and perivascular, perimysial, T cells, B cells, macrophages and plasmacytoid dendritic cells infiltrates.

5. Treatment

The pharmacological management of geriatric DM patients requires a delicate balance between controlling disease activity and minimizing the risk of drug toxicity. Glucocorticoids and conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), such as azathioprine and methotrexate, remain the mainstays of treatment.

However, liver and renal function should be closely monitored in elderly patients. For patients with refractory disease or high inflammatory activity, targeted therapies (e.g., JAK inhibitors, anti-CD20 monoclonal antibodies) offer effective alternatives, although potential risks of infection and metabolic complications must be carefully considered.

5.1. Conventional therapeutic agents

5.1.1. Glucocorticoids

Glucocorticoids are the cornerstone of DM treatment, especially during the acute phase of the disease. Long-term monotherapy with glucocorticoids is prone to adverse effects such as infections and metabolic disturbances, and thus they are often used in combination with other agents [14].

5.1.2. Immunosuppressive agents

Immunosuppressive agents are essential in the treatment of DM, particularly when glucocorticoids are ineffective or poorly tolerated.

5.1.3. Conventional synthetic disease-modifying antirheumatic drugs (csDMARDs)

CsDMARDs form the cornerstone of therapy for geriatric DM patients, controlling disease progression by modulating immune responses and reducing the release of inflammatory mediators. Hydroxychloroquine is the primary csDMARD used in DM treatment and can be employed as first-line therapy. However, its monotherapy efficacy is limited, and it is poorly tolerated by some patients. Studies have shown that monotherapy with hydroxychloroquine is associated with a higher risk of disease relapse in DM; therefore, it is often combined with other agents to enhance therapeutic efficacy [15].

Given the reduced liver and kidney function in elderly patients, treatment typically begins with lower doses (e.g., methotrexate at 7.5 mg/week). Patients with comorbid osteoporosis, cardiovascular disease, or high infection risk should undergo comprehensive evaluation to optimize their treatment plans. Close monitoring of drug toxicity and dose adjustment are crucial when using csDMARDs in elderly patients. Individualized treatment strategies can help optimize outcomes. Through the judicious use of csDMARDs, stable and long-term disease management can be achieved for geriatric DM patients.

5.2. Emerging therapeutic strategies

5.2.1. JAK inhibitors

JAK inhibitors are a novel class of therapeutic agents that target the JAK-STAT signaling pathway. Tofacitinib, a representative JAK inhibitor, has demonstrated promising efficacy in patients with refractory DM.

5.2.2. Biologics

Biologics have also shown potential in the treatment of DM. Rituximab, a chimeric monoclonal antibody targeting the CD20 antigen, effectively depletes B cells and reduces autoantibody production. Other biologics, such as tocilizumab and abatacept, have shown some efficacy in DM treatment, but further research is needed to optimize their use.

5.2.3. Plasma exchange and adsorption therapy

For refractory DM patients, plasma exchange and adsorption therapy can be used as adjunctive treatments. Polymyxin B (PMX), a blood purification technique that directly adsorbs endotoxins, effectively removes circulating endotoxins and inflammatory mediators.

5.2.4. Individualized treatment strategies for geriatric patients

Treatment of DM should be individualized, considering factors such as patient age, disease severity, and comorbidities. Geriatric patients often have multiple chronic conditions, and the benefits and risks of medications must be carefully weighed. For elderly DM patients with ILD, treatment strategies should focus on controlling pulmonary inflammation and improving lung function, with a preference for glucocorticoids combined with immunosuppressive agents. For those with prominent skin symptoms, topical glucocorticoids or calcineurin inhibitors can be used in addition to systemic therapy to control disease activity.

5.2.5. Future research directions

Despite significant progress in DM treatment, many challenges remain. Future research should focus on the following areas:

(1) A deeper understanding of DM pathogenesis, particularly the role of anti-MDA5 antibodies in disease mechanisms, is needed;

(2) More high-quality clinical trials should be conducted in geriatric patients to determine the optimal use and dosing of emerging therapeutic agents;

(3) The exploration of biomarkers in DM diagnosis and treatment monitoring is essential for achieving precision medicine .

6. Conclusion

In summary, the treatment of geriatric DM requires a comprehensive consideration of multiple factors and individualized treatment plans. The combination of conventional therapies and emerging treatments holds promise for improving outcomes in elderly DM patients. As research continues to advance, more precise and effective therapeutic strategies will become available for this patient population.

Disclosure statement

The authors declare no conflict of interest.

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