INVITED ARTICLE

INFLAMMATORY MYOPATHIES

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ABSTRACT

Inflammatory myopathies encompass a wide range of disorders. This article deals with the idiopathic inflammatory myopathies. Classification and diagnostic criteria proposed by Bohan and Peter are still widely used. Diagnosis is based on clinical features, muscle enzyme abnormalities, electromyographic findings and muscle biopsy results. There are known associations with malignancy and lung disease which may affect the prognosis. Management consists of the prudent use of corticosteroids. In refractory cases, cytotoxic agents, cyclosporin and plasmapheresis have been used.

Keywords : inflammatory myopathies, polymyositis, dermatomyositis

SINGAPORE MED J 1992; Vol 33: 186-188

INTRODUCTION

The term "idiopathic inflammatory myopathy" encompasses a variety of diseases. It includes polymyositis, dermatomyositis, cancer-associated myositis, connective tissue disease-associated myositis, childhood dermatomyositis and inclusion body myositis[1-3]. Diagnosis can be difficult, especially in the earlier stages. A patient may present to a family physician, a neurologist, dermatologist or rheumatologist with mild weakness or a rash. Certain differential diagnoses have to be considered. These include endocrine myopathies, toxic myopathies, infective forms, polymyalgia rheumatica, chronic fatigue syndrome, HIV myopathy and other rarer causes such as trichinosis and McArdle's disease. When a diagnosis is made, management involves the prudent use of corticosteroids and immunosuppressive agents. The aim of treatment is to achieve adequate control of the illness while avoiding the side-effects of the medications.

DIAGNOSIS AND CLASSIFICATION

Prior to 1975, diagnosis and classification of this group of disorders did not follow standardised criteria, making it difficult to draw conclusions from studies which employed varying criteria. In that year, Bohan and Peter, [4,5] proposed criteria for both diagnosis and classification which are still the most widely adopted today although newer classifications have been suggested.

The classifications used by Bohan and Peter are as follows:

Group I	-	Primary Idiopathic Polymyositis
Group II	-	Primary Idiopathic Dermatomyositis
Group III	-	Dermatomyositis (or polymyositis) associated with neoplasia
Group IV	-	Childhood dermatomyositis (or polymyositis) associated with vasculitis
Group V	-	Polymyositis or dermatomyositis with associated collagen-vascular disease

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Five major criteria are used for diagnosis:

1) Symmetrical weakness of the limb-girdle muscles and anterior neck flexors over weeks or months.
2) Muscle-biopsy evidence of necrosis of Type I and II fibres, phagocytosis, regeneration with basophilia, large vesicular sarcolemmal nuclei and prominent nucleoli, perifascicular atrophy, variation in fibre size and an inflammatory exudate which is often perivascular.
3) Elevation of serum skeletal muscle enzymes.
4) Electromyographic changes of short, small, polyphasic motor units, fibrillations, positive sharp waves and insertional irritability, and bizarre, high-frequency repetitive discharges.
5) Dermatologic features such as a heliotrope rash and Gottren's sign.

The first four criteria are used to make a diagnosis of polymyositis (PM). The presence of all four is required to make a "definite diagnosis". A "probable diagnosis" requires three and a "possible diagnosis" requires two criteria.

For a diagnosis of dermatomyositis (DM), the dermatologic features have to be present. Of the remaining four criteria, the presence of three or four is required to make a "definite diagnosis". A "probable diagnosis" requires two and a "possible diagnosis"requires one criterion.

Inclusion body myositis is a distinct entity, first characterised by Carpenter et al [6] in 1978. Clinically, it lacks features of a collagen-vascular disease and takes a relatively benign and protracted course. It frequently involves distal muscles and is found mainly in males and it responds poorly to steroid therapy. A definite diagnosis is only possible with the aid of electron microscopy.

