WALDENSTROM'S MACROGLOBULINEMIA PRESENTING WITH PLEUROPULMONARY AND GASTRIC MANIFESTATIONS

J C H Yap, S C Poh

ABSTRACT

A case of Waldenstrom's macroglobulinemia is reported in which the main clinical presentation was related to pulmonary infiltrations and pleural effusion. Serum protein studies demonstrated the characteristic monoclonal increase in immunoglobulin M (IgMK). Pleural and percutaneous lung biopsies showed dense lymphocytic infiltration. Gastric biopsy also showed focal atypical lymphoid hyperplasia. There was good clinical and radiological response to treatment with chlorambucil and prednisolone.

Keywords: Waldenstrom's Macroglobulinemia, pleuropulmonary manifestations

SINGAPORE MED J 1990; Vol 31: 405 - 408

INTRODUCTION

Waldenstrom's macroglobulinemia (WMG) is a rare lymphoproliferative disorder of insidious onset and relatively benign clinical course. It predominantly affects the elderly. This disease is characterised by proliferation of a cell population consisting of lymphoplasmacytoid cells and associated with a monoclonal increase in the serum IgM level. Many cases of WMG have been reported since Waldenstrom reported the first case in 1944, but cases with mainly pleuropulmonary manifestations are rare.

This report describes the clinical, pathological and immunological features of a case of pleuropulmonary and gastric WMG.

CASE REPORT

A 75-year old lady presented with a nine-month history of cough productive of moderate amount of yellow sputum. There was no haemoptysis, pleuritic chest pain or fever. She also noticed exertional dsypnoea and had lost 4 kg of body weight. She denied any other symptoms. He appetite was good. Her diet was assessed to be adequate. She did not smoke.

Physical examination showed a thin and frail-looking lady. Pallor was present. There was no clubbing of fingers. Raynaud's phenomenon was not demonstrated. There was no lymphadenopathy. The cardiovascular system was normal. A left pleural effusion was detected, and there were signs of consolidation of the right upper lobe anteriorly. The liver and spleen were not enlarged. Per rectal examination and protoscopy was normal. Per vaginal speculum examination showed some cervical erosions. There was no abnormality in the neurological system. Fundoscopy was normal.

A chest roentgenogram showed a left pleural effusion and opacities involving the right upper and middle lobes (Fig 1 and 2). She was admitted to hospital for further investigations. Thoracentesis yielded 700 ml of bloodstained pleural fluid with a total protein of 4.6 g/dl. Pleural fluid for acid fast bacilli stain and microscopic examination for malignant cells were negative. However, the fluid was found to have small round and plasmacytoid lymphocytes. Occasional plasma cells were present (Fig 3). The pleural biopsy also showed a similar finding (Fig 4). A subsequent percutaneous lung biopsy was performed and it showed a similar lymphomatous infiltrate. A raised IgM of 2400 mg/dl was found in the pleural fluid. Additional laboratory test results were as follows: Hb 9.8 g/dl, WBC 5,100/ul, platelets 350,000/ul ESR 140 mm/first hr., reticulocyte count 1.6% normal peripheral blood film, normal serum folate and B_{12} levels. The serum iron was 41 µg/dl and TIBC 261 µg/dl with a Fe/TIBC ration of 16%. The serum total protein was 8.5 g/dl, albumin 2.9 g/dl, α_1 globulin 0.2 g/dl, α_2 globulin 1.0 g/dl and the $\beta + \gamma$ globulin 4.4 g/dl. An M-band was seen in the serum. Serum immunoelectrophoresis demonstrated bands for anti-gamma and anti-kappa. Serum IgM estimation was 3950 mg/dl (NR 30 - 160 mg/dl). Bence Jones Protein was not detected in the urine. Serum cryglobulin was absent. Bone marrow aspirate was not diagnostic except for iron depletion. There was no lytic lesion on skeletal survey. A CT scan of her thorax showed bilateral pleural effusion, more on the left side than the right. There were infiltrates in both lungs especially in the right middle lobe. Mediastinal lymph

