

Unusual cause of fever in a 35-year-old man

ECP Yuen

A Chinese man presented to our Accident and Emergency (A&E) department repeatedly for fever and respiratory symptoms. He was finally diagnosed to have polymyositis. Fever and respiratory symptoms are common presenting complaints to our A&E department and this case illustrates the importance of establishing a diagnosis in a patient with fever but without an obvious septic focus. (*Hong Kong j.emerg. med.* 2001;8:34-37)

Keywords: Myalgia, polymyositis, septic focus

Introduction

A 35-year-old man presented to our Accident and Emergency department with fever for 6 days. He enjoyed good past health with no known drug allergy. The fever was associated with chills but there was no respiratory nor urinary symptom. There was no history of recent travel nor insect bite.

On examination he was flushed with a temperature of 38°C. He was tachycardiac with a pulse rate of 130 beats/min. His blood pressure was 130/75 mm Hg, a respiratory rate was 20 breaths/min, and his oxygen saturation was 96% on room air. There was no lymphadenopathy nor jaundice. Examination of the chest and abdomen were normal and there was no signs of meningism.

Urinalysis was positive for red blood cell. Chest radiograph (CXR) showed clear lung fields and radiograph of Kidney, Ureter and Bladder showed no radioopaque calculus. Blood testing including full blood count, renal and liver function urinary tests were performed and mid stream urine (MSU) was sent for culture. The provisional diagnosis was urinary tract infection and patient was discharged with a course of antibiotic and paracetamol. A follow-up appointment was arranged 5 days later.

On the day of follow up, the patient still complained of intermittent fever. He developed productive cough for 2 days with breathlessness on exertion. MSU showed no growth and all the blood tests were normal except an isolated rise in alanine transferase (ALT) to 273 UL. Auscultation of the chest now showed fine crepitation but a repeat CXR showed no significant change from the previous radiograph. The patient was provisionally treated for pneumonia with a course of clarithromycin, and a follow up appointment one week later.

Two days after the second follow-up, i.e. one week after he first presented to us, he attended our department again, this time with new symptoms. His fever had continued and it was already the thirteenth days of his febrile episode. His breathlessness had worsen. He could only walk for 2 minutes on level ground due to breathlessness and severe muscle pain. He also complained of swelling of all four limbs and difficulties in rising from a chair. His urine was frothy. Clinical examination now revealed an oedematous gentleman with fever of 39°C, normal blood pressure and a heart rate of 120/min. There was fine inspiratory crackles audible over the bases of the lungs. Neurologically, there was severe proximal muscle weakness. Urinalysis now showed large amount of red blood cell and protein. The patient was admitted for further investigation.

His creatinine kinase (CPK) level was 26420 UL and his ESR level was 30. His ALT was raised as before. His renal function remained normal. The

Correspondence to:

Yuen Chuek Pun, Eddie, MBChB(Leeds), FRCS(Edin)

Prince of Wales Hospital, Accident and Emergency Department, Shatin, N.T., Hong Kong

Email: eddieyuen2000@hongkong.com

anti-Jo-1 antibodies was positive and all other immune markers were negative. EMG showed myopathic changes and muscle biopsy showed lymphocytic infiltration. The diagnosis of polymyositis was made. He was started on prednisolone with remarkable response. His fever and oedema subsided and muscle power also shown improvement. All the viral markers were checked and possible underlying malignancy was searched, with negative results. The patient was discharged 10 days after admission.

Discussion

Polymyositis is a non suppurative inflammatory disease of the muscle which may occur either alone or in association with another connective tissue disease. It is characterised by symmetrical proximal muscle weakness and myalgia, and when associated with a rash, the term dermatomyositis is used. There is an association with underlying malignancy in a minor percentage for adult patients, some authors quoted a rate of 10% for patient over 40 years old. The peak age of onset is in childhood and the fifth and sixth decade of life.

The aetiology of polymyositis is unknown. Genetic, viral infection and autoimmune mechanism have been postulated. Patients with HLA-DR3 and DRw52 antigens have an increase incidence of the disease. Influenza, Rubella and Coxsackie virus have been implicated in the occurrence of the disease. The presence of antibodies to cytoplasmic ribonucleoprotein like Jo-1 in patient with the disease may represent an immune-mediated process.

There is general lymphopenia with decreased in absolute number of all T-lymphocyte subsets in patient with dermatomyositis, whereas there is a CD8+ T cells activation, leading to muscle injury in patient with polymyositis.¹

Bohan² classified the disease into five groups and this classification is widely accepted.

1. Primary idiopathic polymyositis (Group I), comprises one-third of all the cases. It is a slowly progressive disease of up to years. It may affect

patient of all ages and has a female predominance of 2:1. Truncal, pectoral and pelvic weakness is most marked. Ocular movement is rarely affected. Dysphagia, respiratory impairment and cardiac abnormalities are also present but relatively rare.

2. Primary idiopathic dermatomyositis (Group II) comprise the other one-third of all cases. The skin changes precede the muscle syndrome. The rash ranges from localized erythema to exfoliative dermatitis. Periorbital oedema is also seen. It is mandatory to search for the presence of malignancy in patients over 40 years old.
3. Dermatomyositis (or polymyositis) associated with neoplasia (Group III). It account for more than 8% of all cases. The malignancy may antedate or postdate the onset of myositis by up to 2 years. It is more common in those over 40 years old and the incidence is even higher in the over 60 years old. The most common malignancies are those the lung, breast, ovary, gastrointestinal tract and the lymphoproliferative system.³ The myositis is a paraneoplastic syndrome.
4. Childhood dermatomyositis (or polymyositis) associated with vasculitis (Group IV). The myositis is associated with vasculitis, causing necrotising lesions in skin, ischaemic infarct of the kidney, gastrointestinal tract and brain.
5. Polymyositis (or dermatomyositis) with associated collagen vascular disease (Group V). This is an overlapping group of myositis and make up about one-fifth of all cases. It is associated with several connective tissue disease like systemic sclerosis, mixed connective disease, rheumatoid arthritis.