EPIDEMIOLOGY AND PATHOGENESIS

Idiopathic inflammatory myopathies are fairly uncommon and true incidences are hard to determine. Epidemiological studies report varying figures. In the United States, Medsger et al[7] reported an annual incidence of 5 cases per million in Shelby Country, Tennessee. 2.18 per million for Israel was quoted by Benbasset and colleagues[8]. In general the illness showed a bimodal age distribution with peak incidence rates in the 5 to 14 and 45 to 64 age groups[9]. Most authors note a slight female predominance especially among Negro females. There are no local figures.

There is strong evidence for immune-mediated inflammation in dermatomyositis and polymyositis. Capillary damage in muscle tissue is seen in dermatomyositis. This eventually results in microinfarcts, focal loss of myofibrils and perifascicular atrophy which are all characteristic histological findings[10]. Deposition of the membrane attack complex (C5B-

9) in the capillary bed has been demonstrated[11]. In polymyositis, there is evidence for lymphocyte and macrophage mediated cytotoxic damage[12]. There is strong expression of class I products of the major histocompatibility complex in the sarcolemma of these patients[13]. Although there is some evidence that viral triggers may play a role, causative agents remain unknown.

CLINICAL FEATURES

The major clinical feature is muscle weakness rather than muscle pain or tenderness, although it may not be the presenting feature. In a computer-assisted analysis of 153 patients, Peter and Bohan [4] found that most patients had muscle weakness at some point of time although it was the presenting feature in only 69%. The pathognomonic lesions of dermatomyositis may not be present in 15% of such patients who have more subtle photosensitive or vasculitic lesions. Muscular calcifications and systemic vasculitis are more likely to be found in the childhood forms.

The presence of interstitial lung disease is thought to adversely affect prognosis [15]. It is found in about 10% of patients with DM/PM. Anti-Jo 1 antibody serves as a marker for its presence[16]. As the disease progresses, other pulmonary problems may develop. Of particular concern are aspiration pneumonia and hypoventilation due to muscular weakness, opportunistic lung infections and drug-induced pneumonitis.

Arthralgia, dysphagia, cardiac abnormalities and Raynaud's phenomenon are some of the other less common clinical features found.

Other serological markers such as anti-nuclear antibody and rheumatoid factor are not specific tests. Antibodies such as antibodies to double-stranded DNA, Smith antigen, Ro (SS-A) and ribonucleoprotein may assist in the diagnosis of associated collagen-vascular diseases in the presence of overlap clinical features.

Creatinine kinase evaluation is the most useful of the muscle enzymes, both for diagnosis and for follow-up. It can be normal in 5% of patients. Similarly, muscle biopsy and EMG can be normal in 10% of patients. EMG is not good for assessing activity or for distinguishing between various forms of myositis. The muscle biopsy can provide a more specific diagnosis, the clearest example being inclusion body myositis. In many instances, PM and DM show distinctive histological features. The activity of illness can also be determined from the degree of inflammatory infiltration and follow-up biopsies may contribute to information regarding the progress of the patient. The diagnostic yield of open and needle biopsies is very similar and each technique has advantages and disadvantages. Both techniques can result in sampling error. Results depend on the expertise and experience of the person performing the biopsy, the technician preparing the muscle specimens and the pathologist.

Difficulty arises when one has to distinguish weakness due to steroid myopathy from active inflammatory muscle disease. Muscle biopsy findings are not always helpful and clinical judgement is of great value.

