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Paediatric Idiopathic Inflammatory Muscle Disease

Recognition and Management

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Abstract

The idiopathic inflammatory myopathies (IIM) of childhood are rare, multisystem autoimmune disorders, of which the most common is juvenile dermatomyositis (JDM). The criteria currently used to diagnose the paediatric IIMs, including both JDM and other childhood autoimmune conditions in which myositis may be a prominent feature, are somewhat outdated in relation to paediatric practice. Controversies surrounding the criteria for diagnosis have resulted in an international effort to define both the diagnostic and classification criteria in light of modern investigation and practice.

Clinical features of these IIMs include muscle weakness and skin rash; however, these may be absent at disease onset. JDM patients require careful assessment of multiple organ systems, which can divided into musculoskeletal and extra-musculoskeletal, and examination should include validated disease measurement tools such as the Childhood Myositis Assessment Scale. Investiga-

tions include blood tests to assess generalised markers of inflammation as well as more specific markers of muscle inflammation; organ-specific investigations, such as MRI, and muscle biopsy are also often used.

Treatment and management protocols include corticosteroids, methotrexate and other disease-modifying agents such as ciclosporin (cyclosporin) and intravenous immunoglobulin, as well as newer treatments such as tumour necrosis factor blockade or B-cell depletion. Management of children with JDM requires a multidisciplinary approach, including specialist physiotherapy, occupational therapy and nursing input.

Two major international projects, the International Myositis and Clinical Studies Group (IMACS) and Paediatric Rheumatology International Trials Organisation (PRINTO) aim to standardise the assessment of these patients and measurement of their disease. The efforts of these large collaborative groups should provide much needed networks for mulitcentre trials in the future.

Paediatric idiopathic inflammatory muscle diseases are rare. The most common form is juvenile dermatomyositis (JDM); polymyositis in children is very uncommon. Myositis also occurs as part of other diseases, or so-called overlap syndromes, in children; however, this review focuses predominantly on JDM.

Typical cases of JDM are easy to recognise, but the presentation and course of the disease are variable, with a multisystem form occurring more often in paediatric than adult patients. While JDM is widely felt to be a 'vasculopathy', in severe cases it can also develop into a clinically 'vasculitic' picture, with complications that may be fatal. Early recognition and appropriate treatment is likely to improve long-term outcomes by decreasing mortality and disability. However, there are few published data on long-term outcomes in this disease.

As JDM is rare, no one centre can collect sufficient patients for clinical trials of new therapies. More needs to be known about the early predictors of severe disease; mild symptoms at onset may develop into prolonged, difficult to control disease. Under-treatment by paediatricians with limited experience of this disease can be a problem as signs thought to be associated with a poor prognosis can be subtle. Treatment needs to be tailored early in the course of the disease to prevent fatalities and long-term disability. In order for multicentre collaborations to be successful, there needs to be standardised assessment tools that are robust and sensitive to change. Some are already available, but an assessment tool for overall disease activity and damage is still being developed and validated. Ideally, once these tools have been validated, all patients with JDM would be entered into multicentre studies to allow better understanding of the disease course and the effect of treatments on outcomes.

1. Incidence of Juvenile Dermatomyositis (JDM)

JDM has a reported incidence of between 2 and 5 cases per million children,[1-4] with the incidence varying from one year to another and between different racial groups.[1] There are few good epidemiological studies as JDM is so rare, and these reports are derived by extrapolating from the study of cases at referral centres (with the exception of a UK study performed in 1995, which was a nationwide study over the course of 1 year[4]). The sex ratio also varies in different publications, from 1 : 1.3 (girls : boys) in 5- to 9-year-olds[5] to 5 : 1 (girls : boys) in the UK survey.[4] No association has been found with malignancy, in contrast with adult dermatomyositis. Studies have investigated clustering to see if there is a seasonal variation in onset, implying an infectious or environmental agent could be involved in triggering the disease. One study showed that 55% of the examined cases had onset in February to April.[5] The UK survey identified several clusters that varied with each year of onset with the largest cluster in April to May.[4]