Myositis is also found in infection caused by human immunodeficiency virus (HIV).⁴ It may be the manifestation of the disorder or due to therapy with Zidovudine (AZT). It is dose related and may present after the cessation or reduction of dose.

The diagnosis of the disease depends on the following four modalities:

1. Symptom and sign. These include proximal muscle weakness, muscle pain and tenderness, arthralgia, dysphagia, respiratory muscle weakness. Fibrosing alveolitis may occur.
2. Serology. There is usually an elevation of muscle enzyme, mainly creatinine kinase (CK). Normochromic normocytic anaemia is present and the Erythrocyte sedimentation rate (ESR) is raised. Antinuclear antibodies (ANA) and circulating rheumatoid factor are found. Recent research also indicated the presence of ANA in a significant percentage of first-degree relatives of patient with polymyositis.⁵ Anti-Jo-1 antibodies is also raised and found in the idiopathic type with interstitial lung disease. Recently, enzyme-linked immunosorbent assay (ELISA) is used to detect Anti-Jo-1 antibodies.⁶ Serum neopterin is also raised in a recent study and appears to be a marker of the global disease activity.⁷
3. Electromyography (EMG). The EMG shows myopathy changes. These include short duration, low amplitude, spiky, polyphasic muscle action potential with abnormal early recruitment.
4. Muscle biopsy. There may be inflammatory changes with lymphocytic infiltration and muscle fibre regeneration and necrosis.

The main differential diagnosis are muscular dystrophies, motor neurone disease and drug-induced myopathies. Muscular dystrophies rarely progress as rapidly as polymyositis and there is typically no muscle pain. Upper motor neurone sign and muscle fasciculations are present in motor neurone disease. Various classes of drugs are implicated in the development of myopathies. These includes diuretics, immune modulating agent like AZT, cyclosporin, others like cimetidine, phenytoin, heroin, carbimazole and even growth hormone.

The treatment depends on the severity of the symptoms. The mainstay of treatment is glucocorticoid. Azathioprine is added if response

to steroid is not satisfactory. Other cytotoxic drugs are also used, for example, methotrexate, cyclophosphamide, cyclosporin⁸ as well as total body irradiation.

Patients with mild to moderate symptoms are given low dose prednisone, with dose tapering when the response is satisfactory. The dose is increased if the response is inadequate. Patients with severe symptoms are given high dose prednisone, up to 2 mg/kg/day for up to 3 months. Azathioprine is added if the response is inadequate. High dose intravenous immunoglobulin therapy is also used in refractory cases.⁹

In terms of prognosis, the five year survival is about 75%. Females, blacks, and those with severe symptoms or have prolong delays before receiving treatment have worse prognosis. Adverse prognosis is also associated with dysphagic, neoplasm related, connective tissue diseases related types and presence of anti Jo-1 antibodies. About half of the patients will recover, but 20% will have ongoing disease and 30% will have inactive disease but residual muscle weakness.¹⁰

The lesson learnt in this case is that it is important to look 'further' for other systemic cause in patients presenting with fever without obvious infectious focus.

References

1. Iannone F, Cauli A, Yanni G, et al. T-lymphocyte immunophenotyping in polymyositis and dermatomyositis. *Br J Rheumatol* 1996;35(9): 839-45.
2. Bohan A, Peter JB, Bownan RL, et al. A computer-assisted analysis of 153 patients with polymyositis and dermatomyositis. *Medicine (Baltimore)* 1977;56(4):255-86.
3. Callen JP. Relationship of cancer to inflammatory muscle diseases. *Dermatomyositis, polymyositis, and inclusion body myositis*. *Rheum Dis Clin North Am* 1994;20(4):943-53.
4. Chariot P, Ruet E, Authier FJ, et al. Acute rhabdomyolysis in patients infected by human immunodeficiency virus. *Neurology* 1994;44(9): 1692-6.

5. Valentini G, Improta RD, Resse M, et al. Antinuclear antibodies in first-degree relatives of patients with polymyositis-dermatomyositis: analysis of the relationship with HLA haplotypes. *Br J Rheumatol* 1991;30(6):429-32.
6. Nishikai M, Ohya K, Kosaka M, et al. Anti-Jo-1 antibodies in polymyositis or dermatomyositis: evaluation by ELISA using recombinant fusion protein Jo-1 as antigen. *Br J Rheumatol* 1998;37(4): 357-61.
7. Samsonov MY, Nassonov EL, Tilz GP, et al. Elevated serum levels of neopterin in adult patients with polymyositis/dermatomyositis. *Br J Rheumatol* 1997;36(6):656-60.
8. Dawson JK, Abernethy VE, Lynch MP. Effective treatment of Anti-Jo-1 antibody-positive polymyositis with cyclosporin. *Rheumatology* 1997;36(1):144-5.
9. Dalakas MC, Illa I, Dambrosia JM, et al. A controlled trial of high dose intravenous immune globulin infusion as treatment for dermatomyositis. *N Engl J Med* 1993;329(27):1993-2000.
10. Devere R, Bradley WG. Polymyositis: its presentation, morbidity and mortality. *Brain* 1975; 98(4):637-66.