Department of Medicine III
Tan Tock Seng Hospital
Moulmein Road
Singapore 1130

J C H Yap, MBBS, M Med (Int. Med) (S'pore)
Registrar

S C Poh, MBBS (Mal), AM (S'pore), FRCP (Edin)
Clinical Associate Professor and Head

Correspondence to: Dr J C H Yap

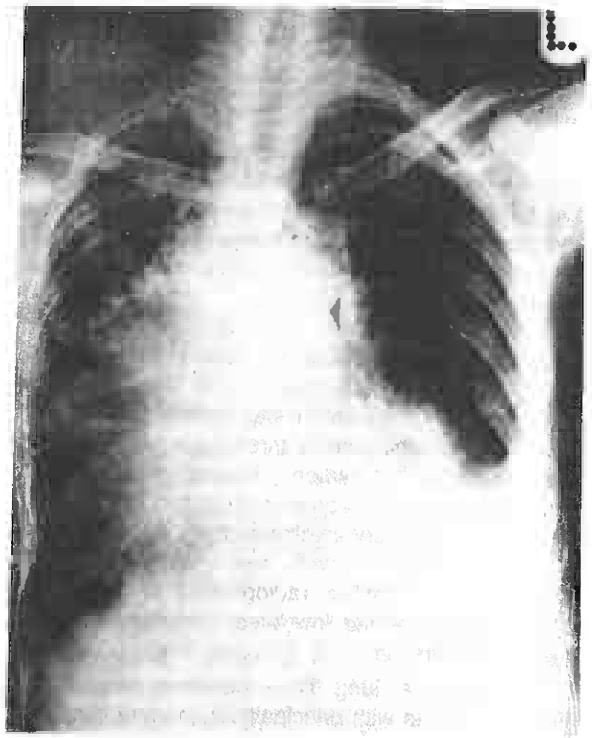
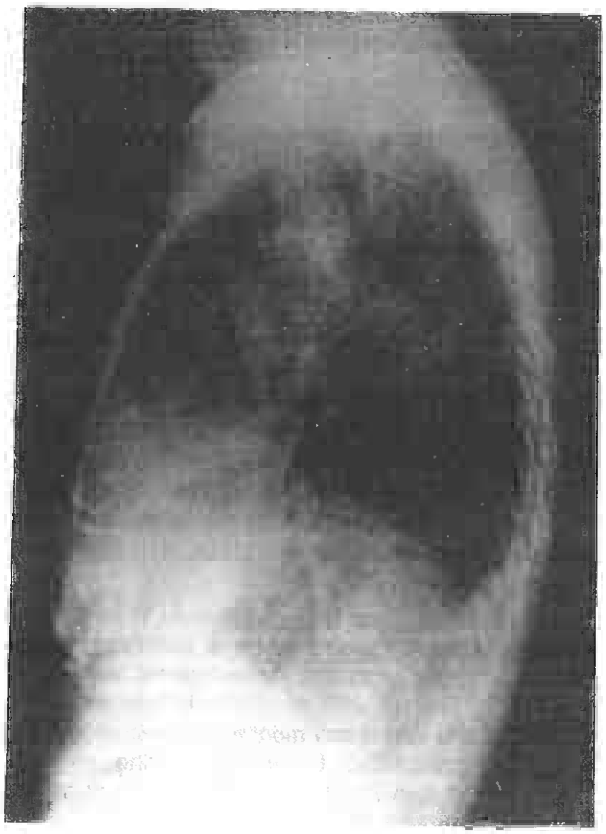


Fig 1 and 2
Chest X-ray films showing a left pleural effusion and right pulmonary opacities.



nodes were not enlarged. The serum uric acid, calcium and phosphate levels were normal. Gastroscopy showed only chronic atrophic gastritis. Biopsy was reported as showing focal atypical lymphoid hyperplasia on histology (Fig 5).

Fig 3
Cytocentrifuge of pleural fluid showing cells with plasmacytoid features. An intranuclear Dutcher body is seen (upper right hand corner arrow). H + E x 250.

