Review

Non-inflammatory mimickers of myositis: a guide for rheumatologists

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ABSTRACT

Muscle dysfunction presenting with weakness and elevated muscle enzymes poses a significant diagnostic challenge for rheumatologists, particularly in differentiating idiopathic inflammatory myopathies (IIM) from other mimicking conditions. This review systematically categorises non-inflammatory muscle diseases, including drug-induced myopathies, endocrine myopathies, genetic muscular dystrophies, metabolic and mitochondrial myopathies, and neuromuscular junction disorders, that can clinically and histologically resemble myositis. We emphasise the importance of a detailed clinical evaluation, including history, pattern of muscle involvement, extramuscular features, and comprehensive laboratory and biopsy investigations, to avoid misdiagnosis. Awareness of these mimickers is crucial for guiding appropriate diagnostic workup and management, given the distinct therapeutic approaches required for each condition. This framework aims to assist rheumatologists in improving diagnostic accuracy, optimising patient management, and enhancing referral decisions in patients presenting with muscle weakness.

Introduction

Skeletal muscle is one of the three major muscle tissues of the human body, able to generate voluntary muscle contraction, force, and movement, sustain body posture and position, and stabilise joints due to its highly organised tissue (Fig. 1) (1). Pathological inflammation (myositis) can lead to muscle weakness, typically proximal, which is the main clinical hallmark of idiopathic inflammatory myopathies (IIM) (2). IIMs are a heterogeneous group of immune-mediated disorders that include several extra-muscular manifestations, such as skin lesions, arthritis, interstitial lung disease, and heart involvement (2). Apart from an elevation of the muscle enzymes' serum concentration, autoantibodies can be found in up to 60% of patients and help establish a diagnosis. Myositis-specific autoantibodies (MSAs) are associated with particular organ manifestations and disease subgroups (3). IIMs can be classified into several subgroups, including dermatomyositis (DM), antisynthetase syndrome, immune-mediated necrotising myopathy (IMNM), inclusion body myositis (IBM), and overlap myositis, according to different combinations of clinical phenotypes, autoantibody profile, and histopathological findings (4-6). However, clinical and laboratory parameters suggestive of myositis are insufficient to establish a diagnosis due to several mimicking diseases that should be considered (7). Apart from IIM, numerous genetic, endocrine, immune-mediated, or toxic conditions can cause muscle weakness, myalgia, or high serum concentrations of muscle enzymes (8). Therefore, it is key to consider more prevalent conditions that present similarly.

This review aims to summarise the different types of non-inflammatory muscle diseases, providing a framework to assist rheumatologists in differentiating these conditions from IIM, supporting accurate diagnosis and optimal patient referral and management.

Which drugs commonly used in Rheumatology can induce myopathy?

A thorough history of drug consumption is essential in the evaluation of patients presenting with muscle disorders. This includes prescription medicines (*e.g.* Zidovudine), over-the-counter drugs (*e.g.* red rice), and illicit drugs (*e.g.* cocaine) (8). Some drugs familiar to rheumatologists should be

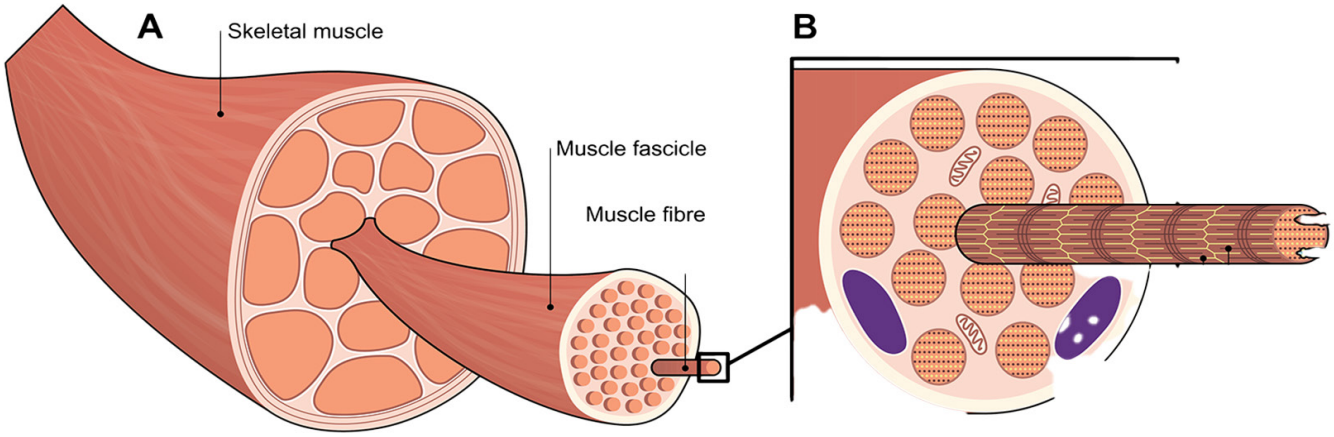

Fig. 1. Structure of skeletal muscle. The skeletal muscle is a highly organised tissue composed of bundles of fascicles, each composed of muscle fibres called myofibres (**A**). Myofibres are multinucleated cells with an essential structural and functional unit responsible for muscle contraction, the sarcomere. The sarcomere comprises three critical key components, namely thin filaments, thick filaments, and support proteins, that are organised to efficiently generate force and contract muscle in an ATP-dependent process (**B**). Nuclei are in the cell's periphery, adjacent to its membrane, the sarcolemma. The sarcolemma is a tubular sheath that encases each muscle fibre, forming a barrier between the extracellular and intracellular compartments with different calcium (Ca2+) levels.

Table I. Clinical and histological characteristics of toxic myopathies.

Drug	Prevalence of myopathy	Symptoms	Muscle biopsy
Statins* (10)	10-29%	Myalgia and tenderness (proximal muscles) Fatigue Muscle weakness (lower limbs) CK elevation (severe cases of rhabdomyolysis)	Necrotic muscle fibres Regenerating fibres Minimal or absent inflammation
Glucocorticoids (14)	10-60%	Proximal muscle weakness Muscle atrophy [Does not present myalgia, and CK levels can be normal]	Selective type 2 fibre atrophy No significant inflammation
Colchicine (18)	1-2%	Proximal muscle weakness Myalgia Elevation of CK (severe cases of rhabdomyolysis)	Vacuolar myopathy Lipid accumulation Muscle fibre degeneration Mild or absent inflammation
Chloroquine, hydroxychloroquine (17)	12.9% (particularly after years of therapy)	Proximal muscle weakness Fatigue Muscle atrophy Cardiomyopathy	Vacuolar myopathy Myofibrillar disorganisation Phospholipid inclusions (lamellar bodies)
Antiretroviral drugs (particularly Zidovudine) (98)	1-5% (17-20% Zidovudine)	Muscle weakness (legs and arms) Exercise intolerance Fatigue Elevation of CK (severe cases of rhabdomyolysis)	Ragged-red fibres on Gömöri trichrome stain, increased number of swollen and abnormal mitochondria Muscle fibre atrophy Mild necrosis and regeneration
Alcohol (99)	Acute alcoholic myopathy: 5-10% Chronic alcoholic myopathy: 40-60%	Acute myopathy: Sudden onset of myalgia, weakness, and swelling. Chronic myopathy: Proximal muscle weakness and muscle fibre atrophy and wasting	Muscle fibre atrophy (both type 1 and type 2 fibres, but type 2 fibres are more severely affected) Necrosis of muscle fibres (acute alcoholic myopathy) Fatty infiltration (chronic alcohol use) Absence of inflammation
Amiodarone (21)	<1%	Proximal muscle weakness Fatigue	Lipid accumulation Mitochondrial changes Muscle fibre necrosis Mild or absent inflammation
Tacrolimus and cyclosporine (21)	<5%	Proximal muscle weakness Elevation of CK (severe cases of rhabdomyolysis)	Type 2 muscle fibre atrophy Minimal or no inflammation Vacuolar changes Mitochondrial dysfunction may occasionally be present
Interferon-alpha (20)	5-10%	Myalgia Proximal muscle weakness (can cause inflammatory myositis)	Muscle fibre atrophy and necrosis Perivascular and endomysial inflammation with T-cell infiltrates

*Does not include immune-mediated necrotising myopathy (IMNM). CK: creatine kinase.