2. Criteria for Diagnosing Paediatric Idiopathic Inflammatory Myopathies

The criteria currently used for the diagnosis of dermatomyositis are those published by Bohan and Peter[6,7] in 1975, which define dermatomyositis as the presence of a typical rash plus three of four criteria. The typical rash includes purplish discolouration of the eyelids, described as a heliotrope rash, with periorbital oedema, and Gottron's papules over the metacarpophalangeal or proximal interphalangeal (PIP) joints, or over the extensor surfaces of the elbow or knee joints. The four criteria are:

- progressive muscle weakness that is symmetrical and affects the proximal muscles including the limb-girdle and neck flexor muscles;
- an increase in serum muscle enzymes such as creatine kinase (CK), lactate dehydrogenase (LDH), AST or aldolase;
- a muscle biopsy consistent with myositis (perifascicular atrophy, perivascular inflammatory infiltrates, internal myonuclei and necrosis of muscle fibres);
- an electromyogram (EMG) showing myopathy and denervation.

These criteria are used for both adult and paediatric cases of dermatomyositis. However, the criteria do not always work well, even for typical cases, and are somewhat outdated in relation to paediatric practice. Muscle biopsies or EMGs may be negative because the inflammation is patchy between muscle groups and can be patchy within a muscle. Some paediatricians are reluctant to perform biopsies on children who have classic clinical features of JDM as the biopsy necessitates a general anaesthetic, and because biopsies from early JDM may be 'normal' by conventional histology, even when the child is clinically weak. However, using modern techniques, muscle biopsies from patients with early disease may show subtle signs of inflammation, such as up-regulation of major histocompatibility complex (MHC) class I, before the histopathological features described. These signs may provide valuable prognostic information.[8] As magnetic resonance imaging (MRI) has become more widely available, it has become commonly used as a diagnostic tool for demonstrating myositis, although there is no agreed scoring system nor any standardisation of the reading of MRI information in the diagnosis of myositis.

These criteria are also used for polymyositis. This is defined as dermatomyositis without a rash, and it is extremely rare in childhood. It is seen more commonly in adult patients, and has different features on muscle biopsy, with inflammatory infiltrates, in particular of CD8+ T cells, being widespread within the muscle. The diagnostic criteria do not specifically cover patients who have features of dermatomyositis and other autoimmune inflammatory conditions such as scleroderma or systemic lupus erythematosus. These so-called overlap syndromes are when the features of two or more conditions present in the same patient. Such syndromes may develop over time and may not be apparent at presentation. The clinical course of these conditions has not been well characterised and may be associated with a different response to treatment than classical JDM. There is still considerable controversy about the classification and diagnostic criteria of myositis.[9-11] In addition, the Bohan and Peter[6,7] criteria do not differentiate between the various neuromuscular disorders that may be in the differential diagnosis of JDM. Recent controversy concerning diagnosis and classification of both childhood and adult myositis has reopened discussion.[10,12-14] An international effort is currently underway to define both diagnostic and classification criteria in light of modern investigation and practice.[15]

3. Clinical Assessment: History

A careful history needs to be taken to elicit information concerning the presence of symptoms of proximal muscle weakness. Children may complain of difficulty getting up from the floor (e.g. after assembly at school) or they may have difficulty coming downstairs. Their muscles can be painful and tender (myalgia), and children will not differentiate this from joint pain due to an associated arthritis. Parents do not always notice that their child's voice may have become more nasal, and children seldom notice that food may be sticking 'on the way down' because of swallowing difficulties. Patients can also be short of breath because of respiratory muscle weakness, or in more severe cases because of inflammation within the lung, leading to interstitial lung disease.

Patients of any age with JDM, but especially children under the age of 7 or 8 years, are often irritable in a way that is not seen in children with other inflammatory conditions such as juvenile idiopathic arthritis (JIA). This can be a valuable marker of disease activity, since an increase in irritability often precedes a relapse. Other general symptoms include recurrent fever, abdominal pain and tiredness.

In a report on 79 children with JDM studied from disease onset, rash and weakness were seen in 100%, while 73% had myalgia, 65% had fever, 44% had dysphagia, 43% had a hoarse voice and 35% had arthritis.[16] However, both a study of a cohort of 105 children with JDM from Canada[17] and our own experience with the first 114 patients recruited into the UK National Registry and Repository for JDM, showed that rash and/or weakness may be absent at disease onset.[18] These differences may reflect subtly different uses of diagnostic criteria, further illustrating the need for an international agreement to standardise these guidelines.