ASSOCIATION WITH MALIGNANCY

The association of PM/DM with malignancy remains controversial. Figures ranging from 10-70% have been quoted. Most of the studies do not involve control populations. Manchul et al[17] did a controlled study and found no increase in the number of malignancies subsequent to the diagnosis of DM/PM. There was however an association with malignancies diagnosed at or before the diagnosis of DM/PM. It is generally accepted that patients with dermatomyositis and males and older patients have a higher risk of malignancy. However, extensive screening tests should be guided by a thorough clinical history and examination, including per rectal, breast, ENT and gynecological examinations. Simple tests such as a full blood count, chest X-ray, urinalysis, liver function tests and fecal occult blood testing are also indicated. In a cohort of DM patients, Cox et al[18] showed that extensive screening tests such as barium enema, barium meal, gastroscopy, intravenous urography, mammography, laparoscopy and CT scanning of the abdomen did not increase the number of malignancies diagnosed in patients in whom the history, physical examination and simple tests were normal. A recent study by Basset-Seguin et al [19] found cutaneous necrosis and an elevated erythrocyte sedimentation rate to be potential markers for malignancy in adult DM.

PROGNOSIS AND TREATMENT

Mortality figures vary between 14-50% and various factors have been proposed to predict an unfavourable outcome, although none has been found to do so consistently. Some of these factors include the presence of malignancy, pulmonary complications, age greater than 50, dysphagia, severity of weakness, childhood onset and a longer duration of weakness prior to diagnosis[21-23]. Common causes of death include malignancy, pulmonary complications and ischaemic heart disease.

Although corticosteroids are widely accepted as the initial therapy of choice, no controlled trials have been performed to assess their efficacy. The most common regime involves the use of prednisolone or its equivalent in a dose of 1mg/kg for one to two months, after which a slow tapering of about 10mg per week is instituted until a maintenance dose of 5 to 10mg per day is reached at four months [24]. There are variations in steroid therapy involving alternate day doses and intravenous pulses of methylprednisolone. Treatment has to be tailored to the individual's needs. In general, clinical improvement lags behind a fall in creatinine kinase by several weeks or months. One has to consider weakness arising from corticosteroid therapy or hypokalemia while a patient is receiving treatment. If remission is achieved, maintenance treatment should be continued for at least one year before complete withdrawal of drugs. Long term follow up is advisable as relapses can occur.

There is a group of patients in whom corticosteroids alone produces an inadequate response or no response at all. Methotrexate, azathioprine and cyclophosphamide have been found to be of benefit in such patients[24,25]. In patients who are extremely refractory to therapy, there are anecdoctal reports of success with plasmapheresis, cyclosporin, total body irradiation and combination immunosuppressive treatment [26-30].

CONCLUSION

Idiopathic inflammatory myopathies, although uncommon, make a considerable impact on the lives of those who are afflicted. An early diagnosis, a competent assessment and skilled management can make a tremendous difference to the prognosis of the patient.

REFERENCES

1. Bradley WG. Inflammatory diseases of muscle. In: Kelly WN. et al, eds. Textbook of rheumatology, 2nd ed. Philadelphia: WB Saunders, 1985:1225-45
2. Mastaglia FL, Ojeda VJ. Inflammatory myopathies: Part 1. Ann Neurol 1985; 17: 215-7
3. Urbano-Marquez A, Casademont J, Josep MG. Polymyositis/ Dermatomyositis: the current position. Ann Rheum Dis 1991; 50: 191-5
4. Bohan A, Peter JB. Polymyositis and dermatomyositis (First of two parts). N Engl J Med 1975; 292:344-7
5. Bohan A, Peter JB. Polymyositis and dermatomyositis (Second of two parts). N Engl J Med 1975; 292-403-7
6. Carpenter S, Karpati G, Heller I, Eisen A. Inclusion body myositis: a distinct variety of idiopathic inflammatory myopathy. Neurology 1978; 28: 8-17

