

A case of mixed connective tissue disease combined with sarcoidosis

Mixed connective tissue disease (MCTD) is an overlap syndrome accompanied by high levels of anti-ribonucleoprotein (RNP) antibodies and RNase-sensitive anti-ENA antibodies.^{1,2} Sarcoidosis, on the other hand, is a systemic granulomatous disease with reduced cellular immunity and increased humoral immunity.³

We report a case of MCTD associated with sarcoidosis. The patient was a 61 year old Japanese woman complaining of exertional dyspnoea and Raynaud's phenomenon. A chest x ray showed fine reticular/granular shadows in both lower lung fields with slight swelling of the hilar lymph nodes. A superficial lymph node was palpable in the left neck (10 mm diameter) and the right supraclavicular fossa (2–3 mm diameter). Heart sounds were regular, no murmurs were audible. Fine crackles were heard on auscultation in both lower lung fields. There was scleroderma of the fingertips on both hands as well as a swollen right fourth finger. Mild anaemia (RBC $3.22 \times 10^6/\text{mm}^3$, Hb 10.7 g/dl, Ht 31.7%) and mild leukopenia ($3,600/\text{mm}^3$) were observed. Arterial blood gas analysis revealed pH 7.434, PaO₂ 72.7 mm Hg, PaCO₂ 37.3 mm Hg, HCO₃⁻ 24.8 mEq/l, BE + 0.8 mEq/l, and oxygen saturation 94.8%, indicating reduced pulmonary diffusing capacity. Pulmonary function test also revealed decreased diffusing capacity (DL_{CO} 67.4%), whilst neither constrictive nor obstructive change was noticed. The erythrocyte sedimentation rate (ESR) was 118 mm/hour. CRP was negative. Acetylcholine esterase level was at the upper limit of normal range (19.4 IU/l), lysozyme was slightly elevated (18.0 mg/ml), antinuclear antibodies (++, speckled pattern), RNase-sensitive anti-ENA antibodies ($\times 20480$), anti-RNP antibodies ($\times 16$) and anti-DNA antibodies

($\times 160$) were positive, but anti-Sm, anti-Scl, anti-Jol, and anti-double-stranded DNA antibodies (IgG), and the LE test were negative. The rheumatoid factor level, immune complexes and the CH₅₀ were within normal range.

A CT scan of the thorax showed slight enlargement of the hilar lymph nodes and infiltration mainly in the lower lung fields (fig A, B), and a Ga scintiscan revealed diffuse isotope accumulation in both lung fields. She had polyarthralgia in her hand and knee joints and was therefore diagnosed as having MCTD. A transbronchial lung biopsy revealed granulomas associated with epithelioid cells within the pulmonary tissue (fig C). Increase of total cell count ($1.2 \times 10^3/\text{ml}$) with considerable lymphocytosis (68.6%) was observed in bronchoalveolar lavage fluid, which was compatible with sarcoidosis. Sputum and gastric juice were negative for tubercle bacilli. The tuberculin reaction was negative. A diagnosis of associated sarcoidosis was made.

On day 51 the onset of intercurrent iritis was noted. An associated heart lesion was suspected because of multifocal paroxysmal ventricular contractions. Oral prednisolone (30 mg/day) was administered for three weeks and the dose was decreased. All her signs and symptoms improved. The arterial blood gas data were normal, lysozyme levels and all the autoantibody titres had decreased, and the infiltration shadows on the chest x ray and CT scan gradually improved.

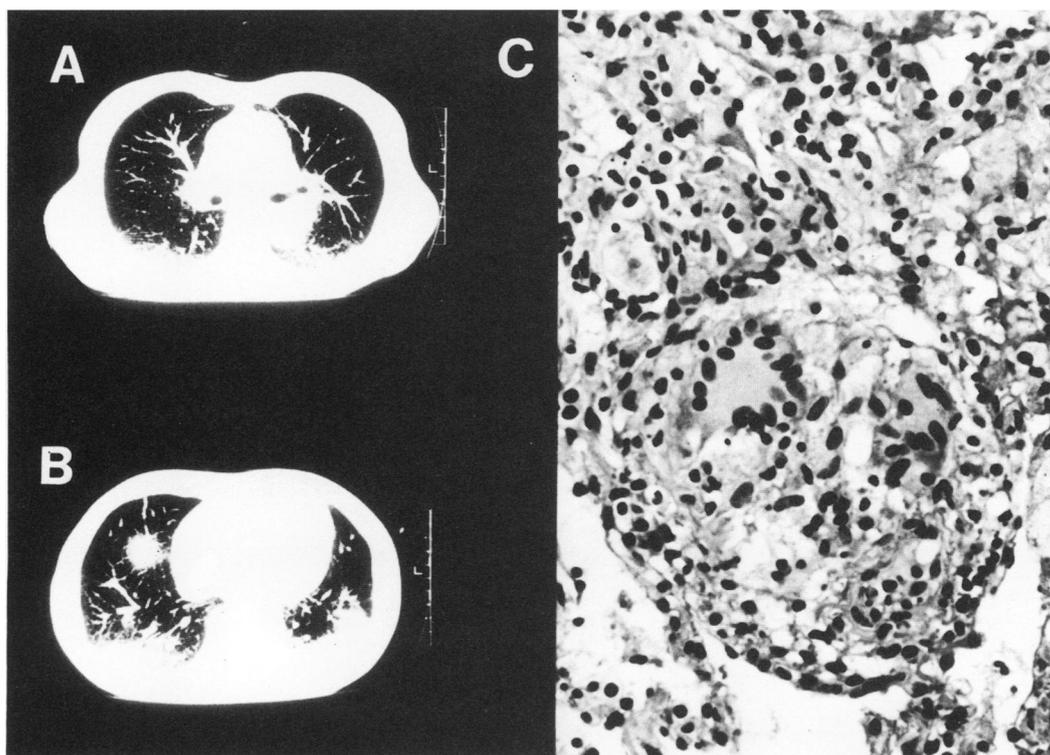
Collagen disease-type symptoms sometimes occur in sarcoidosis, while non-caseating epithelioid cell granulomas are sometimes observed in the spleen and other organs in systemic lupus erythematosus (SLE),⁴ and in aponeuroses in progressive systemic sclerosis (PSS).⁵ The concomitant progression of MCTD and sarcoidosis and their remission by steroid treatment in our patient suggest that the two diseases are immunologically related. The increased humoral immunity and decreased cellular

immunity seen in sarcoidosis is reported to closely resemble SLE and the autoimmune disease model in New Zealand mice.⁶ To date only one case of an association between MCTD and sarcoidosis has been reported.⁷ There have been occasional reports of sarcoidosis associated with SLE,⁶ PSS,⁶ RA⁸ and primary biliary cirrhosis.⁹

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Pulmonary CT scans (A and B) and histology of the lung tissue obtained by a transbronchial biopsy (C). Enlargement of hilar lymph nodes (A) and infiltration mainly in the lower lung fields (B) were observed on CT scans. Histology (C) showed epithelioid cells and Langhans-type giant cells in granulomas (H & E; original magnification $\times 200$).