4. Clinical Assessment: Examination

JDM patients require careful assessment of multiple organ systems, which can be divided into musculoskeletal (muscles, joints and bone) and extramusculoskeletal (skin, gastrointestinal tract, neurological, haematological) categories. This approach has been used to develop standardised disease activity and damage tools (see sections 4.1 to 4.6 and sections 8.1 and 8.2) for myositis, which are currently being validated. There are assessment tools available for measurement of muscle power, muscle function and generalised health, but not as yet for the measurement of disease activity in the skin or the assessment of the more widespread features of the vasculitic form of JDM.

4.1 Skin Assessment

Full assessment of the skin is essential. When present, the rash associated with JDM can be very variable. Patients may have a 'classical' heliotrope tinge over the eyelids, mild purple veining on the eyelids or a more severe rash around the eyes that looks like 'raccoon eyes'. They may have a rash behind the ears or anywhere on the trunk. Gottron's patches may start as erythema over the metacarpophalangeals or PIP joints, elbows or knees, thickening to become plaques later in disease. Early in the disease, these may be mistaken for psoriasis or eczema. Occasionally, patients will have small plaques on their PIP joints, which can be mistaken for warts. The skin may be more widely involved, with inflammation causing a 'vasculitic' appearance. This can create a marbling effect on the skin (livedo reticularis), can lead to small skin 'pits' on the fingertips, or small ulcers can develop. The nail beds may become inflamed (periungual erythema and swelling), leading to dilated capillary loops and eventually capillary loop dropout. Nail-fold capillaroscopy is a valuable examination tool that is noninvasive and simple to learn; appearance of new lesions is associated with active disease and severe nail-fold abnormalities have been associated with a poor prognosis.[17,19,20] Deposition of calcium within the skin and other tissues (calcinosis) may occur and needs to be documented. Calcinosis can be in large clumps, subcutaneous plaques or sheet-type calcification.[21,22] Ulcerative skin lesions, although rare at onset, have been associated with a poor prognosis.[19]

At present, there is no internationally recognised standardised assessment system for the different skin rashes seen in JDM, although these have been proposed, for example, as part of a disease activity score (DAS).[23] In the Canadian cohort, features at presentation included Gottron's papules in 91% of patients, heliotrope rash in 83%, facial rash in 42% and nail-fold changes in 80% of patients.[24]

4.2 Muscle Assessment

Muscles can be assessed for their strength and function. There are now recognised tools for assessing these two aspects of the effect of inflammation on muscles, which are used internationally and have been validated in several centres.

4.2.1 Manual Muscle Testing

Manual Muscle Testing (MMT)-8 tests the power of eight muscle groups, including the neck flexors, proximal upper and lower limb muscles, the shoulder and pelvic girdle muscles, the abdominal muscles and Gower's sign, where children are observed getting up off the floor. Each muscle is given a score

out of 10 (rather than the Medical Research Council score of 5 for muscle power), with a maximum score for the MMT-8 of 80.[25]

4.2.2 Childhood Myositis Assessment Scale

The Childhood Myositis Assessment Scale (CMAS) assesses muscle strength, function and endurance. It has 14 items, including timed tests such as how long a patient can hold their head up off a bed. It is applicable for children ≥4 years old and has a maximum score of 53. It has been validated,[26] and has been shown to correlate well with the MMT-8 (with which it is complementary but overlapping) as well as the Childhood Health Assessment Questionnaire (CHAQ).[27]

The clinical entity of 'amyopathic dermatomyositis' is also recognised; that is, patients with a rash typical of dermatomyositis but no apparent muscle involvement, although this entity appears to be rare in children.[24,28,29] Mild muscle weakness can be asymptomatic and may be overlooked if patients do not undergo a full systematic musculoskeletal examination, but may show as abnormalities upon MRI or magnetic resonance spectroscopy.[30]

