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Case Reports

Pulmonary fibrosis in polymyositis with the Jo-1 syndrome: an unusual mode of presentation

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Introduction

The development of pulmonary fibrosis in polymyositis is not rare (1–3), particularly in polymyositis characterized by the presence of anti-Jo-1 (antihistidyl-tRNA synthetase) antibodies (4), referred to as the 'Jo-1 syndrome' or 'anti-synthetase syndrome' (5). These antibodies appear to be specific for polymyositis (6) and correlate strongly with the presence of interstitial lung disease (5). However, pulmonary fibrosis rarely precedes the clinical recognition of polymyositis (3) and is an indicator of poor prognosis (1). We describe a case where interstitial lung disease preceded the diagnosis of polymyositis by 12 months, and describe possible factors related to therapy which delayed the definitive diagnosis.

Case Report

A 66-year-old man presented with a 3 weeks' history of fatigue, dry cough and dyspnoea on exertion. He had no previous illnesses and was a lifelong non-smoker. He was on no medication. Physical examination revealed a low grade pyrexia, resting tachypnoea, bi-basal crepitations on chest auscultation, and no finger clubbing.

Resting arterial oxygen tension (PaO_2) was reduced at 9·3 kPa breathing room air, and arterial carbon dioxide tension ($PaCO_2$) was 4·8 kPa. Pulmonary function tests showed a restrictive pattern on spirometry with forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) both 51% of the predicted normal values. The transfer factor (DICO) was 46%. Laboratory investigations demonstrated a neutrophil leukocytosis ($16 \times 10^9\,l^{-1}$) with a normal eosinophil count, erythrocyte sedimentation rate (ESR) of $30\,mm\,h^{-1}$ and hypoalbuminaemia (serum albumin $23\,g\,l^{-1}$). A chest radiograph (Plate 1) and computed tomographic (CT) scan (Plate 2) indicated bilateral interstitial pulmonary infiltrates.

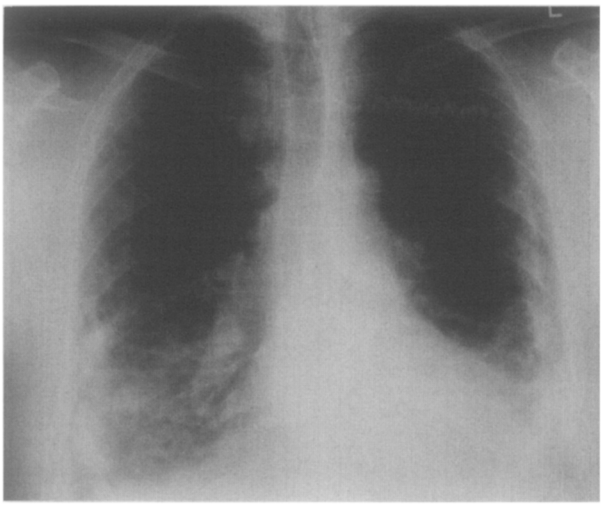

PLATE 1. Chest radiograph on initial presentation showing extensive bi-basal infiltrates.

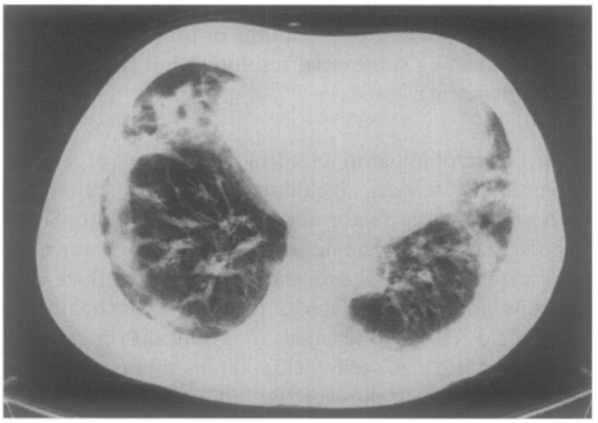

PLATE 2. CT thorax on initial presentation showing extensive bi-basal infiltrates, predominantly sub-pleural in distribution.

