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EDITORIAL

Idiopathic inflammatory myopathies: new therapeutic horizons

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Idiopathic inflammatory myopathies (IIM) constitute a heterogeneous group of rare autoimmune disorders characterised by chronic muscle inflammation, progressive weakness and a broad spectrum of extra-muscular manifestations[1]. Despite substantial advances in immunology and disease classification over the past two decades, the management of these conditions remains challenging. Therapeutic strategies continue to rely heavily on empirical approaches, reflecting both the rarity of the diseases and the limited availability of robust clinical trial data[2,3].

For many years, glucocorticoids have remained the cornerstone of treatment. Their rapid anti-inflammatory effect makes them indispensable in the initial control of disease activity. However, prolonged corticosteroid use carries well-recognized risks, including metabolic complications, infection, osteoporosis and cardiovascular morbidity. As a result, the need for effective steroid-sparing strategies has become increasingly apparent. In clinical practice, conventional immunosuppressive agents such as methotrexate, azathioprine and mycophenolate mofetil are frequently introduced early in the disease course to facilitate glucocorticoid tapering and improve long-term outcomes[4,5].

While these therapies remain widely used, their efficacy varies considerably between patients and across disease subsets. Moreover, their use is often supported more by clinical experience than by high-quality evidence[6]. The relative scarcity of randomised controlled trials in IIM continues to represent a major limitation in guiding treatment decisions[7]. Consequently, clinicians are frequently required to rely on observational data, small cohort studies and expert consensus when tailoring therapy to individual patients.

In recent years, the therapeutic landscape of IIM has begun to evolve, driven by advances in disease characterisation and a better understanding of immunopathological mechanisms. One of the most significant developments has been the increasing use of intravenous immunoglobulin (IVIG)[8]. Evidence supporting the efficacy of IVIG has strengthened considerably, particularly following the results of controlled clinical trials demonstrating meaningful improvements in muscle strength and overall disease activity in dermatomyositis[9]. These findings have led to regulatory approval of IVIG for dermatomyositis in several jurisdictions and have reinforced its role as an important therapeutic option, particularly in patients with refractory disease or intolerance to conventional immunosuppressants.

Beyond its effects on muscle involvement, IVIG may also provide benefits in selected extra-muscular manifestations, including severe cutaneous disease and dysphagia[10].Nevertheless, questions remain regarding optimal dosing strategies, duration of therapy and long-term cost-effectiveness. Given the high economic burden associated with IVIG treatment, careful patient selection and ongoing evaluation of therapeutic response are essential.

Parallel to these developments, biologic therapies have increasingly attracted attention as potential targeted treatments for IIM. Among these, B-cell depletion with rituximab has been one of the most extensively studied approaches[11]. Although the results of large clinical trials have been somewhat inconclusive, subsequent analyses and real-world studies suggest that certain patient subsets may derive significant benefit, particularly those with specific myositis-related autoantibodies or severe refractory disease[12]. These observations underscore the importance of recognising the immunological heterogeneity of IIM and suggest that future therapeutic strategies may need to be guided by more refined patient stratification.

Other biologic agents are also being explored. T-cell co-stimulation blockade with abatacept has shown encouraging signals in early studies, reflecting the central role of adaptive immune mechanisms in the pathogenesis of inflammatory myopathies[13]. Although further clinical trials are needed to clarify its efficacy, such approaches illustrate the growing interest in therapies targeting specific immune pathways rather than relying solely on broad immunosuppression.

More recently, small-molecule inhibitors have emerged as promising additions to the therapeutic armamentarium. In particular, Janus kinase (JAK) inhibitors have generated considerable interest in dermatomyositis, where interferon-mediated signalling pathways appear to play a pivotal pathogenic role. Early clinical reports and small case series suggest that JAK

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inhibition may lead to improvements in both muscle and cutaneous manifestations, particularly in patients with refractory disease. However, the long-term safety and effectiveness of these agents in IIM remain to be fully established[14,15].

Despite these encouraging developments, several important challenges persist. Perhaps the most fundamental issue is the marked heterogeneity of IIM itself. The spectrum of disease includes polymyositis, dermatomyositis, immune-mediated necrotising myopathy and inclusion body myositis, each with distinct pathological and clinical characteristics[16]. In addition, the identification of myositis-specific autoantibodies has further refined disease classification, revealing subsets associated with particular clinical features, prognostic implications and therapeutic responses.

This increasing complexity highlights the limitations of traditional "one-size-fits-all" treatment approaches. Instead, a more personalised strategy may be required, integrating clinical phenotype, autoantibody profile and organ involvement. Achieving this goal will depend not only on improved understanding of disease mechanisms but also on the development of reliable biomarkers capable of predicting treatment response.

Another persistent obstacle is the limited number of well-designed clinical trials in this field[17]. The rarity of IIM poses significant difficulties in patient recruitment and trial design, often resulting in small sample sizes and heterogeneous study populations[18]. International collaboration and the use of standardised outcome measures will therefore be essential to generate more robust evidence. Initiatives such as collaborative research networks and multinational registries may play a crucial role in addressing these challenges[19–21].

Importantly, optimal management of IIM extends beyond pharmacological therapy. Multidisciplinary care remains fundamental, particularly given the potential involvement of multiple organ systems. Respiratory disease, interstitial lung disease, cardiac complications and dysphagia may all contribute substantially to morbidity and mortality. Close collaboration between rheumatologists, neurologists, pulmonologists and rehabilitation specialists is therefore essential to ensure comprehensive care.

Rehabilitation and structured exercise programmes also represent key components of management. Historically, concerns were raised regarding the potential exacerbation of muscle inflammation with physical activity. However, accumulating evidence suggests that appropriately supervised exercise can improve muscle strength, endurance and functional capacity without worsening disease activity. Integrating rehabilitation strategies alongside immunosuppressive therapy may therefore enhance long-term outcomes and quality of life[22,23].

Looking forward, advances in translational research are likely to further reshape the treatment landscape of IIM. Increasing insights into the molecular pathways involved in disease pathogenesis—including interferon signalling, complement activation and antibody-mediated mechanisms—may lead to the development of more targeted therapeutic interventions. At the same time, the integration of biomarker-driven approaches and precision medicine strategies may help identify patients most likely to benefit from specific therapies.

Equally important is the growing recognition of patient-centred outcomes. Beyond improvements in muscle strength or laboratory parameters, treatment strategies should also aim to address fatigue, physical function and overall quality of life. Incorporating patient-reported outcome measures into both clinical trials and routine care will be essential to ensure that therapeutic advances translate into meaningful benefits for those living with these chronic conditions[24–26].

In conclusion, the treatment of idiopathic inflammatory myopathies is entering a period of significant transformation. While glucocorticoids and conventional immunosuppressants continue to form the backbone of therapy, the emergence of biologic agents, targeted immunomodulators and small-molecule inhibitors is gradually expanding the therapeutic repertoire. However, the complexity and heterogeneity of these disorders demand a more personalised and evidence-based approach. Continued research, international collaboration and improved disease stratification will be crucial to fully realise the potential of these emerging therapies and ultimately improve outcomes for patients with IIM.

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