4.3 Childhood Health Assessment Questionnaire

The CHAQ is the most widely used health questionnaire in paediatric rheumatology. It has been validated in JIA[31]and JDM,[32] and has been translated into numerous languages. It comprises questions asking how the illness has affected the child over the past week. It has eight sections, with an increasing score denoting increasing disability.[33]

4.4 Joint Assessment

Joints should always be assessed for arthritis (swelling, heat, tenderness on movement and loss of normal range) and for contractures. While arthritis at JDM onset has been reported to occur in approximately 5% of patients, arthritis at any time in the course of JDM may occur in as many as 61%[34] and joint contractures at long-term follow-up have been reported, in one series, to have a prevalence as high as 40%.[35]

5. Investigation of Suspected Cases of JDM

5.1 Blood Tests

Blood tests are used to assess generalised markers of inflammation (such as anaemia and an elevated erythrocyte sedimentation rate, which may be mild and is seen in about 45% of patients), as well as more specific markers of muscle inflammation such as the muscle enzymes that may be raised at onset: CK, AST, ALT and LDH. However, the finding of normal muscle enzymes does not exclude a diagnosis of JDM. There is controversy about the best enzyme with which to measure disease activity. It is widely recognised that CK can be a poor correlate of disease activity, since it may be normal in classic cases of JDM and may not correlate with later disease flares, even in those children who present with a raised CK. Some data suggest that LDH may be a better disease correlate, especially later in the disease, and that aldolase and AST may also be useful indices of disease activity.[36]

Antibodies associated with autoimmune inflammation may be positive in JDM; in particular, antinuclear antibody and rheumatoid factor. There are specific myositis-associated antibodies found in adult dermatomyositis patients that are associated with different disease courses. These have not been found to characterise paediatric patients in the same way and it may be that different myositis-associated antibodies may be important in children.[30,37]

5.2 Organ-Specific Investigations

Many centres with access to MRI use this as a diagnostic tool or as a tool to guide surgeons during the biopsy of involved muscles. One study has shown that quantification of muscle inflammation based upon T2-weighted relaxation times correlates well with disease activity; this method has not yet been standardised between different centres.[38] Some centres use ultrasound scanning as an alternative, although this is heavily dependent upon the expertise of the operator. EMG can also be useful; however, many children find the procedure painful. Speech therapy assessment of swallowing can be valuable but video fluoroscopy is a more definitive investigation. If there is any sign of aspiration sec-

ondary to swallowing problems (and this is often seen much earlier with a video fluoroscopy than on a chest radiograph), pulmonary function tests and a high-resolution computed tomography (CT) of the chest may be needed. Symptoms of interstitial lung disease may include mild shortness of breath on exercise and any respiratory symptoms warrant pulmonary function tests. Muscle weakness can cause a restrictive defect, which corrects as muscle strength returns. Pulmonary function tests should include measurement of the diffusion factor, in order to detect inflammation or fibrosis affecting the ability of the lung to exchange gases. High-resolution CT scanning allows visualisation of the inflammatory and fibrotic processes, although it cannot always differentiate between the two. If there are any clinical signs of cardiac involvement, an ECG and echocardiogram should be considered.

5.3 Muscle Biopsy

A recent worldwide survey of paediatric rheumatologists caring for children with inflammatory myopathies revealed that only 60% routinely include muscle biopsy in their diagnostic workup,[39] although the appearance of muscle tissue upon biopsy is still part of the Bohan and Peter[6,7] criteria. Features typical of dermatomyositis that are frequently seen include perivascular inflammatory infiltrate, perifascicular atrophy, fibre necrosis and degeneration, and increased connective tissue (see figure 1). In addition, the 'vasculopathy' may be evidenced by capillary dropout, endothelial deposition of complement components and/or IgM, and endothelial cell hyperplasia and tuboreticular changes.[6,7,10,40] It is possible for a child with characteristic rash and weakness to have apparently 'normal' muscle tissue on standard histology. However, a recent study of biopsy material from patients with early-stage JDM showed that, in these apparently 'normal' biopsies, early immunological abnormalities, including the up-regulation of MHC class l protein, are in fact present.[8] An international group of experts on muscle biopsy features in JDM is currently planning a collaborative project to generate a scoring system for JDM biopsy material, which may provide prognostic information in the future.