The patient continued to have intermittent pyrexias over the next 4 weeks despite empiric broad-spectrum antibiotic

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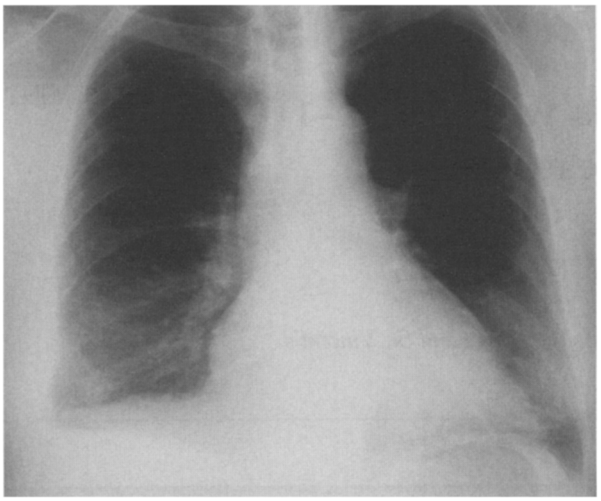

PLATE 3. Chest radiograph following 9 months of oral steroid therapy, indicating significant resolution.

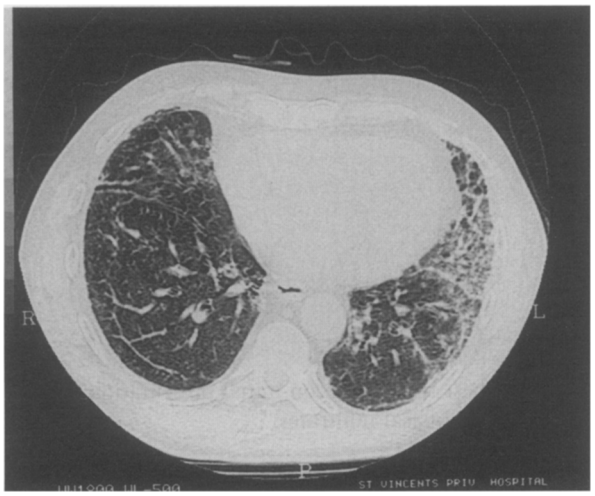

PLATE 4. CT thorax after 9 months of oral steroid therapy indicating substantial resolution but residual scarring persisting.

therapy. Microbiological cultures yielded no organisms. Autoantibody screens, including antinuclear antibodies (ANA), rheumatoid factor and antineutrophil cytoplasmic antibodies (ANCA), were negative. HIV serology was negative. Flexible fibre-optic bronchoscopy revealed thick clear secretions and diffuse mucosal oedema. Bronchoalveolar lavage fluid (BAL) indicated a significant increase in neutrophils (12% of cell yield). Trans-thorascopic lung biopsy indicated a non-specific interstitial pneumonitis without granulomata or angiopathy. He was commenced on high-dose prednisolone (60 mg) after which his pyrexia resolved and his dyspnoea improved. Over the next several months, improvements were noted in radiological appearances on CXR (Plate 3) and CT thorax (Plate 4). Improvements in pulmonary function were also observed, with FEV_1 increasing to 61%, FVC to 65% and transfer factor to 52%. However, after 6 months of continuous prednisolone therapy he developed proximal muscle weakness which was

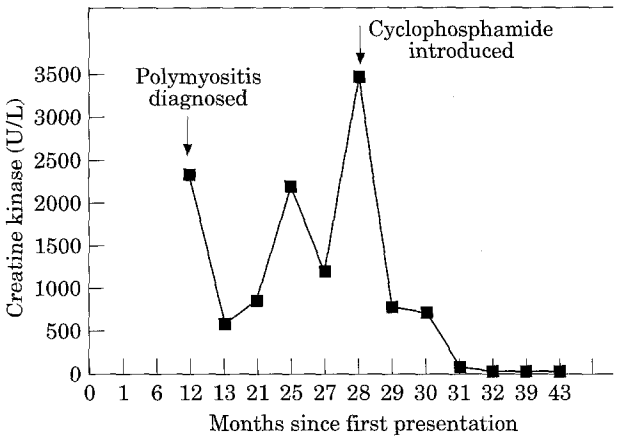

FIG. 1. Creatine kinase activity from diagnosis of polymyositis to present.