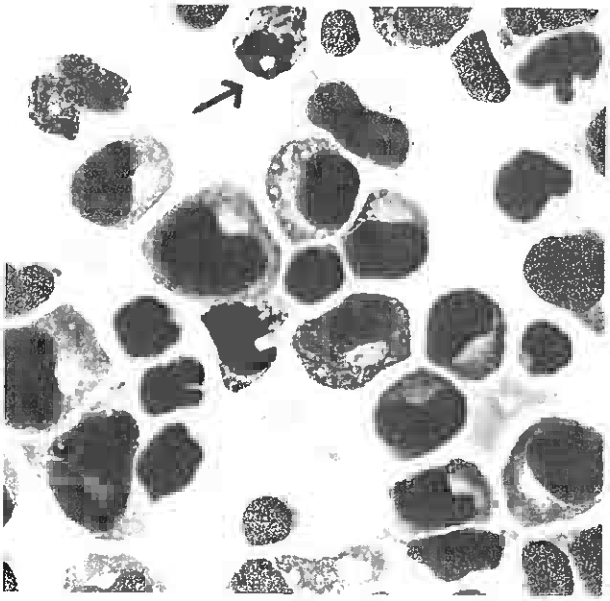
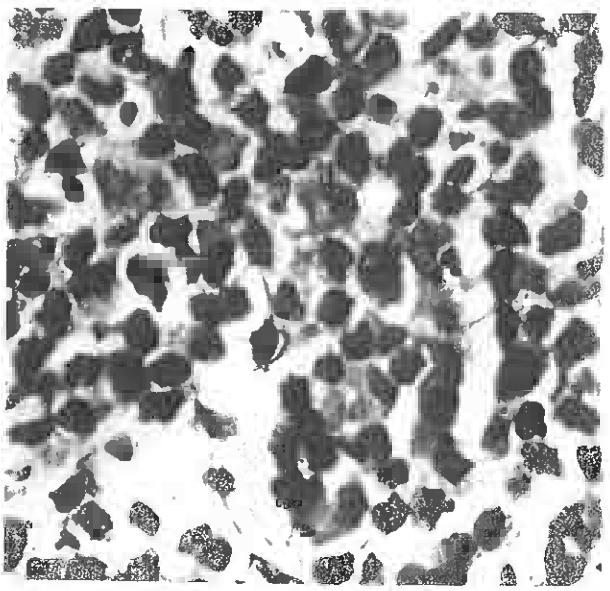


Fig 4
Pleural biopsy showing small round and plasmacytoid lymphocytes together with mature plasma cells. Cells with similar cytologic features were obtained from the fine needle aspirate of the right lung. H + E x 100.



The patient was discharged after a ten day course of chlorambucil 9 mg/day and prednisolone 40 mg/day. She was admitted again two weeks later for supraventricular tachycardia which responded to an intravenous dose of verapamil. There was no clinical or ECG evidence of heart disease. Her thyroid function tests were normal. She was given digoxin orally and had a second course of chlorambucil and prednisolone. An X-ray of the chest showed partial resolution of the right lung opacities and the left pleural effusion (Fig 6). Her serum IgM level decreased to 176 mg/dl. She was less symptomatic.

Fig 5
Fundic glands in gastric biopsy are widely separated by an infiltrate of a typical lymphoid cells in the lamina propria. H + E x 25.