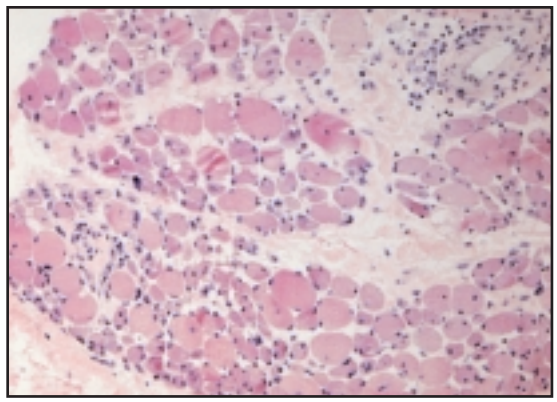

Fig. 1. Muscle biopsy (×20 magnification) from a child with juvenile dermatomyositis, stained with haematoxylin and eosin, showing marked inflammatory infiltrate, perifascicular atrophy, fibre size variation and increase in connective tissue.

5.4 Poor Prognostic Features

In order to tailor treatment, it is important to take into account the severity of the disease and the presence of poor prognostic indicators. Most experts agree that ulcerative skin disease, severe gastrointestinal tract involvement (such as gut vasculopathy, which may lead to perforation), lung involvement with interstitial lung disease and CNS involvement are associated with a poor prognosis.[30,35,41] Lung involvement may include severe respiratory muscle weakness, aspiration pneumonia secondary to abnormal swallowing (which can be seen to be surprisingly severe upon imaging) or interstitial lung disease, which can cause severe fibrosis and be fatal.[42] CNS involvement, usually seen as part of the severe widespread vasculopathy, may be visualised on MRI and can be fatal.[43] Cardiac involvement, although rare, can be serious, and ranges from conduction abnormalities to pericardial tamponade and myocarditis.[41,44]

Another poor prognostic indicator is the presence of calcinosis.[45] This implies ongoing disease activity and treatment needs to be intensified to bring the inflammation under control. When extensive, calcinosis can lead to severe disability. There is no clear understanding of why calcinosis occurs in JDM nor any evidence as to what causes the different patterns of calcium deposition that are seen.

6. Treatment and Management

Patients with JDM may have a one-off episode of disease (monocyclic), a polycyclic course with several relapses or a long-term persistent course, lasting for many years without periods of remission. The outcome of JDM has improved, but there are many variations in treatment protocols and few published long-term outcome studies. In a retrospective study of 65 patients with JDM (median follow-up of 7.2 years), 37% had a monocyclic course of disease and 63% had a long-term or polycyclic course. Ninety-five percent had been treated with corticosteroids, yet, at the time of follow-up, 40% still had rash and 23% were still weak.[46] Severely affected patients are at risk of death and may be left with considerable disability.

All JDM patients should be treated with corticosteroids. Oral corticosteroids improve outcomes, although there is little evidence on the optimal route of administration or dosage. Either high-dose oral prednisolone (2 mg/kg/day), with slow reduction, or infusions of intravenous methylprednisolone, can be given. The latter appears to give faster symptom control, which may be due to decreased gastrointestinal absorption secondary to the vasculopathy affecting the gut with oral therapy,[47] but there is no evidence of a change in long-term outcome.

The main dilemma in treating patients with JDM is judging the severity of the disease; under-treatment leads to life-threatening illness or severe lifelong disability. There is evidence that corticosteroids and the early use of methotrexate improve outcomes and reduce calcinosis.[48] The principle of treatment in our centre is to induce remission rapidly (once the diagnostic investigations have been performed) using intravenous methylprednisolone, followed by oral prednisolone 1 mg/kg. Methotrexate is introduced as a disease-modifying drug within 2–6 weeks of starting corticosteroids. Typically, dosages of 10–15 mg/m^2/week are used and the widespread use of methotrexate in children with JIA has provided evidence for a good safety record of methotrexate at these dosages.[49] However, children with JDM may have poor absorption of methotrexate when it is administered orally;[47] therefore, it is advisable to consider subcutaneous administration in all children with moderate-to-severe disease, and in young children. When methotrexate is given by this route, children generally tolerate the weekly injection well and, in many families, parents can readily learn to administer the injections. Local anaesthetic cream can be used for injections, where required. Evidence from the treatment of children with JIA suggests that better disease control is achieved,[49] and there are fewer problems with nausea, when methotrexate is given subcutaneously. Folic acid supplementation with methotrexate therapy is standard practice to help prevent adverse effects. Active disease and treatment with corticosteroids are associated with increased calcium turnover and osteoporosis; calcium and vitamin D supplementation during corticosteroid treatment may help to prevent this.