Table II. Clinical and histological characteristics of endocrine myopathies.

Endocrine disorder	Prevalence of myopathy	Symptoms	Ancillary exams
Hypothyroidism (34)	30-80%	Myalgia, cramps and stiffness Proximal muscle weakness Delayed relaxation of deep tendon reflexes Pseudomyotonia	Elevated TSH Elevated CK (variable, but can be very high) Electromyography can be normal or demonstrate myopathic changes (lack of fibrillation potentials)
Hyperthyroidism (100)	60-80%	Proximal muscle weakness Muscle wasting Fatigue Fine muscle tremors Periodic paralysis (rare)	Reduced TSH Normal CK Electromyography may be normal or demonstrate myopathic changes (lack of fibrillation potentials)
Acromegaly (101)	30-50%	Proximal muscle weakness Muscle hypertrophy Fatigue	Elevated serum IGF-1 Elevated CK Nonspecific findings on electromyography
Hyperparathyroidism (36)	20-50%	Proximal muscle weakness Fatigue Hyperreflexia (Mimics motor neuron disease)	Elevated PTH Normal CK Nonspecific findings on electromyography
Hypoparathyroidism (33)	Rare	Muscle cramps Stiffness Mild weakness Distal paraesthesia Tetany (low calcium levels)	Reduced PTH Levels of CK are variable (elevation tends to be more pronounced in those with severe or chronic hypocalcaemia) Nonspecific findings on electromyography
Adrenal insufficiency (102)	20-40%	Fatigue Myalgia Cramps Generalised muscle weakness (particularly in periods of adrenal crisis)	Reduced cortisol levels CK can be elevated Nonspecific findings on electromyography
Cushing syndrome (103)	40-70%	Proximal muscle weakness Muscle atrophy	Elevated cortisol levels Normal CK levels Non-specific findings on electromyography
X-liked hypophosphataemia (XLH) (39)	1 in 20,000 to 60,000 live births Mutations in PHEX gene Inherited X-linked dominant	Myalgia Muscle weakness Fatigue (Rickets/osteomalacia, lower limb deformities, enthesopathy, short stature)	Low serum phosphate (due to renal phosphate wasting) Inappropriately normal/low 1,25-OH_2 vitamin D Normal ALP (or high for age)
Hypophosphatasia (HPP) (40)	1 in 6,000 Mutations in ALPL gene Inherited autosomal dominant or recessive	Fatigue Proximal weakness Exercise intolerance (Rickets/osteomalacia, fractures, premature loss of deciduous teeth, variable severity)	Persistently low serum alkaline phosphatase Calcium and phosphate usually normal

ALP: alkaline phosphatase; CK: creatine kinase; IGF-I: insulin-like growth factor-I; PTH: parathyroid hormone; TSH: thyroid-stimulating hormone.

considered when evaluating a patient (Table I).

Rheumatic diseases are consistently associated with high cardiovascular risk, and rheumatic patients are often treated with statins. Statins are commonly associated with muscle-related adverse events, which are reported in up to 27% of patients (9). The most common are myalgia in proximal muscles and high serum creatine kinase (CK) levels, which typically occur at the beginning of the treatment (10). Rarely, patients can also develop statin-induced IMNM, which is classically associated with the presence of anti-3-hydroxy-3-methylglutaryl-coenzyme antibodies (anti-HMGCR), which target an enzyme involved in cholesterol synthesis (11). The estimated incidence rate of IMNM is 2-3/100,000 patients using statins (12). From all patients with anti-HMGCR IMNM, around 44% had statin exposure (13). Of note, statins should not be reintroduced in patients with statin-induced IMNM. However, statins are not contraindicated in patients with other IIMs.

Glucocorticoids can induce two types of myopathies. Acute glucocorticoid-induced myopathy is uncommon and might occur in patients treated with doses greater than 60 mg of prednisone equivalents per day for five to seven days. Chronic myopathy is more common, usually associated with the prolonged administration (>4 weeks) of doses greater than 10 mg of prednisone equivalents per day, and can occur in up to 60% of patients. It usually affects proximal muscles and is typically painless (14). Even more complex is the evaluation of patients with IIM after prolonged treatment with glucocorticoids, since proximal muscle weakness in these patients may be due to either persistent disease activity or glucocorticoid-induced muscle damage. Of note, there can be an absence of inflammatory cell infiltrates on muscle biopsy after treatment with glucocorticoids, which can make it harder to distinguish glucocorticoid-induced myopathy from active myositis.

Hydroxychloroquine can also lead to similar confusion since it is sometimes used to treat skin manifestations of DM (15). More often, it is used to treat systemic lupus erythematosus, a disease that can also cause myositis in 4–16%

of patients (16). Muscle biopsy can help distinguish myositis from hydroxychloroquine-induced myopathy, which can occur in 12.9% of patients (17). Hydroxychloroquine-induced myopathy usually has no inflammatory cell infiltration and may have typical vacuolar inclusions in the muscle histopathology (17).

Colchicine-induced myopathy is uncommon (<2%) and is usually associated with peripheral neuropathy, gastrointestinal adverse events, and bone marrow aplasia (18). These accompanying features are essential to distinguish it from IIM, since it may also induce proximal muscle weakness with high CK levels.

Interferon-alpha is used in the treatment of viral hepatitis, cancer, and severe and refractory Behçet's disease (19). Interferon-alpha-induced myopathy can occur in 5–10% of patients and presents similarly to an IIM, with symptoms developing in weeks to months (20). It is key to determine the temporal relationship between symptom onset and interferon therapy (20).

Specific muscle biopsy findings can occur in certain drug-induced myopathies (21). Key features, such as muscle fibre necrosis, vacuolar changes, mitochondrial abnormalities, and the absence of inflammation, can help differentiate drug-induced myopathies from other muscle diseases, such as IIM. However, these findings are not always present, and biopsy findings must be correlated with clinical and drug exposure history and laboratory findings for an accurate diagnosis. Discontinuing or modifying the offending medication often leads to improvement, and treatment typically involves supportive care, such as physical therapy and pain management.