7. Medsger TA, Dawson WN, Masi AT. The Epidemiology of polymyositis. Am J Med 1970; 48: 715-23
8. Benbassat J, Geffel D, Zlotnick A. Epidemiology of polymyositis-dermatomyositis in Israel, 1960-76. Isr J Med Sci 1980; 16:197-200
9. Rose AL, Walton JN. Polymyositis: A survey of 89 cases with particular reference to treatment and prognosis. Brain 1975; 89: 747-68
10. Whitaker JN, Engel WK. Vascular deposits of immunoglobulin and complement in idiopathic inflammatory myopathy. N Engl J Med 1972; 286: 333-8
11. Kissel JT, Mendel JR, Rammohan KW. Microvascular deposition of complement membrane attack complex in dermatomyositis. N Engl J Med 1986; 314: 329-34
12. Dawkins RL, Mastaglia FL. Cell-mediated cytotoxicity to muscle in polymyositis. N Engl J Med 1973; 288: 434-8
13. Karpati G, Poliot Y, Carpenter S. Expression of immunoreactive major histocompatibility complex products in human skeletal muscles. Ann Neurol 1988; 23: 64-71
14. Bohan A, Peter JB, Bowman RL, Pearson CM. A computer-assisted analysis of 153 patients with polymyositis and dermatomyositis. Medicine 1977; 56: 255-86
15. Arsura EL, Greenburg AS. Adverse impact of interstitial pulmonary fibrosis on prognosis in polymyositis and dermatomyositis. Semin Arthritis Rheum 1988; 18:29-37
16. Bernstein RM, Morgan SH, Chapman J et al. Anti-Jo-1 antibody: a marker for myositis with interstitial lung disease. Br Med J 1984; 289: 151-2
17. Manchul LA, Jin A, Pritchard KI et al. The frequency of malignant neoplasms in patients with polymyositis-dermatomyositis. Arch Intern Med 1985; 145: 1835-9
18. Cox NH, Lawrence CM, Langtry JAA, Ive FA. Dermatomyositis. Disease associations and an evaluation of screening investigations for malignancy. Arch Dermatol 1990; 126:61-5
19. Basset-Seguin N, Roujeou JC, Gherardi R, Guillaume JC, Revuz J, Tourine R. Prognostic factors and predictive signs of malignancy in adult dermatomyositis. Arch Dermatol 1990; 126: 633-7
20. Plotz PH. Current concepts in idiopathic inflammatory myopathies: polymyositis, dermatomyositis and related disorders. Ann Intern Med 1989; 111: 143-57
21. Medsger TA, Robinson H, Masi AT. Factors affecting survivorship in polymyositis. A life-table study of 124 patients. Arthritis Rheum 1971; 14:249-58
22. Benbassat J, Gefel D, Larholt K, Sukenik S, Morgenstern V, Zlotnick A. Prognostic factors in polymyositis/dermatomyositis: A computer-assisted analysis of ninety-two cases. Arthritis Rheum 1985; 28:249-55
23. Tymms KE, Webb J. Dermatopolymyositis and other connective-tissue diseases: a review of 105 cases. J Rheumatol 1985; 12: 1140-8
24. Oddis CV, Medsger TA. Current management of polymyositis and dermatomyositis. Drugs 1989; 37:382-90
25. Metzger AL, Bohan A, Goldberg LS, Bluestone R, Pearson CM. Polymyositis and dermatomyositis: combined methotrexate and corticosteroid therapy. Ann Intern Med 1974; 81: 182-9
26. Dau PC. Plasmapheresis in idiopathic inflammatory myopathy: experience with 35 patients. Arch Neurol 1981; 38: 544-52
27. Heckmatt J, Hasson N, Saunders C et al. Cyclosporin in juvenile dermatomyositis. Lancet 1989; i: 1063-6
28. Gruhn WB, Diaz-Buxo JA. Cyclosporine treatment of steroid resistant interstitial pneumonitis associated with dermatomyositis/polymyositis. J Rheumatol 1987; 14: 1045-7
29. Morgan SH, Bernstein RM, Coppen J, Halnan KE, Hughes GRV. Total body irradiation and the course of polymyositis. Arthritis Rheum 1985; 28: 831-5
30. Wallace DJ, Metzger AL, Ehite KK. Combination immunosuppressive treatment of steroid-resistant dermatomyositis/polymyositis. Arthritis Rheum 1985; 28:590-2