Ciclosporin (cyclosporin) is also used as a disease-modifying agent in JDM,[42,50,51] although many paediatric rheumatologists prefer methotrexate. A placebo-controlled trial has shown benefit with intravenous immunoglobulin (IVIg) in adult dermatomyositis,[52] and safety and efficacy have also been demonstrated in a small series of children with JDM.[53] However, IVIg is a blood product and its efficacy may vary between different preparations in different countries. To date, there have been no head-to-head comparisons of different second-line agents in JDM.

A recent retrospective review of 12 patients with severe JDM treated with cyclophosphamide found it to have considerable clinical benefit with little evidence of short-term adverse effects.[54] Indications for considering this therapy include severe muscle weakness, ulcerative skin disease and other organ involvement such as gastrointestinal ulceration, interstitial lung disease and CNS disease.

Over the past 5 years there have been significant developments in the use of biological treatments in inflammatory diseases, including recombinant products to block tumour necrosis factor (TNF) and B-cell depletion using anti-CD20 monoclonal antibody therapy. To date, only a small number of myositis patients have been treated with anti-TNF, although these initial results have been encouraging.[55-58] The use of anti-TNF therapy in the form of the soluble TNF receptor etanercept, combined with the bisphosphonate pamidronate, has been noted to have benefit in patients with calcinotic skin disease.[57]

Early reports of success with B-cell depletion using the anti-CD20 antibody rituximab in dermatomyositis have included small numbers of children with JDM.[59,60] More evidence-based studies involving larger numbers of patients are awaited in order to gain a full knowledge of the role of these biologics in the treatment of severe JDM.

The management of children with JDM requires a multidisciplinary approach, including specialist physiotherapy, occupational therapy and nursing input. In addition to their drug treatment, patients with JDM need physiotherapy to prevent joint contractures and to rebuild muscle strength. Despite concerns about the effects of exercise on inflamed muscles, there is no good evidence for any damage to muscles caused by exercise in patients with JDM; a recent study using MRI before and after a controlled exercise programme in children with JDM showed no change in levels of muscle inflammation, at least over a short time period.[61] Aerobic exercise testing using a treadmill in patients with JDM has revealed an impairment in their maximal aerobic exercise capacity, stressing the importance of a supervised exercise programme to rebuild strength.[62] Occupational therapy is also important for activities of daily living, as well as helping to solve schooling problems secondary to illness and fatigue. Good nursing and vigilance against infections is essential, especially with the heavily immunosuppressive treatments now being used.

7. Clinical Dilemmas

The dilemma facing clinicians is which medication should be given in which circumstances. All patients should receive corticosteroids, and those with mild JDM may need only corticosteroids. However, if the disease does not improve quickly, or if there are features present that indicate a poor prognosis, an immunosuppressive agent should be added to treatment. This situation may be difficult to assess, unless treatment is being administered at a unit with experience of dermatomyositis. General paediatricians may only see one or two cases in their career, and many regional centres will see only one or two cases per year; it is therefore difficult to build up sufficient expertise. Hence, most patients should be referred to a paediatric rheumatology or neurology specialist who has an interest in JDM for a second opinion or shared care.