A special consideration for immune checkpoint inhibitors

Immune checkpoint inhibitors (ICIs), which target the T-cell cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) or the programmed cell death(-ligand) one pathway (PD-1/PD-L1), have revolutionised the treatment of many types of cancer by enhancing anti-tumour immune responses. However, with the expanding indications of these drugs, ICI-associated immune-related adverse events are increasingly recognised (22). Among them, myopathy and myositis represent important toxicities. ICI-induced myopathy may range from asymptomatic serum CK elevation to severe weakness with respiratory failure leading to death (23). Myalgia is a common but non-specific complaint in ICI trials and often precedes the development of symmetrical proximal muscle weakness, frequently involving the pelvic girdle and neck extensors, contrasting with the flexor predominance seen in IIMs (24). Besides, 0.1–1% of treated patients might develop ICI-related myositis, which is usually a severe and life-threatening condition (25). PD-1 inhibitors are more frequently associated with ICI-myositis and with overlap syndromes. For example, pembrolizumab has been associated with fulminant myositis complicated by myocarditis and myasthenia gravis (called the "3M overlap") (26), and nivolumab (27) has been reported to cause severe myasthenia–myositis overlap requiring intensive care. In addition, atezolizumab (28) (PD-L1) has been implicated in the development of concurrent myositis and myocarditis with acute respiratory failure. A study based on a real-world pharmacovigilance database, EudraVigilance, found that avelumab (PD-L1), durvalumab (PD-L1), and pembrolizumab (PD-1) were associated with a higher likelihood of developing myositis (29). Ipilimumab (30) (CTLA-4) is more associated with myositis in combination regimens with nivolumab. Although rare, it is important to keep in mind that ICI-related myositis is usually a severe and life-threatening condition, as it can lead to profound muscle weakness, respiratory failure, and cardiac complications. Besides, the absolute number of incident cases is expected to rise as the use of ICIs to treat cancer becomes more widespread. According to EULAR recommendations, rapid initiation of treatment is essential: discontinuation of the ICI alone is rarely sufficient. High-dose glucocorticoids are first-line therapy, while refractory or fulminant cases may require additional immunosuppressive measures, including intravenous immunoglobulin, plasma exchange, or other steroid-sparing immunosuppressants, to avert fatal outcomes (31).

Which endocrine disorders should be ruled out when evaluating a patient with muscle weakness?

Several endocrine disorders may lead to proximal muscle weakness, myalgia, or additional rheumatic symptoms, such as arthralgia (32). While these disorders are common in the general population, the exact prevalence of neuromuscular complications secondary to endocrine dysfunctions is unknown and is likely to be underestimated (33).

In hypothyroidism, symptoms are initially nonspecific and constitutional. Deposition of glycosaminoglycans in the sarcomere impairs the contractility of the actin-myosin unit and slows down motor activity (34). Commonly presenting with proximal muscle weakness and high CK serum levels, hypothyroid myopathy may be mistaken for IIM if thyroid function tests are not included in the diagnostic workup (35, 36).

Hyperparathyroidism and hypoparathyroidism have been linked to muscle dysfunction, primarily due to hypercalcaemia and hypocalcaemia, respectively (36).

Both adrenocortical overproduction and adrenal insufficiency can cause myopathy. Cushing's syndrome's clinical presentation and pathophysiology may be similar to exogenous glucocorticoid-induced myopathy. In Addison's disease (chronic adrenal insufficiency), muscle tenderness is commonly reported with generalised muscle weakness (37). Electrolyte imbalance, such as hyperkalaemia or severe hyponatraemia, can also lead to myopathic changes (38).

There is increasing evidence that conditions related to hypophosphataemia, such as osteomalacia and X-linked hypophosphataemia, can lead to myopathy. Muscle weakness, rhabdomyolysis, and myoglobinuria may occur due to phosphorus depletion (39). Hypophosphatasia (HPP), a rare inherited metabolic disorder, should also be considered in the differential. Persistently low serum alkaline phosphatase