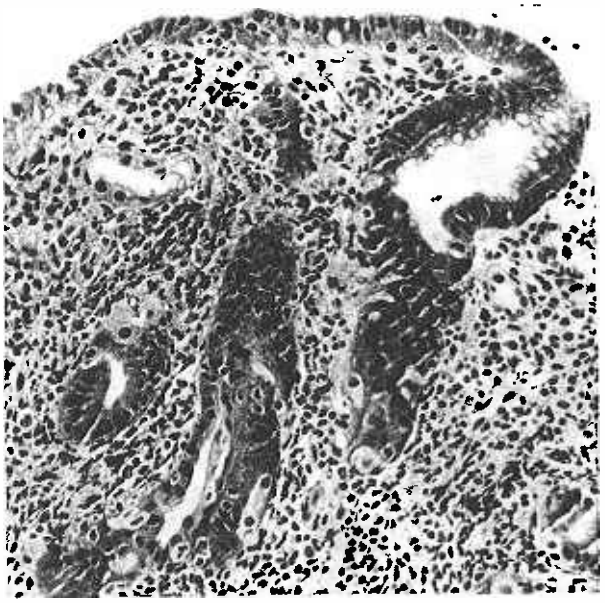
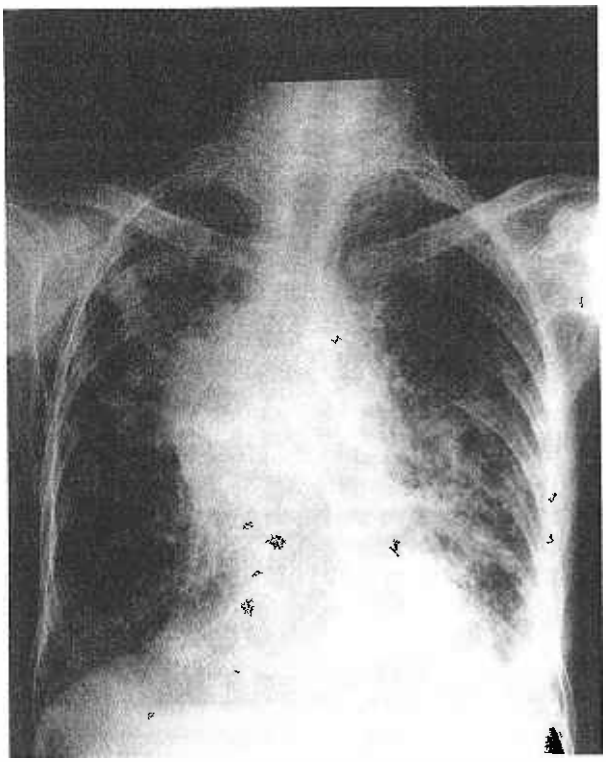


Fig 6
Chest X-ray film showing some resolution of the right lung opacities and the left pleural effusion



Four weeks later, she was re-admitted for a chest infection. While in the ward, She had another episode of supraventricular tachycardia which responded to intravenous verapamil. She was subsequently put on oral verapamil. The fever from the chest infection settled with intravenous ampicillin. However, she went into respiratory failure on the ninth day of admission. The arterial blood gas on intranasal oxygen 3 l/min showed PaO_2 137.1 mmHg, $PaCO_2$ 93.1 mmHg, pH 7.187 and bicarbonate 25.1 mmol/l. She was intubated and resuscitated. Post resuscitation chest X-ray did not show worsening of her lung lesions. She improved and was extubated 3 days later, but collapsed suddenly on the following day and could not be resuscitated. There was no autopsy.

DISCUSSION

Waldenstrom's macroglobulinemia (WMG), first described in 1944, is a rare disease of unknown aetiology. It is characterised by proliferation of lymphoplasmacytoid cells and monoclonal increase in the serum level of IgM. The clinical features of Waldenstrom's macroglobulinemia include anemia, fatigue, lymphadenopathy, hepatosplenomegaly and visual disturbance. Generally, infiltration of lymphocytic cells is seen in the lymph nodes, bone marrow, liver and spleen. The first case of WMG with pulmonary involvement was reported by Noach [1] in 1956. This was followed by three large reviews [2-4] and case reports [5-9] which showed that pulmonary involvement is more common than thought previously. Therefore, pulmonary involvement should be suspected in any case of WMG with abnormal chest X-ray film findings. The common radiographic findings include diffuse reticulonodular infiltrates, parenchymal masses and pleural effusion.

Although the lung is a common site of WMG infiltration, cases with principally pulmonary involvement are rare [2, 5-8]. The classic features of WMG are absent. Our case presented only with pulmonary complaints. There were no classic features such as lymphadenopathy, hepatosplenomegaly and hyperviscosity symptoms. Investigations showed lymphocytic infiltrations only in the lung parenchyma, pleura and stomach. A monoclonal gammopathy of IgM was found. Her serum IgM was 3950 mg/dl. A similar raised IgM level was also found in the pleural fluid.

