Case report

Efficacy of intravenous immunoglobulin in shrinking lung syndrome associated with mixed connective tissue disease: a case report

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ABSTRACT

Shrinking lung syndrome is a rare manifestation of connective tissue diseases, namely systemic lupus erythematosus. It is characterised by reduced lung volumes and extra-pulmonary restrictive ventilatory pattern with good response to high-dose glucocorticoids alone or in combination with a second immunosuppressive agent. Here, we describe a case associated with mixed connective tissue disease and effectively treated with intravenous immunoglobulin.

Introduction

Shrinking lung syndrome (SLS) is a rare and poorly understood manifestation of connective tissue diseases (CTDs) (1). It affects more frequently systemic lupus erythematosus (SLE) patients (approximately 1%) (2). However, this involvement has been described in other CTDs, including mixed connective tissue disease (MCTD) (1, 3-5). It is characterised by reduced lung volumes and extra-pulmonary restrictive ventilatory pattern (1, 2). We report a case of SLS associated with MCTD treated with intravenous immunoglobulin (IVIg).

Case report

A 42-year-old woman presented with a six-month history of symmetric polyarthritis, involving proximal interphalangeal and metacarpophalangeal joints, wrists, elbows and knees, puffy hands and a triphasic Raynaud's phenomenon without digital ulceration. In addition, in the previous three months, she reported fatigue and mild exertional dyspnoea. Her medical history was unremarkable except for a diagnosis of arterial hypertension treated with candesartan/hydrochlorothiazide 16/12.5 mg daily and she reported no history of tobacco, alcohol, or illicit drug use. Laboratory results showed a normocytic anaemia (haemoglobin 10.1 mg/dL) with normal leukocytes (5230 /L) and platelets (220000 /L), elevated C-reactive protein (1.92 mg/dL) and erythrocyte sedimentation rate (120 mm/hour) with normal renal and liver parameters. Protein electrophoresis revealed an increased gamma globulin (3 g/dL), which was confirmed as a reactive IgG polyclonal gammopathy after immunofixation. Antinuclear antibodies were positive with a speckled immunofluorescence pattern and anti-U1RNP specificity (>6438 U/L). Other autoantibodies (including anti-dsDNA, anti-Sm and anti-Ro) were negative and complement levels were normal. Anti-hepatitis B surface antibody and anti-hepatitis B core antibody were positive and serum hepatitis B surface antigen and viral DNA were negative. Anti-hepatitis C virus, anti-HIV-1 and anti-HIV-2 antibodies were negative. Chest and joints radiographs were normal, without erosions, and fingernail capillaroscopy excluded a scleroderma pattern. A diagnosis of MCTD was made and treatment with prednisolone 10 mg daily and methotrexate up to 20 mg weekly was started. Arthritis remission was achieved after 8 weeks, but dyspnoea was progressively worse [Modified Medical Research Council (mMRC) dyspnoea scale 2] and associated with episodic pleuritic chest pain. A chest computed tomography revealed left diaphragmatic elevation and left basal atelectasis with no parenchymal abnormalities (Fig. 1). Pulmonary function tests (PFT) revealed a severe restrictive pattern with a decreased forced vital capacity (FVC; 37%), maximal inspiratory pressure (MIP; 55%) and diffusing capacity for carbon monoxide (DLCO; 63%) with normal DLCO

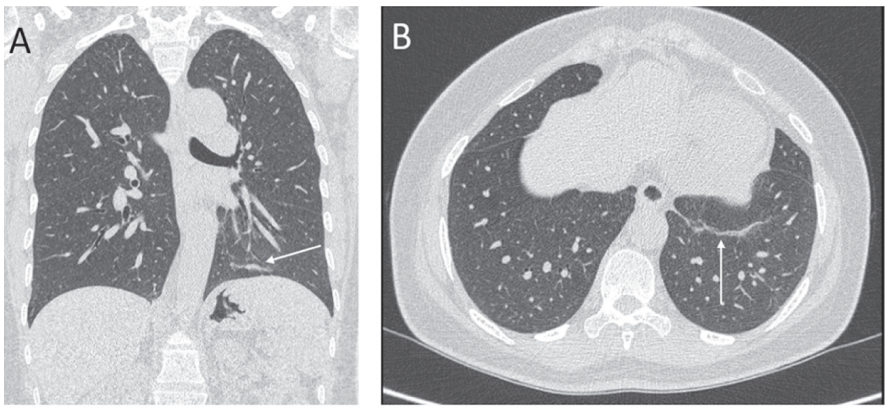

Fig. 1. Longitudinal plane CT scan (A) and axial plane CT scan, at the level of the eight thoracic vertebra (B) showing slightly elevated left diaphragmatic dome and linear atelectasis (white arrow) without signs of interstitial lung disease.

corrected for alveolar volume. Muscle strength was preserved and muscle enzymes were within the normal range. Despite that, we performed phrenic nerve conduction studies and limbs electromyograms, which excluded a subclinical myopathic involvement and a diagnosis of SLS was assumed. Given the joint involvement and active therapy with methotrexate, rituximab was the preferred treatment for SLS. However, due to the presence of anti-hepatitis B core antibody she was referred for further hepatology evaluation and, meanwhile, bridge therapy with IVIg 2g/Kg (150g total) was added on a 4-week basis. After three months of IVIg, the patient reported progressive symptomatic improvement (mMRC 1) and an almost complete normalisation of the PFT was documented with an increased in FVC to 65% and DLCO to 120%, with normalisation of MIP (89%). Considering the clinical and functional improvement, IVIg was stopped at this time. Three months later, the patient remains stable on the initial methotrexate dose of 20 mg weekly and low dose prednisolone (6.25 mg daily), with minimal exertional dyspnoea. The initiation of rituximab was withheld, pending symptomatic and PFT evolution.

Discussion

SLS is rarely described in association with MCDT and its treatment is derived from the limited evidence of the management of SLS associated with SLE, which includes moderate to high-dose glucocorticoids (GC) alone or in combination with a second immunosuppressive agent, azathioprine, methotrexate or cyclophosphamide (1, 2, 6). Recently, rituximab has been used in refractory SLS (2, 5, 7, 8). Overall, there is a good clinical and functional response irrespective of the treatment strategy (2, 8).

The underlying mechanisms of SLS are yet to be elucidated, but several studies suggest the contribution of myopathic damage. An extra-pulmonary restrictive pattern with decreased respiratory pressures is seen in most patients without other clinical or enzymatic evidence of myopathy, suggesting the involvement of respiratory muscles (2, 8). Having this rational in mind and considering the efficacy of IVIg in idiopathic inflammatory myopathies, we added IVIg to the patient's treatment strategy with an excellent clinical and functional response with no need to increase the dose of GC. To the best of our knowledge this is the first report of IVIg use in SLS.

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