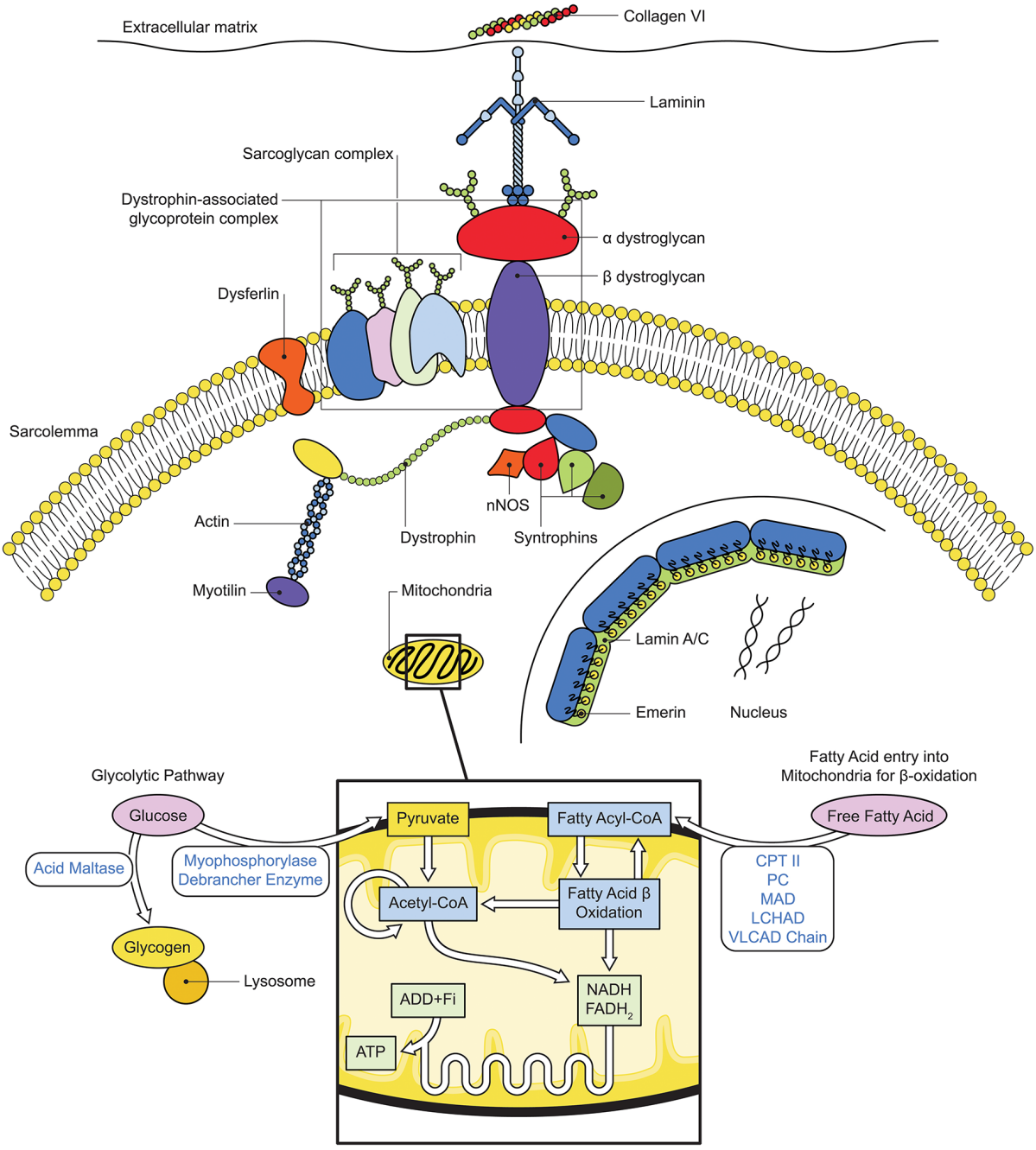

Fig. 2. Proteins and enzymes important for the functioning of the muscle cell. Collagen VI, laminin, and alpha-dystroglycan anchor the sarcolemma to the extracellular matrix. The dystrophin-associated glycoprotein complex helps connect the internal cytoskeleton of muscle fibre to the extracellular matrix. The anchoring of the muscle fibre to the extracellular matrix is essential to keep the structural integrity of the muscle cell, especially during muscle contraction. Apart from being an essential structural protein of the cytoskeleton, actin is also one of the sarcomeric proteins with a contractile function. Lamin A/C and emerin are crucial in stabilising the nuclear envelope structure and keeping its integrity. Abnormalities in all these proteins can lead to different myopathies. Glycogen is a critical energy storage molecule for muscle cells, serving as a rapidly mobilisable source of glucose during physical activity. The regulation of glycogen involves two primary reactions: glycogen synthesis and breakdown. These reactions are tightly controlled to balance energy storage and usage based on cellular energy demands. When glycogen supplies are insufficient, fatty acid metabolism is crucial in providing energy for ATP production. Deficiency of numerous enzymes are recognised to cause myopathies: acid maltase, myophosphorilase, debrancher enzyme, causing glycogen storage diseases; carnitine palmitoyltransferase II (CPT II), primary carnitine (PC), very-long-chain acyl-CoA dehydrogenase (VLCAD), multiple acyl-CoA dehydrogenase (MAD), long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHA), causing lipid storage myopathies. The metabolism depends on converging enzymatic pathways in the cellular mitochondria. Mitochondria are also essential for generating energy in muscle cells since they allow the production of ATP through oxidative phosphorylation. Besides, mitochondria are central to muscle cell calcium homeostasis and cellular signalling. Mutations of key enzymes in these metabolic pathways may lead to a lack of glycogen storage, lipid deposition, or an inability to produce sufficient energy for muscle contraction.
Note: The structures are not shown to scale.
ADP: adenosine diphosphate; ATP: adenosine triphosphate; CPT II: carnitine palmitoyltransferase II; $FADH_2$: flavin adenine dinucleotide; LCHA: long-chain 3-hydroxyacyl-CoA dehydrogenase; MAD: multiple acyl-CoA dehydrogenase; NADH: nicotinamide adenine dinucleotide; nNOS: neuronal nitric oxide synthase; PCR: primary carnitine; Pi: inorganic phosphate; VLCAD: very-long-chain acyl-CoA dehydrogenase.

Table III. Epidemiological, clinical and histological characteristics of muscular dystrophies.

Condition	Prevalence of myopathy	Mutation	Symptoms	Muscle biopsy
Myotonic dystrophy (104)	1 in 8,000 individuals	CTG repeat expansions in the *DMPK* gene (Type 1) or CCTG repeat expansions in the *CNBP* gene (Type 2) Autosomal dominant	Type 1: Muscle waste, distal muscle involvement, myotonia, cataracts, cardiac arrhythmias, and endocrine issues. Type 2: More prominent proximal muscle weakness; other features are milder when present.	Muscle type 1 fibre atrophy Hypertrophic fibres Nuclear internalisation Ring fibres Fibrosis Mild inflammatory changes.
Duchenne muscular dystrophy(49)	1 in 3,500 to 5,000 male births Early childhood onset	*DMD* gene (encodes dystrophin) X-linked recessive	Progressive muscle weakness Loss of ambulation Cardiac involvement Respiratory involvement CK elevation	Muscle fibre necrosis and regeneration Inflammatory infiltration Fibrosis Fatty replacement **Absent or significantly reduced staining for dystrophin in immunohistochemistry.**
Becker muscular dystrophy (50)	1 in 18,000 male births Later-onset and milder form than DMD	*DMD* gene (mutation results in a partially functional dystrophin protein) X-linked recessive	Milder than DMD Muscle weakness Sower progression (patients may remain ambulatory into their 30s or 40s) CK elevation (milder than DMD) Cardiomyopathy	Mild muscle fibre degeneration Myofibrillar disorganisation Inflammatory infiltrates Fibrosis Fibroblast and fatty infiltration **Reduced dystrophin staining in immunohistochemistry.**
Facioscapulohumeral muscular dystrophy (54)	1 in 20,000 individuals	Deletion in the D4Z4 region on chromosome 4, with dysregulation of the *DUX4* gene Autosomal dominant	Weakness in facial, shoulder, and upper arm muscles Can potentially involve legs (foot drop) Asymmetric muscle weakness is common Mild CK elevation	Type I fibre atrophy Endomysial fibrosis Mild inflammatory infiltration Normal dystrophin staining
Limb-girdle muscular dystrophy (57)	1 in 14,500 to 1 in 123,000, depending on subtype	Mutations in various genes affecting proteins involved in muscle structure (*e.g. CAV3, CAPN3, DYSF, SGCA, SGCB, SGCG*) Autosomal dominant or recessive	Weakness in limb-girdle muscles Progressive muscle wasting Variable cardiomyopathy Respiratory involvement (depending on subtypes) CK elevation	Muscle fibre atrophy Muscle fibre degeneration Regenerated fibres with centrally located nuclei Vacuoles Endomysial and perimysial fibrosis Mild inflammatory infiltrates **Immunohistochemical abnormalities in specific muscle proteins (*e.g.* sarcoglycans, dysferlin)**
Congenital muscular dystrophies (73)	1 in 20,000 to 1 in 50,000 individuals Present at birth or early infancy	Mutations in various genes that affect muscle, eye and brain development (*e.g. MDC1A, LAMA2, COL6A1, FKTN, POMT1*) Autosomal dominant or recessive	Hypotonia Delayed motor milestones Progressive muscle weakness Some forms involve brain abnormalities (Some cases can present before birth with reduced foetal movement and polyhydramnios)	Muscle type 1 fibre atrophy Muscle fibre degeneration Regenerated fibres with centrally located nuclei Fibrosis Mild inflammatory changes **Abnormalities in merosin, collagen, alpha-dystroglycan, or other structural proteins, depending on the disease subtype in immune-histochemistry**
Emery-Dreifuss muscular dystrophy (42)	1 in 100,000 individuals	*EMD* gene (emerin) or *LMNA* gene (lamin A/C) X-linked recessive or autosomal dominant	Progressive muscle weakness in biceps and calves Early contractures of the elbows, Achilles tendons, neck and spine Respiratory involvement Cardiac arrhythmias (Ventricular arrhythmias) Dilated cardiomyopathy CK elevation	Muscle type 1 fibre atrophy Muscle fibre degeneration and regeneration Fibrosis Mild inflammatory changes Mitochondrial changes **Abnormalities in structural proteins (*e.g.* lamin, emerin) in immune-histochemistry**
Distal muscular dystrophy (59)	Rare Specific prevalence varies by subtype	Mutations in various genes (*e.g.* MYOT, DYSF, TTN) Autosomal dominant or recessive	Weakness and wasting of the muscles in the hands, feet, and lower legs Slower progression than other forms of muscular dystrophy	Muscle type 1 fibre atrophy Muscle fibre degeneration Internal structure alterations (*e.g.* rimmed vacuoles, cytoplasmatic bodies, myofibrillar aggregates) Fibrosis Mild inflammatory infiltration **Abnormalities in structural proteins (*e.g.* myotilin, desmin) in immune-histochemistry**

CK: creatine kinase; DMD: Duchenne muscular dystrophy.

should alert to this condition. Enzyme replacement therapy can improve not only skeletal outcomes but also muscle strength and motor function (40).

The diagnosis of endocrine myopathies does not depend on muscle biopsy, as muscle findings are mostly non-specific and non-diagnostic (33). Diagnosing these myopathies mostly depends on a careful clinical evaluation and blood and/or urine workup, including the measurement of some hormones (Table II). The role of muscle biopsy in these cases is to exclude other non-endocrine aetiologies.

Which genetic muscle diseases should be kept in mind when myositis is suspected?

Myofibres rely on numerous structural and metabolic proteins (Fig. 2) (41). Mutations affecting these proteins cause inherited myopathies, broadly classified into muscular dystrophies, metabolic myopathies, mitochondrial myopathies, and congenital myopathies (42, 43).