considered to be related to his steroid therapy, despite a gradual reduction in prescribed steroids. His steroid dose was further reduced to 10 mg daily. However, his muscle weakness increased, and he was hospitalized for investigation. CXR appearances remained stable but creatine kinase activity of 3500 $U\,l^{-1}$ (normal range 0–185 $U\,l^{-1}$), electromyography (EMG), skeletal muscle biopsy and the presence of a positive anti-Jo-1 antibody titre confirmed the diagnosis of polymyositis. ANA was retested at this time and was positive (1:400 dilution) with a nucleolar pattern. EMG confirmed a myopathic process without neuropathy. The muscle biopsy reported the presence of a light mixed inflammatory cell infiltrate extending from muscle fascia into muscle fascicles, intimately associated with degenerating fibres. Some fibres had undergone frank necrosis and showed replacement by macrophages. Neither ragged red fibres nor inclusion bodies were present, nor were rimmed vacuoles or Nemalin rods. There was no evidence of selective atrophy or selective hypertrophy. Myophospharylase, phosphofructokinase and cytochrome oxidase studies were normal. The overall appearances were those of a sub-acute inflammatory myopathic process consistent with polymyositis. His steroid dosage was increased and azathioprine commenced with reduction in creatine kinase activity and improvement in muscle power. Over the next 12 months, his polymyositis followed a relapsing course (Fig. 1) but his pulmonary infiltrates and lung function remained relatively unchanged. Cyclophosphamide, 100 mg daily, in place of azathioprine, resulted in remission of his polymyositis, normalization of creatine kinase activity and muscle strength, and no deterioration in pulmonary function.

Discussion

Polymyositis is an inflammatory condition of skeletal muscle with one-third of cases occurring between 45 and 60 years of age (2). Clinical suspicion of polymyositis is high where muscle pain or tenderness is obvious, but these symptoms may only occur in 50% of cases (7). Sub-acute polymyositis is much more common with features of progressive weakness and atrophy of proximal muscle groups.

Laboratory investigation usually indicates elevated serum creatine kinase activity but definitive diagnosis may depend upon a combination of clinical findings, electromyography and muscle biopsy. Several respiratory complications have been associated with polymyositis. Respiratory muscle weakness, reduction in lung volumes, basal atelectasis, aspiration pneumonia due to reduced cough reflex or involvement of pharyngeal muscles, respiratory failure due to hypoventilation, and adult respiratory distress syndrome have been reported (8,9). Pulmonary fibrosis may occur in 5–10% (3,10) and the presence of anti-Jo-1 antibodies increases this likelihood (3). This case is unusual in that dyspnoea due to pulmonary infiltrates was the presenting feature rather than muscle weakness or pain. This sequence of events is rare in polymyositis, even in the anti-Jo-1 syndrome, where the diagnosis of polymyositis often precedes any pulmonary involvement. As the pulmonary infiltrates and respiratory symptoms were considered to be due to a steroid-responsive cryptogenic fibrosing alveolitis, treatment with corticosteroids was appropriate, although this therapy may have delayed the diagnosis of polymyositis. The development of proximal muscular weakness during therapy was initially considered to be a result of chronic steroid therapy, and the correct aetiology only became clear when reduction of the steroid dosage led to worsening of muscle weakness. This clinical pattern suggested the presence of polymyositis which was subsequently confirmed. The presence of anti-Jo-1 antibodies may explain the responsiveness of the pulmonary infiltrates to steroid therapy as the presence of this antibody seems to suggest a more favourable response to steroids (5).

We conclude that corticosteroid therapy, although successfully treating the pulmonary pathology, may have obscured the underlying diagnosis and delayed definitive therapy due to the unusual mode of presentation. Clinicians should therefore consider measuring serum creatine kinase and anti-Jo-1 antibody when investigating atypical cases of interstitial lung disease.

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