Case report

Minimal-change disease in association with sarcoidosis

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Introduction

Sarcoidosis is a multisystem disorder characterized by non-caseating granulomata which most frequently presents with bilateral hilar lymphadenopathy, pulmonary infiltrates, and skin lesions [1]. Its renal manifestations are usually that of a granulomatous interstitial nephritis, hypercalcaemia, and hypercalciuria and rarely a glomerulonephritis of which membranous is the most common [2].

Minimal-change disease in association with sarcoid is very rare and has only been reported previously with other diseases (IgA [3,4] and Graves’ disease [5]). We report a case of steroid-resistant nephrotic syndrome secondary to minimal-change disease in a patient with sarcoidosis.

Case report

A 43-year-old woman was admitted to our unit in 1994 for investigation of a 2-week history of ankle swelling and shortness of breath. Sarcoidosis had been diagnosed 14 years earlier on the basis of bilateral nodular shadowing on X-ray, with fibrosis on lung biopsy. She was treated with prednisolone but this was stopped after 3 months due to problems with weight gain and mood swings. She experienced premature menopause at 24 years. She was on no medication.

Examination revealed pitting oedema to the knees. Blood pressure was 125/80 mmHg with no postural drop. Respiratory, cardiovascular, neurological, and skin examinations were normal. Initial investigations showed blood urea 5.1 mmol/l, creatinine 0.07 mmol/l, calcium (corrected) 2.59 mmol/l, phosphate 0.99 mmol/l, albumin 20 g/l, haemoglobin 148 g/dl, platelets 428, total white cell count 9.4 and ESR was 76 mm/h. Chest X-ray revealed bilateral interstitial shadowing consistent with pulmonary fibrosis. Anti-DNA antibodies and ANCA were negative, complement levels were normal and protein electrophoresis showed no evidence of a paraprotein. Proteinuria and haematuria was present on urinalysis. Twenty-four-hour urinary protein excretion was 8.4 g. Urine microscopy revealed no casts. Respiratory function tests showed reduction in total lung capacity, residual volume, and transfer factor consistent with pulmonary sarcoid. Serum ACE level was 60 (normal range 13–40 u/l) and 24-h urinary calcium excretion was within normal limits.

Renal biopsy showed two granulomata in the interstitium but glomerular light-microscopy, immunofluorescence, and electron-microscopy revealed only mild non-specific changes consistent with minimal-change disease.

Prednisolone at an initial dose of 60 mg/day was commenced. This was continued for 6 weeks before being slowly tapered to 5 mg/day. After 3 months the patient still had marked proteinuria at 5.7 g/l with a serum albumin of 24 g/l. Her exercise tolerance had improved, her serum ACE level had returned to normal, and respiratory function tests had shown some improvement.

Further investigation of the patient’s ‘early menopause’ revealed hyperprolactinaemia, 5300 mu/l (normal <600 mu/l). MRI pituitary scan showed no micro- or macroadenoma, and cerebrospinal fluid ACE level was low, <5 u/l. The most likely diagnosis was thought to be neurosarcoidosis. She was started on bromocriptine but because of persistent nausea this was stopped and she was commenced on hormone replacement therapy.

In view of her steroid-unresponsive proteinuria, the diagnosis of minimal-change disease was queried and in March 1995 the patient underwent repeat renal biopsy. The specimen contained 25 glomeruli, two showing global sclerosis while the others were normal or had slight mesangial expansion. There were no segmental sclerosing lesions. Immunofluorescence was negative. Electron-microscopy was not performed. She was commenced on cyclophosphamide at 2 mg/kg whilst continuing prednisolone at 5 mg/day. In July 1995 after 3 months treatment her albumin was 24 g/l and 24-h urinary protein was 15.3 g. Due to further problems with nausea she stopped the cyclophosphamide. Cyclosporin was commenced in August 1995 at an initial dose of 3 mg/kg/day. Isotope GFR measurement at that stage was 43 ml/min/1.73 m² (serum creatinine 0.12 mmol/l). Subsequently the patient had
subjective improvement in symptoms of tiredness and nausea. In April 1996 her albumin had improved to 26 g/l with minimal proteinuria on urinalysis. The prednisolone was tapered and withdrawn. Her serum creatinine had deteriorated to 0.41 mmol/l by July 1996 and the cyclosporin was stopped. In September 1996 the lung sarcoid flared with cough and worsening respiratory function tests and she was recommenced on prednisolone 50 mg/day for 2 weeks before dose tapering. She had no flare of her nephrotic syndrome at this time.

The patient currently remains well with serum creatinine of 0.43 mmol/l.

Discussion

Glomerular involvement in sarcoid is rare and minimal-change nephrotic syndrome is rarer still. This patient had onset of a nephrotic syndrome associated with a flare of her sarcoidosis. It is possible the two events are related, however; following steroid treatment her sarcoid improved but her nephrosis did not and a later flare of pulmonary sarcoid was not associated with relapse of nephrotic syndrome. Steroid resistance is unusual in minimal-change disease but is well described [6]. She could not tolerate cyclophosphamide but had a partial response to cyclosporin therapy at the expense of worsening creatinine.

A few previous reports have highlighted the association between sarcoid and minimal-change disease but only in the context of other diseases [3–5]. This is the first report of minimal-change disease alone in a patient with sarcoid. As discussed by Mündlein and colleagues [5] clustering of immune disorders in individuals is well recognized and we report this case as a further example of this.

References


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