Muscular dystrophies

Muscular dystrophies typically present with progressive weakness and elevated CK, sometimes with inflammatory biopsy changes, which often make them misdiagnosed as IIM (44). There are over a hundred types of muscular dystrophies, with many genes and their respective proteins (Fig. 2) implicated in their pathogenesis (Table III).

Myotonic dystrophy type 1 (MD1) is the most frequent type of muscular dystrophy worldwide. Together with myotonic dystrophy type 2 (MD2), they represent autosomal dominant disorders presenting with progressive proximal muscular weakness, myotonia, cardiac conduction disturbances, and cataracts (45). Other characteristics include frontal alopecia, cognitive impairment, endocrine disturbances, and an increased risk of cancer (46). MD1 also typically presents distal weakness of the dorsiflexors and long finger flexors (47). The presence of myotonia with other clinical and histological features supports the diagnosis of a myotonic disorder. Genetic testing is often required to confirm the diagnosis. Family history can also provide important clues, especially due to anticipation phenomena (48).

Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) are both dystrophinopathies and represent the second most common cause of muscular dystrophy (42). DMD is the most prevalent and severe phenotype, affecting 1 in 5000 male live births. Generally asymptomatic at birth, male infants exhibit difficulty in ambulation after the age of 3 and later scoliosis, upper limb dysfunction, respiratory insufficiency, and cardiomyopathy. Survival expectation is usually no longer than the late twenties. Clinical examination may reveal muscular pseudohypertrophy in the calf muscles, while limb-girdle muscles exhibit atrophy (49). The severity spectrum of BMD is substantially milder and encompasses a broader spectrum, depending on the levels of dystrophin activity (50). Importantly, cardiac involvement with dilated cardiomyopathy can be prominent, and its severity does not necessarily correlate with skeletal muscle involvement (51). Of note, dystrophinopathies are not exclusive to the male gender, and different presentations can be found in women, such as myalgia, increased CK serum levels, or isolated cardiomyopathy (52). However, given the prevalence of this condition, it is not uncommon for a rheumatologist to come across a female patient with dystrophinopathy. Most female carriers of the abnormal dystrophin gene have few or no symptoms (53). The history of affected male patients in their families is helpful but can be lacking, and the disease is sometimes diagnosed after the birth of a male child.

Facioscapulohumeral dystrophy (FSHD) typically presents in young adults who complain of asymmetrical upper limb weakness. Besides, as suggested by its name, weakness of the shoulder girdle muscles, scapular winging, and facial weakness are usually present (54). FSHD is most often inherited in an autosomal dominant fashion, but several genetically distinct forms have been identified (55). Patients with early-onset FSHD worsen rather quickly since they tend to have more severe muscular weakness and manifest systemic symptoms more frequently than those with adult-onset FSHD. One-third of patients have inflammatory muscle biopsies with $CD4^+$ and $CD8^+$ T-cell infiltrates (56).

Limb-girdle muscular dystrophies (LGMD) are a heterogeneous group of inherited neuromuscular disorders due to mutations in more than thirty different genes. Typically, patients present with significant proximal muscle weakness and typical scapular winging (57). The assessment of different proteins by immunohistochemistry in muscle specimens, suggestive patterns on muscle imaging, and gene sequencing can help guide the diagnostic process (57, 58).

Distal myopathies are a heterogeneous group of rare, genetically inherited muscle disorders primarily affecting distal muscles (59). Welander distal myopathy has an autosomal dominant inheritance and typically presents in adults around 40–50 years old (60). Since it usually involves the hand and forearm first, fine motor skills, such as gripping or writing, are often affected first and progressively spread to the lower limbs later. This clinical pattern might be confused with IBM, although the latter affects mainly the deep flexors of the fingers and the former the extensors. Genetic and histological findings might differentiate between these two conditions. Regarding other subtypes of distal myopathies, considering their distal-predominant weakness pattern and age of onset, they should not be confused with IIM (59).

Metabolic myopathies

Metabolic myopathies result from inherited enzymatic defects that impair energy production within muscle tissue, encompassing conditions such as glycogen storage diseases (GSD) and fatty acid oxidation disorders (FAOD) (43).

There are more than a dozen different known GSDs, but only some involve the skeletal and cardiac muscle, such as GSD Type II, III, V, and VI (Table IV) (61). Patients with McArdle disease (GSD type V) typically experience early fatigue, muscle pain, stiffness, or even cramps due to their inability to effec-

Table IV. Clinical and histological characteristics of metabolic myopathies.

Name	Prevalence of myopathy	Mutation and enzyme deficiency	Symptoms	Muscle biopsy findings
Glycogen storage disease				
McArdle disease (glycogen storage disease type V) (62)	1 in 100,000 individuals can present in childhood or early adulthood	PYGM gene (encodes the enzyme myophosphorylase) autosomal recessive	Myalgia, cramps and fatigue during exercise Exercise intolerance "Second wind" phenomenon Markedly elevated CK levels (often over 10,000 IU/L) Myoglobinuria	Variability in muscle fibre size Subsarcolemmal glycogen accumulation in PAS staining Absent myophosphorylase on enzyme histochemistry Muscle can have a normal appearance at rest, but necrosis and muscle damage can be seen after exercise.
Infantile onset Pompe disease (glycogen storage disease type II) (64)	1 in 100,000 to 1 in 40,000 live births	GAA gene (encodes the enzyme acid maltase)	Severe muscle weakness Respiratory failure Cardiomyopathy Early death (if untreated)	Variability in muscle fibre size PAS staining shows excessive glycogen accumulation in lysosomes and the cytoplasm Glycogen-filled vacuoles Lysosomal enlargement Fibre necrosis and regeneration (advanced disease) (Acid alpha-glucosidase enzyme activity is not commonly measured in muscle tissue, but in blood)
Late-Onset Pompe Disease (glycogen storage disease type II) (64)	1 in 40,000 to 1 in 60,000	GAA gene (encodes the enzyme acid maltase)	Progressive muscle weakness Respiratory insufficiency (no heart involvement)	
Cori disease (glycogen storage disease type III) (61)	1 in 100,000 individuals Onset is typically in childhood.	AGL gene (encodes the debranching enzyme)	Proximal muscle weakness Liver enlargement Hypoglycaemia Cardiomyopathy	PAS staining shows excessive glycogen (with abnormal branching and structure) accumulation in the cytoplasm Cytoplasmic vacuoles Type 1 fibre hypertrophy Muscle fibre degeneration and regeneration (more advanced cases or following exercise) Mitochondrial accumulation.
Glycogen storage disease type IV (Anderson disease) (61)	1 in 800,000 to 1 in 1,000,000 individuals Typically, it presents in infancy or childhood, but some later-onset muscular forms exist.	GBE1 gene (encodes the glycogen branching enzyme)	Progressive muscle weakness Liver dysfunction Neurological involvement Cardiomyopathy	Muscle fibre size variability Abnormal glycogen structure (polyglucosan) positive in the PAS staining Vacuoles containing these abnormal deposits Fibre degeneration and fibrosis Occasionally, some biopsies may show inflammatory cell infiltration in the damaged muscle.
Lipid storage myopathies				
Carnitine palmitoyl-transferase II (CPT II) deficiency (68)	1 in 40,000 to 100,000 individuals There are three forms: neonatal, infantile, and adult myopathic form (most common)	CPT2 gene (enzyme CPT II is essential for transporting long-chain fatty acids into the mitochondria for β-oxidation)	Myalgia Muscle weakness Rhabdomyolysis (triggered by prolonged exercise, fasting, or illness). Severe neonatal forms can also lead to life-threatening multi-organ dysfunction.	Excessive lipid droplets in muscle fibres are revealed by lipid staining with Oil Red O or Sudan Black B Ragged red fibres stained with Gomori trichrome stain Lipid-filled vacuoles Mitochondrial changes on electron microscopy Absence of inflammation
Very-long-chain acyl-CoA dehydrogenase (VLCAD) deficiency (105)	1 in 30,000 to 100,000 individuals	ACADVL gene (encodes the VLCAD enzyme involved in mitochondrial fatty acid oxidation)	Muscle weakness Hypoglycaemia Cardiomyopathy Rhabdomyolysis The severe form may manifest in infancy with liver failure, heart problems, and rhabdomyolysis.	
Primary carnitine deficiency (PCD) (106)	1 in 100,000 individuals	SLC22A5 gene (encodes the carnitine transporter)	Muscle weakness Fatigue Hypoglycaemia Cardiomyopathy (during physical stress or fasting)	
Multiple acyl- CoA dehydrogenase deficiency (MADD) (107)	1 in 200,000 live births	ETFDH, ETFA, ETFB genes (impaired fatty acid β-oxidation and amino acid metabolism)	Muscle weakness Exercise intolerance Hypoglycaemia Rhabdomyolysis	
Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency (108)	1 in 250,000 births	HADHA gene (encodes the enzyme LCHAD)	Muscle weakness Hypoketotic hypoglycaemia Cardiomyopathy Hepatopathy Rhabdomyolysis.	

