Respirology (2003) **8**, 396–397

CASE REPORT

Antinuclear antibody positive pleural effusion in a patient with tuberculosis

THIDA WIN, ASHLEY M. GROVES AND GERRARD D. PHILLIPS

Dorset County Hospital, Dorchester, Dorset, United Kingdom

Antinuclear antibody positive pleural effusion in a patient with tuberculosis
WIN T, GROVES AM, PHILLIPS GD. *Respirology* 2003; **8**: 396–397
Abstract: A patient with tuberculosis presented with a pleural effusion that was highly positive for antinuclear antibody (ANA). The pleural fluid autoimmune profile was positive for ANA IgG at a titre of 1 : 1280. Antibodies to double-stranded DNA were not detected in the pleural fluid or in serum. The serum autoimmune profile was positive for ANA IgG at 1 : 160 and IgM at 1 : 40. Pleural fluid was positive on culture for *Mycobacterium tuberculosis* after 8 weeks. Pleural biopsy for histology showed chronic inflammation and culture revealed no growth. The pleural fluid resolved with the antituberculous treatment, and signs and symptoms of systemic lupus erythematosus or malignancy did not occur, which suggests that tuberculous pleural effusion is one of the causes of high ANA in pleural fluid.

CASE REPORT

A 47-year-old woman presented with a 4-week history of right-sided pleuritic chest pain and worsening exertional dyspnoea. She reported no cough or sputum. She was an ex-smoker of 30 years, having smoked five to 10 cigarettes per day for 10 years. She had been exposed to asbestos and had visited Singapore recently.

On examination she was breathless on minimal exertion. Her temperature was 38°C. Chest examination was compatible with a large right-sided pleural effusion, which was confirmed by the CXR.

Her haemoglobin was 10.5 g/dL, WCC 10.6×10^9/L (neutrophils 8.5×10^9/L) and her ESR was 94 mm in 1 h. Renal function was normal but liver function was slightly impaired, alkaline phosphatase 494 IU/L (normal value 100–300 IU/L), gamma GT 128 IU/L (normal value 5–32 IU/L).

Pleural aspiration and biopsy were undertaken. The pleural fluid was clear, straw-coloured and had a protein content of 64 g/L. Cytological examination revealed predominantly lymphocytes, some of which appeared reactive and mildly atypical. Gram stain and staining for acid-fast bacilli were negative. Pleural fluid was positive on culture for *Mycobacterium tuberculosis* after 8 weeks. Pleural biopsy for histology showed chronic inflammation and culture revealed no growth. Polymerase chain reaction for mycobacterium was requested but no result was obtained due to insufficient material being available.

The pleural fluid autoimmune profile was positive for ANA IgG at a titre of 1 : 1280 with speckled pattern. Antibodies to double-stranded DNA were not detected in serum or pleural fluid. The serum autoimmune profile was positive for ANA IgG at 1 : 160 and IgM at 1 : 40. Therefore her pleural fluid to serum ANA ratio was > 1. Her Heaf test was grade II, but she had been given a BCG vaccination when she was young.

The technique we used for autoimmune profiling was immunofluorescence. Fluorescein labelled anti-human immunoglobulin (sheep) (Binding Site PF002), fluorescein labelled anti-human IgG (sheep) (Binding Site PF004) and fluorescein labelled anti-human IgM (sheep) (Binding Site PF012) reagents were used. Tissue sections were incubated with serum that possibly contained autoantibodies. If present, these antibodies would bind to specific antigenic sites within the tissues. Excess serum was washed off and the antigen/antibody complex was detected using an antihuman conjugate linked to a fluorescent dye (fluorescein isothiocyanate, FITC). The fluorescence was visualized using an ultraviolet microscope. If autoantibodies were detected, we proceeded to titration. For antinuclear factor, rat liver was used.

A presumed diagnosis of tuberculosis (TB) was made and the patient was treated with a standard regimen of isoniazid, rifampicin and pyrazinamide. Her

Correspondence: Thida Win, Thoracic Oncology Unit, Papworth Hospital, Papworth Everard, Cambridge, CB3 8RE, UK. Email: thida.win@papworth-tr.anglox.nhs.uk

Received 20 September 2002; accepted for publication 26 November 2002.

response was slow. However further investigations including a CT of the thorax and abdomen, bronchoscopy and ventilation perfusion scan were unrevealing. After 2 weeks of anti-tuberculous treatment, prednisolone 60 mg/day was added to her regimen. She began to improve clinically 1 week after starting steroid treatment.

The repeat CXR after 2 weeks of anti-tuberculous therapy showed a reduction in size of the pleural effusion, which completely resolved 8 weeks after starting chemotherapy. She received 6 months of treatment in total, without any side effects. We followed her for a further 6 months and she remained completely asymptomatic with a normal CXR and blood tests. In particular, she failed to develop any signs or symptoms of systemic lupus erythematosus (SLE) or malignancy.