The differential diagnosis in a case of WMG with only pleuropulmonary manifestation include multiple myeloma [10,11], lymphocytic interstitial pneumonia [12-14] and lymphocytic lymphoma [15]. It is difficult to determine clinically whether the disease is pulmonary WMG or some other lung disease in a patient with a raised IgM. Histologic examination of biopsy specimens does not often show specific changes. Immunologic tests for monoclonal IgM, eg. by the peroxidase-antiperoxidase method, is more important in the diagnosis of pulmonary WMG.

Although the patient had no gastrointestinal symptoms, a gastroscopy was performed to exclude any occult bleeding from the stomach that could account for the iron deficiency anaemia. Of interest was the finding of focal atypical lymphoid hyperplasia consistent with a diagnosis of gastric WMG.

Chlorambucil has been reported to be of value and at present seems to be a promising form of therapy [2,4-6,8,9]. Our patient showed partial resolution of chest X-ray findings with symptomatic improvement at the end of one and a half months. Her serum IgM was reduced significantly. Unfortunately she suddenly collapsed and died whilst recovering from an episode of acute respiratory failure.

ACKNOWLEDGEMENT

We wish to thank Dr Elizabeth Cheah and Dr Jean Ho of the Department of Pathology, Singapore General Hospital, for the histology reports.

REFERENCES

1. Noach AS. Pulmonary Involvement In Waldenstrom's Macroglobulinemia. Naderi T Geneesk 1956; 100: 3881 - 7.
2. Winterbauer RH, Riggins RC, Griesman FA, Bauermeister DE. Pulmonary Manifestations Of Waldenstrom's Macroglobulinemia. Chest 1974; 66: 368 - 75.
3. Rausch PG, Herion JC. Pulmonary Manifestations Of Waldestrom's Macroglobulinemia. Am J Hematol 1980; 9: 201 - 9.
4. McCallister BD, Bayrd ED, Harrison EG Jr, McGuckin WF. Primary Macroglobulinemia: Review With A Report on Thirty One Cases And Notes On The Value Of Continuous Chlorambucil Therapy. Am J Med1967; 43: 394 - 434.
5. Kobayashi H, Ii K, Hizawa K, Maeda T. Two Cases Of Pulmonary Waldenstrom's Macroglobulinemia. Chest 1985; 88: 297 - 9.
6. Major D, Meltzer MH, Nedwich A, Hayes B, Oaks WW. Waldenstrom's Macroglobulinemia Presenting As A Pulmonary Mass. Chest 1973; 64: 760 - 2.
7. Strunge P. Waldenstrom's Macroglobulinemia. An Unusual Case Having Only Pleuropulmonary Manifestations. Acta Med Scand 1969; 185: 83 - 7.
8. Rabiner SF, Aprill SN, Rabiner DB. Waldenstrom's Macroglobulinemia. Report Of A Case With Pulmonary Involvement And Improvement In Pulmonary Symptoms Only Following Chlorambucil Therapy. Am J Med 1972; 53: 685 - 9.
9. Furgerson WB, Bachman LB, O'Toole WF. Waldenstrom's Macroglobulinemia With Diffuse Pulmonary Infiltration. Lung Biopsy And Response To Chlorambucil Therapy. Am Rev Respir Dis 1963; 88: 689 - 97.
10. Sekulich M, Pandola G, Simon T. A Solitary Mass In Multiple Myeloma. Dis Chest 1965; 48: 100 - 3.
11. Gabriel S. Multiple Myeloma Presenting As Pulmonary Infiltration. Dis Chest 1965; 47: 123 - 6.
12. Montes M, Tomasi TB, Noehren TH et al. Lymphoid Interstitial Pneumonia With Monoclonal Gammopathy. Am Rev Respir Dis 1968; 98: 277 - 80.
13. Young RC, Tillman RL, Burton AF et al. Lymphoid Interstitial Pneumonia With PolyClonal Gammopathy. J Nat Med Assoc 1968; 61: 310 - 4.
14. Moran TJ, Totten HS. Lymphoid Interstitial Pneumonia With Dysproteinemia. Am J Clin Path 1970; 51: 747 - 56.
15. Turner R R, Colby TV, Doggett RS. Well-Differentiated Lymphocytic Lymphoma. A Study Of Forty Seven Patients With Primary Manifestation In The Lung. Cancer. 1984; 54: 2088 - 96.