CK: creatine kinase; CPT II: carnitine palmitoyl-transferase II; LCHAD: long-chain 3-Hydroxyacyl-CoA dehydrogenase; MADD: multiple acyl-CoA dehydrogenase deficiency; PAS: periodic acid-Schiff; PCD: primary carnitine deficiency; VLCAD: very-long-chain Acyl-CoA dehydrogenase.

Table V. Clinical and histological characteristics of mitochondrial myopathies.

Condition	Prevalence of myopathy	Mutations	Symptoms
Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) (99)	1 in 4,000 to 10,000 individuals Onset usually in childhood or early adulthood	MT-TL1 gene (mitochondrial tRNA for leucine); other mtDNA mutations	Muscle weakness Headache Stroke-like episodes Seizures Lactic acidosis Hearing loss
Kearns-Sayre syndrome (KSS) (100)	1 in 100,000 individuals Onset is usually before age 20	Large deletions in mtDNA	Muscle weakness Ataxia Progressive external ophthalmoplegia Ptosis Pigmentary retinopathy with progressive degeneration Cardiac conduction defects
Myoclonic epilepsy with ragged-red fibres (MERRF) (101)	< 1 in 100,000 individuals	MT-TK gene (mitochondrial tRNA for lysine)	Muscle weakness Myoclonus Seizures Ataxia Hearing loss
Mitochondrial DNA Depletion Syndrome (MDDS) (67)	Rare Onset varies but often starts in infancy or early childhood	Mutations in genes involved in mtDNA replication (*e.g.* TK2, POLG, DGUOK).	Severe muscle weakness Exercise intolerance Encephalopathy Hepatopathy Respiratory failure

mtDNA: mitochondrial DNA.

tively use glycogen as a source of energy during the onset of exercise (62). After a few minutes of low-intensity exercise, there is a marked improvement in symptoms and a renewed ability to continue exercising, due to the use of alternative energy sources from the bloodstream, bypassing the defective glycogenolytic pathway. This unique characteristic is known as the "second wind phenomenon", distinguishing myophosphorylase deficiency from other metabolic myopathies (63). Muscle weakness is less prominent than in other muscle diseases and predominantly affects proximal muscles. Patients typically do not report muscle fatigue between episodes but can have moderately elevated CK levels, even after prolonged rest. Clinical manifestations of patients with GSD Type II, or Pompe disease, vary according to the age of onset, which depends on the nature of the mutations and the residual enzymatic activity levels (64). Late-onset or non-classic form Pompe disease (LOPD) can occur at a young or adult age and present different features, including progressive proximal myopathy, exercise intolerance, and respiratory insufficiency. The diaphragm tends to be more severely involved than other skeletal muscles, and a low forced vital capacity on pulmonary function testing should raise suspicion for acid maltase deficiency (65). Other GSDs involving the musculoskeletal system are extremely rare, with some, such as Types VII, IX, X, and XI, having only a few reports in the literature (61).

Lipid storage myopathies (LSM) encompasses a group of inherited metabolic myopathies characterised by defects in fatty acid metabolism, resulting in abnormal utilisation of lipids by the muscle (66). Since fatty acids are a crucial energy substrate for skeletal muscle, particularly during periods of exercise or fasting, individuals with LSM typically present with muscle weakness, myalgia, myoglobinuria, and exercise intolerance. LSMs are part of a larger group of disorders known as lipid storage diseases and can present a range of symptoms and multi-organ involvement (Table IV) (67). The most common is a mutation in the *CPT2* gene, responsible for carnitine palmitoyl-transferase II deficiency (68). As well as GSDs, LSMs can cause cardiomyopathy. Blood tests may reveal elevated levels of muscle enzymes during episodes of muscle damage, and acylcarnitine profiles, even outside episodes, can indicate defects in fatty acid metabolism. Muscle biopsy is often normal or only mildly changed. In some cases, skin fibroblast studies and specialised metabolic testing may be used to assess fatty acid oxidation. Genetic testing is crucial for identifying the specific mutation responsible for the disorder and can aid in confirming the diagnosis, determining prognosis, and guiding treatment (67).

Mitochondrial myopathies

Mitochondrial myopathies are another rare heterogeneous group of inherited disorders that profoundly impact muscle and nerve function due to energy production defects, which usually present in childhood or early adulthood. However, there are reports of late-onset forms manifesting in middle age or even later (68). These conditions result from mutations in mitochondrial DNA (mtDNA) or nuclear DNA affecting the function of mitochondria, the energy-producing organelles in cells. They can have a classical maternal inheritance or follow a Mendelian pattern (69). The clinical presentation is highly variable, depending on the specific mutation and the extent of mitochondrial dysfunction (Table V) (70). The most common symptoms include muscle weakness, fatigue, exercise intolerance, neurological symptoms, vision and hearing loss, arrhythmia, and lactic acidosis. Some patients may experience mild symptoms and have a near-normal life expectancy, while others, in contrast, may have a more severe disease course with significant disability or early death (69). Progressive external ophthalmoplegia is one of the most common clini-

cal manifestations of mitochondrial diseases and does not occur due to IIM, which makes it a key finding in distinguishing these two groups of myopathies (71). Muscle biopsy can present lipid droplets and an increased number of swollen and abnormal mitochondria, with an absence of inflammation (72).

Congenital myopathies

Congenital myopathies usually begin in the first year of life, with a non-progressive or very slowly progressive global weakness over decades and resulting in tetraparesis with axial, abdominal, cervical, and facial involvement. CK is normal, and there is usually no extramuscular involvement other than some degree of facial dysmorphia (73). Due to the age of onset, they are usually not a consideration for differential diagnosis of IIM, but many times, patients with these disorders only seek medical attention in their adult life, and the diagnosis can be delayed if the history of weakness during childhood or infancy is not ascertained through a detailed clinical history. Besides, later onset forms are increasingly recognised. The late-onset variants are often considered milder with slower progression (74). Diagnosis can be made through a combination of genetic testing and muscle biopsy (73).

Can neuromuscular junction disorders mimic myositis?