DISCUSSION

This present case of tuberculous pleural effusion is unusual in that there was a very high pleural fluid titre of ANA, with a pleural fluid : serum ratio > 1. Antibodies to double-stranded DNA were absent in both the pleural fluid and serum and she had no clinical evidence of SLE.

In many parts of the world TB remains one of the most common causes of pleural effusion.[1] Tuberculous pleural effusions are usually clear, straw-coloured exudates with a predominance of lymphocytes.[1] Acid-fast bacilli in a smear from pleural fluid are seen in < 10% of cases. Multiple samples from closed pleural biopsy are positive in 50–80% of the cases, while positive cultures are obtained from 30 to 70% of cases. With all methods combined, the yield is close to 95%.[2] There is very little data about the relationship between ANA positive pleural fluid and tuberculous pleural effusions.[1–5]

The main cause of a positive test for ANA in pleural fluid is lupus pleuritis.[3,4,6] Weakly positive results may be found in normal individuals, especially the elderly. Other causes include autoimmune diseases, acute viral infections, chronic inflammatory processes, malignant disease and congestive cardiac failure.[5,6] A recent report has suggested that the other main cause of a highly positive ANA titre is malignancy.[6] Bronchogenic carcinoma is the malignancy most commonly associated with high ANA titre and it can be as high as 1 : 51 206 in this disease. The other causes of a high ANA titre in pleural effusion include TB and amoebiasis.[6]

We can find only one previous report of positive pleural fluid ANA titre in TB.[6] Wang *et al.* reported that the ANA titre was positive in four out of 16 samples from tuberculous pleural effusion. One of those effusions showed a titre of 1 : 320 with speckled pattern. In the same report, pleural fluid to serum ANA ratio > 1 was found in malignancy, TB and SLE.

Khare *et al.* discussed the importance of the staining pattern as SLE usually showed a homogenous pattern.[5] They suggested that a low ANA titre and speckled staining pattern in pleural fluid are usually found in diagnoses other than SLE. The report from Wang *et al.* does not support that statement.[6] Their results showed that a high ANA titre is not diagnostic for lupus. At the same time, the staining pattern and the pleural fluid to serum ANA titre ratio were not reliable clues in identifying lupus.

There are some reports that identify an association between positive antineutrophil cytoplasmic antibodies and TB.[7–9] As such we would suggest that TB should be added to the differential diagnosis of a patient who presents with pleural effusion with high ANA. However, we believe that the cause of positive ANA titre in our patient's pleural effusion was TB.

ACKNOWLEDGEMENT

We would like to thank Mrs Lindsay Morgen, Laboratory Manager, Immunology Department, Southampton General Hospital, Southampton, for kindly contributing to the laboratory technique used in this study.

REFERENCES

1 Light RW. Disorders of the Pleura, Mediastinum and Diaphragm. Harrison text book. *Principles of Medicine*, 13th edn. 1994; 1231–2.
2 Bartolome R. Diseases of the Diaphragm, Chest wall, Pleura and Mediastinum. *Cecil Text Book of Medicine*, 20th edn, 1996, 446.
3 Good JT Jr, King TE, Antony VB, Sahn SA. Lupus pleuritis; clinical features and pleural fluid characteristics with special reference to pleural fluid anti-nuclear antibodies. *Chest* 1983; **84**: 714–18.
4 Leechawengwong M, Berger HW, Sukumaran M. Diagnostic significance of anti-nuclear antibodies in pleural effusion. *Mt Sinai J. Med.* 1979; **46**: 137–9.
5 Khare V, Bethge B, Lang S, Wolf RE, Campbell GD Jr. Anti-nuclear antibodies in pleural fluid. *Chest* 1994; **106**: 866–71.
6 Wang DY, Yang PC, Yu WL, Kuo SH, Hsu NY. Serial antinuclear antibodies titre in pleural and pericardial fluid. *Eur. Respir. J.* 2000; **15**: 1106–10.
7 De Clerck LS, Van Offel JF, Smolders WA *et al.* Pitfalls with antineutrophil cytoplasmic antibodies (ANCA). *Clin. Rheumatol.* 1989; **8**: 512–16.
8 Adebajo AO, Charles PJ, Hazleman BL, Maini RN. Antineutrophil cytoplasmic antibody titres in patients with recent infection. *Br. J. Rheumatol.* 1993; **32**: 941–2.
9 Habegger de Sorrentino A, Motta P, Iliovich E, Sorrentino AP. Anti-neutrophil cytoplasmic antibodies (ANCA) in patients with symptomatic and asymptomatic HIV infection. *Medicina* 1997; **57**: 294–8.