At present, there are no trials directly comparing the two medications most commonly used to treat JDM: ciclosporin and methotrexate. Neurologists caring for patients with JDM tend to use ciclosporin, whereas most paediatric rheumatologists use methotrexate. Our own experience has been that methotrexate is more effective but some patients will need both. As a specialist referral centre, where the case mix typically comprises patients with moderate and severe disease, all of our patients receive a minimum treatment of corticosteroids and methotrexate. Internationally, it is agreed that the presence of skin ulcers, a 'vasculitic' skin rash, calcinosis, and lung, gastrointestinal or CNS involvement are all predictors of a poor prognosis. In our unit, we add a course of intravenous cyclophosphamide to the corticosteroid and methotrexate treatment received by these patients. Future long-term follow-up of these patients is needed to provide outcomes data. The success of the medication protocol is highly dependent on all patients being carefully monitored for infections, since this is the most important adverse effect in the short-term. In countries where infections may be more of a problem, or close monitoring cannot be relied on, this treatment regimen may be unsuitable.

At present, management protocols and criteria for defining severe JDM vary between centres, countries and, to some extent, specialties. However, in the future, internationally agreed criteria for dividing the disease into mild, moderate or severe, based upon core measures of disease activity and damage (see section 8), would be highly valuable tools, both to guide choice of medications and to define the inclusion criteria for multicentre trials.

8. International Collaboration

Over the past few years it has been recognised that there is a need for international collaboration to collect enough patients for therapeutic trials in JDM, and for long-term outcome studies to enable a better understanding of the disease processes and effects of treatment. To this end two international groups have been working to develop tools that will allow for multicentre studies.

8.1 International Myositis and Clinical Studies Group (IMACS)

The International Myositis and Clinical Studies Group (IMACS) brought together international experts from the adult and paediatric arenas, to develop disease activity and damage tools for myositis; two activity and two damage tools[63,64] were produced. The Myositis Intention to Treat Index (MITAX) and the Myositis Disease Activity Assessment Visual Analogue Scale (MYOACT) assess presence and extent of disease activity in seven systems: constitutional, articular, cardiac, pulmonary, gastrointestinal, cutaneous and skeletal muscle. The Myositis Damage Index (MDI) and the Myositis Disease Damage Assessment Visual Analogue Scale (MYODAM) are tools that identify the presence and severity of damage. The reliability of the tools and inter-rater reliability were assessed as fair to good in real patient exercises and are now undergoing further multicentre validation studies.

8.2 Paediatric Rheumatology International Trials Organisation (PRINTO)

A different approach was taken to produce core sets of measures for disease activity and damage[65] for JDM by the Paediatric Rheumatology International Trials Organisation (PRINTO) in collaboration with the Pediatric Rheumatology Collaborative Study Group (PRCSG). Two questionnaire surveys were sent to 267 clinicians from 46 countries asking them to select and rank response variables that they used for assessing clinical response. Forty experienced paediatric rheumatologists who attended a consensus conference selected the domains and variables to be included in the preliminary disease activity and damage core sets for JDM and juvenile systemic lupus erythematosus.[65]

The domains for disease activity included the physician's global assessment (Visual Analogue Scale [VAS] or Likert scale), muscle strength assessment (CMAS or MMT), functional ability assessment (CHAQ), muscle enzymes, global assessment by parents/patients and a global JDM disease activity tool (DAS, or MITAX/MYOACT). The domains for disease damage included the physician's global Assessment (VAS or Likert scale), muscle strength assessment development and a global JDM disease damage tool (MDI/MYODAM).

The activity core set proposed by PRINTO is very similar to that proposed by IMACS. However, the activity and damage core sets include both muscle strength and functional assessments: by themselves they cannot distinguish between the two. Prior damage (such as contractures) can interfere with activity assessments.[66] A further complicating factor is that many features considered by adult physicians to be damage (e.g. calcinosis)[2] are reversible in children. Therefore, a different definition of damage may be needed in children. Through a large-scale international collection, these two groups are currently prospectively validating these core sets as well as working on a definition of flare and of remission.

9. Conclusions

The recognition and treatment of JDM has changed considerably in the past few years, with earlier introduction of immunosuppressive agents and aggressive early treatment aimed at the long-term prevention of complications and disability. In patients whose disease does not respond quickly to oral corticosteroids, or where complications are suspected, referral to a large centre with experience in the field is recommended. The international collaborative efforts focused on classification, diagnostic features, disease measurement and now planning clinical trials, will provide an invaluable network through which to continue improving the outcomes in children with this group of debilitating diseases.

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