Neuromuscular junction disorders (NMJD) are a group of conditions that affect signal transmission between motor nerves and skeletal muscles at the neuromuscular junction, leading to muscle weakness and fatigability. Although rare, they have been increasingly recognised. The most common NMJDs include myasthenia gravis (MG), Lambert-Eaton myasthenic syndrome (LEMS), botulism, and congenital myasthenic syndromes with autoimmune, toxic, or genetic causes (75).

MG is caused by antibodies that bind acetylcholine receptors at the neuromuscular junction. Involvement of the extraocular muscles, including the *levator palpebrae superioris*, is the most common finding, but the clinical spectrum can range from a purely ocular form to association with severe weakness of the limbs, bulbar muscles, and respiratory muscles. Muscle weakness is typically due to muscle fatigability. In other words, weakness is usually prominent after the repetitive use of a certain muscle group. Symptoms vary in duration from hours to days and can be aggravated by hormonal variation, ambient temperature, emotional stress, medications that interact with the postsynaptic neuromuscular junction (Table VI), infections, and physical exercise (76). The age of onset varies from childhood to late adulthood, with disease peaks in younger adult women and older men. Antibodies against the acetylcholine receptor (AChR), MuSK, or LRP4 proteins can be found, and patients commonly have thymic abnormalities. Nerve conduction studies have an important role in diagnosis, where a characteristic pattern of decremental response after repetitive nerve stimulation is observed (77).

LEMS is rarer and is associated with antibodies that target voltage-gated calcium channels at the presynaptic neuromuscular junction, leading to reduced acetylcholine release. It affects adults in the sixth and seventh decades of life. Patients present with a triad of proximal muscle weakness, autonomic dysfunction, and hyporeflexia/areflexia (78). It can occur with milder involvement of the oculobulbar and axial muscles, and respiratory muscle weakness is rare. In about 50 to 60% of cases, LEMS is associated with malignancy, particularly small-cell lung carcinoma (79).

Table VI. Drugs to avoid in patients with myasthenia gravis.

Anaesthetic agents	Neuromuscular blocking agents (*e.g.* rocuronium, vecuronium, succinylcholine)
Antibiotics	Antibiotics Aminoglycosides (*e.g.* amikacin, gentamicin, neomycin, tobramycin) Fluoroquinolones (*e.g.* ciprofloxacin, levofloxacin, moxifloxacin, ofloxacin) Macrolides (*e.g.* azithromycin, clarithromycin, erythromycin) Penicillamine
Cardiovascular drugs	Beta blockers (*e.g.* atenolol, labetalol, metoprolol, propranolol) Procainamide Quinidine
Immune checkpoint inhibitors	Atezolizumab, ipilimumab, nivolumab, pembrolizumab
Antimalarials	Hydroxychloroquine, chloroquine
Glucocorticoids*	Dexamethasone, prednisone
Others	Statins (*e.g.* atorvastatin, pravastatin, rosuvastatin) Botulinum toxin Intravenous Magnesium (*e.g.* with magnesium sulphate, magnesium chloride)

*Glucocorticoids at high dose may cause transient worsening of symptoms during first one to two weeks of treatment.

In summary, what should we be aware of when evaluating a patient with muscle weakness and/or elevation of muscle enzymes?

The evaluation of patients with muscle weakness can be challenging (Fig. 3). First, the assessment of muscle strength can be subjective and vary between assessors (80). Additionally, patients with various conditions can present muscle weakness mimicking myositis (8). Therefore, a careful clinical assessment must be undertaken to exclude alternative diagnoses and manage these patients appropriately.

Since most muscular dystrophies are more prevalent than IIM, there is a high probability that rheumatologists evaluate patients with these disease conditions. Earlier age of onset, disease evolution, and family history can help differentiate these entities. With the notable exception of juvenile myositis, IIM patients are often middle-aged adults, unlike patients with genetic muscle diseases, who have an earlier onset of symptoms (2, 42). However, it is important to keep in mind that some muscular dystrophies, such as LGMD, and metabolic myopathies can have a later onset and that family history can be lacking primarily if there is an autosomal recessive inheritance pattern (81-84). The pattern of muscle weakness, as well as the presence of muscle atrophy, can be key in the differential diagnosis of myopathies. In contrast to muscle inflammation, which often evolves rapidly if not treated promptly, inherited myopathies develop progressively and

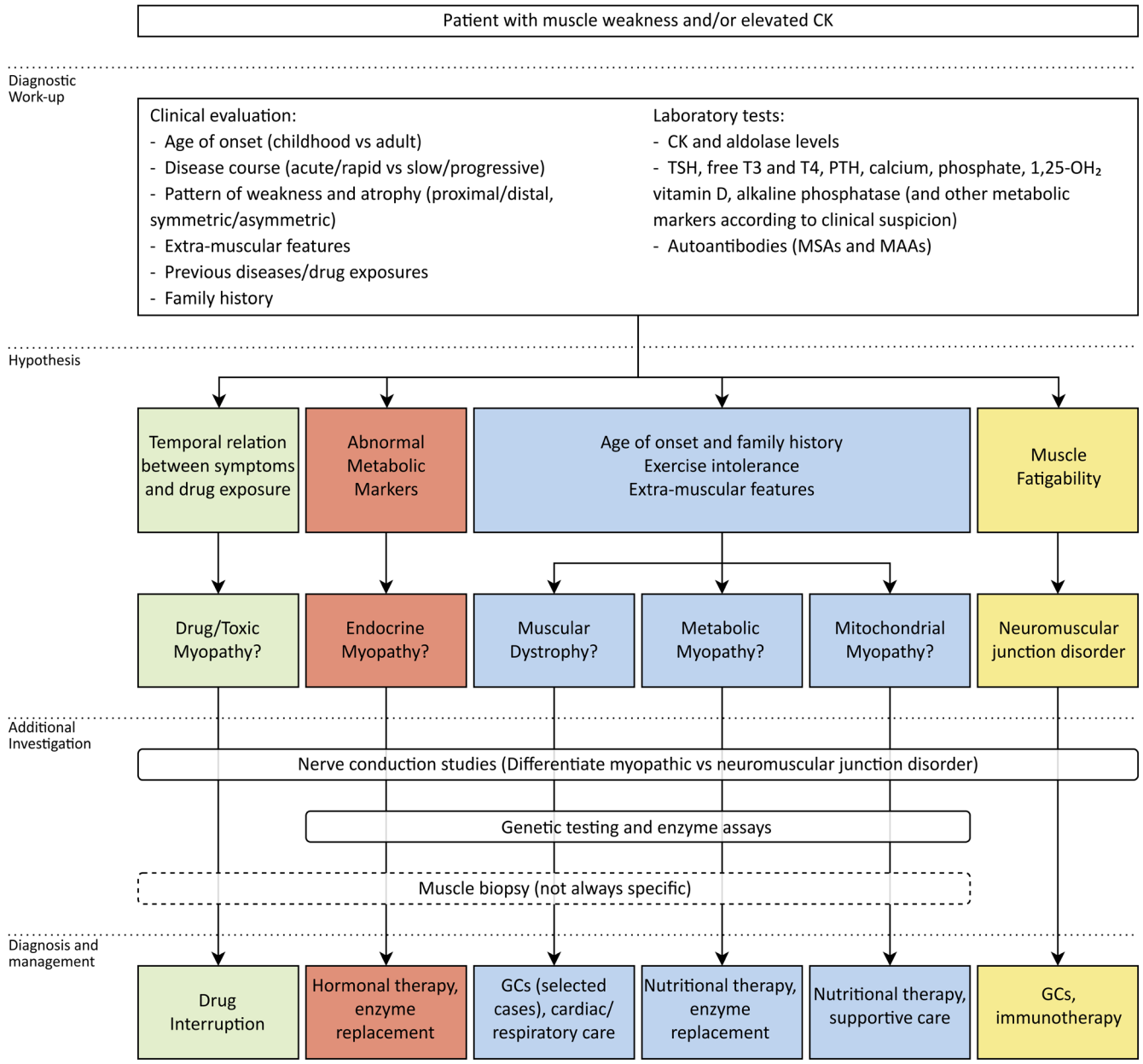

Fig. 3. Diagnostic algorithm for the evaluation of muscle weakness and elevated CK. The evaluation of patients with muscle weakness and/or elevated CK should follow a standardised approach. A careful clinical assessment (age of onset, disease course, family history, pattern of weakness, and extra-muscular features) is the first step. Laboratory testing should include CK, endocrine/metabolic markers, and autoantibodies, keeping in mind that false positives are common with immunoblotting. Electromyography can help distinguish myopathic from neuromuscular junction disorders. A muscle biopsy can help provide supportive histology, though findings are not always specific. Genetic testing and enzyme activity assays are crucial when inherited or metabolic myopathies are suspected. The results must be integrated into a comprehensive clinical judgement to differentiate between idiopathic inflammatory myopathies, genetic myopathies, endocrine/metabolic disorders, and drug-induced myopathies, each of which has distinct management strategies ranging from immunosuppression to enzyme replacement or supportive therapies. CK: creatine kinase.

may go unnoticed for long periods (85). The identification of some clinical features can help the physician strongly consider non-inflammatory myopathies in the differential diagnosis (Table VII). A thorough extra-muscular evaluation is also essential. Dyspnoea can be a sign of interstitial lung disease (ILD) in IIM (86-88) or weakness of respiratory muscles, which can also occur in non-inflammatory myopathies with varying prognoses (65, 89). Neurological symptoms and vision and hearing loss can skew the diagnosis towards a mitochondrial myopathy (66).

The assessment of serum CK is an integral part of evaluating muscle weakness. However, high serum CK levels are not always present in IIM patients, and high serum levels of CK are not always abnormal (90). Beyond CK, the investigation should include endocrine and metabolic markers, such as thyroid and parathyroid hormones. Autoantibodies can also help in the diagnosis. MSAs suggest IIM, although false positives are common with immunoblotting, mandating a strong clinical-serological correlation (91, 92). In contrast, myositis-associated antibodies

Table VII. Differential diagnosis and diagnostic workup according to different clinical and laboratory features.

Features	Differential diagnosis	Possible ancillary exams (diagnostic workup)
Myalgia	Toxic: statins, colchicine, alcohol. Endocrine: hypothyroidism; hypoparathyroidism; diabetic amyotrophy; adrenal insufficiency; hypophosphataemia. Metabolic myopathies: glycogen storage diseases; lipid deposition myopathies.	Drug history. Blood tests: thyroid and parathyroid hormones; cortisol and ACTH; glucose; phosphorus. Muscle biopsy. Genetic testing.
Progressive proximal weakness	Idiopathic inflammatory myopathies. Toxic: glucocorticoids; colchicine; hydroxychloroquine; zidovudine; amiodarone; interferon alpha; alcohol. Endocrine: hypothyroidism; hyperthyroidism; hyperparathyroidism; diabetic amyotrophy; acromegaly; adrenal insufficiency (adrenal crisis); hypophosphataemia. Muscular dystrophies: Duchenne and Becker dystrophy; myotonic dystrophy; limb-girdle muscular dystrophy type 2.	Drug history. Blood tests: thyroid and parathyroid hormones; cortisol and ACTH; glucose; phosphorus; anti-nuclear antibodies, MSA and MAA. Muscle biopsy. Genetic testing.
Distal weakness	Inclusion body myositis. Muscular dystrophies: myotonic dystrophy type 1; distal muscular dystrophy; Udd distal myopathy.	Anti-cn1A antibodies. Muscle biopsy. Genetic testing.
Exercise Intolerance	Muscular dystrophies. Metabolic myopathies; glycogen storage diseases; fatty acid oxidation disorders; lipid deposition myopathy. Neuromuscular junction diseases.	Muscle biopsy. Genetic testing. Electromyography.
Facial weakness	Facioscapulohumeral muscular dystrophy. Type 1 myotonic dystrophy. Myasthenia gravis.	Genetic testing.
Respiratory involvement	Idiopathic inflammatory myopathies: interstitial lung disease or respiratory muscle involvement. Muscular dystrophies: Duchene muscular dystrophy; limb-girdle muscular dystrophy (respiratory muscles involvement). Pompe disease (respiratory muscles involvement).	Chest X-ray. Spirometry with DLCO. Chest HRCT Electromyography. Blood tests: anti-nuclear antibodies, MSA and MAAs. Muscle biopsy. Genetic testing.
Cardiac involvement	Idiopathic inflammatory myopathies Toxic: hydroxychloroquine (cardiomyopathy). Muscular dystrophies: Duchene muscular dystrophy; limb-girdle muscular dystrophy (cardiomyopathy); myotonic dystrophies. Infant-Onset Pompe Disease (cardiomyopathy). Mitochondrial Myopathies.	Electrocardiogram. Echocardiography. Blood tests: CK, troponin I, myoglobulin, anti-nuclear antibodies, MSA and MAA. Muscle biopsy. Genetic testing.
Muscle hypertrophy	Endocrine: acromegalia; hypothyroidism (pseudo-hypertrophy). Duchene muscular dystrophy (calf pseudo-hypertrophy).	Blood tests: thyroid hormones. Muscle biopsy. Genetic testing.

ACTH: adrenocorticotropic hormone; CK: creatine kinase; DLCO: diffusing capacity for carbon monoxide; HRCT: high-resolution computed tomography; IIM: idiopathic inflammatory myopathies; MAA: myositis-associated autoantibodies; MSA: myositis-specific autoantibodies.

(MAAs) are not exclusive to IIM and are also detected in other connective tissue diseases, particularly in overlap syndromes. Although muscle biopsy can provide specific diagnostic information, distinguishing findings are not always present, underscoring the need for thorough clinical evaluation. Electromyography and nerve conduction studies can help to differentiate neuromuscular junction or myopathic disorders. Enzyme activity assays and genetic testing can be key to reaching a diagnosis. Still, it must be reinforced that normal results generally do not rule out a condition, and abnormal results are rarely diagnostic of a particular condition. Test results should be integrated with clinical evaluation and judgement.

The distinction between the different myopathies is essential since different conditions have different targeted treatments. IIM and autoimmune NMJD are managed with immunosuppression and physical therapy (93, 94). Some genetic myopathies also improve with treatment with glucocorticoids, such as dystrophinopathies and some LGMD (95). However, genetic myopathies may have targeted treatment, such as nutritional guidance in metabolic myopathies or enzyme replacement therapy in Pompe disease (96) or HPP (40). Other myopathies still lack specific treatments, and non-pharmacological management is key to improving the quality of life of those patients (97). Additionally, the correct diagnosis of genetic myopathies is vital to refer patients to clinical genetic and fertility clinics for genetic counselling and family planning. Finally, drug history must always be checked even after IIM diagnosis since drug adverse events can be interpreted as disease activity and lead to unnecessary increment of therapy.

Conclusion

Rheumatologists must recognise myositis and its main mimickers, which include many conditions of varying aetiologies and severities. Several myopathies have higher prevalence than myositis. We described and compared different myopathies to help physicians run a comprehensive diagnostic approach. It is crucial to establish the correct diagnosis to refer and manage myopathic patients correctly.

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