

Immunocytoma (polymorphous subtype IgA/ λ) of the lung

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Only 4-5% of the relatively rare extranodal malignant non-Hodgkin lymphomas occur in the lung¹ and most of these seem to be immunocytomas* of the IgM type.² Only a few well documented cases of the IgG and IgA type have been reported.³⁻⁵ We present a case of extranodal pulmonary immunocytoma with production of IgA-lambda.

Case report

The patient, a 56 year old male sports manager, became ill with a "protracted cold." He suffered from hoarseness, productive cough, nocturnal chills, a fever up to 38°C, and undefined chest pain. After a period of five months, during which the symptoms persisted, he was admitted to the hospital.

A chest radiograph showed a well defined opacity in the left upper lobe (fig 1). No endobronchial tumour was seen at bronchoscopy and bronchial biopsy and cytological examination of bronchial secretions yielded no abnormal findings. Three months later the patient was examined at the outpatient service for pulmonary diseases of the Basle University Hospital. At this time he refused invasive diagnostic procedures (mediastinoscopy, open lung biopsy). Treatment with corticosteroids was started on the assumption that he might have chronic pneumonia. The pulmonary opacity seemed to recede temporarily. After a further six months herpes labialis developed and his general condition deteriorated alarmingly. The patient agreed to further biopsy procedures. Bronchial biopsy showed infiltration of the bronchial mucosa by many lymphocytes and plasma cells, suggesting chronic bronchitis. At mediastinoscopy lymph nodes were found to be free of tumour. Cytological examination of sputum and bronchial secretion showed a striking number of small lymphocytes and some plasma cells, but the cytological criteria of malignancy were not met.

Laboratory findings The erythrocyte sedimentation rate was 37-75 mm in one hour, white blood cells $10 \times 10^9/l$, platelets $413 \times 10^9/l$. The differential blood count was within normal limits; only during operation did some atyp-

ical lymphocytes and plasma cells appear in the peripheral blood. Total serum protein was moderately increased at 99.0 g/l, and slight proteinuria (32-48 g/l/24 h) was seen. Serum electrophoresis carried out before operation showed a striking increase of β globulin at 52.7 g/l and of the IgA fraction at 42.0 g/l. All excess immunoglobulin was of the λ type. Other serum proteins were within the normal range: albumin 30.5, α_1 globulin 5.9, α_2 globulin 5.6, γ globulin 4.3, IgM 0.6, and IgG 6.6 g/l. Three weeks after operation the total serum protein fell to the normal value of 63.0 g/l; the β globulin and IgA concentrations remained slightly raised at 19.3 and 8.7 g/l.

The final diagnosis was not made before thoracotomy. The surgeon found an encapsulated sanguinous pleural effusion compressing the left lower lobe. The upper lobe was slightly shrunken and diffusely infiltrated by tumour.

The whole lobe apart from a thin marginal zone was diffusely infiltrated by a greyish fleshy tumour. The bronchi were filled with a friable greyish pink material. The hilar lymph nodes were inconspicuous. Lung tissue infiltrated by tumour was fixed in 2.5% buffered glutaraldehyde and processed as usual for electron microscopy. The remaining lobe was inflation fixed by transbronchial instillation of 4% saline formaldehyde and then cut in 1 cm thick sagittal slices. Paraffin sections were deparaffinised, brought into phosphate buffered saline (PBS), and treated with trypsin (Sigma, type V, 0.1%, pH 7.8, 30 min at 37°C). The sections were incubated by the PAP procedure* with antisera

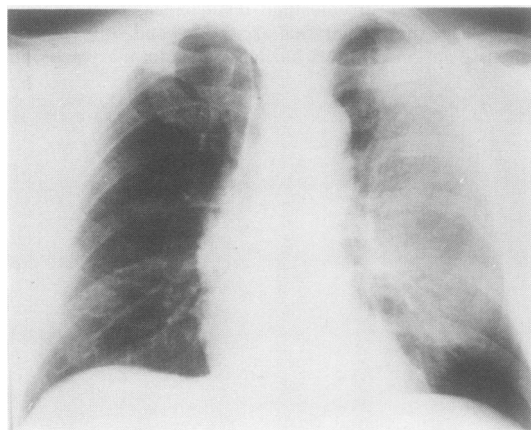


Fig 1 Malignant lymphoma of the lung: chest radiograph showing diffuse opacity of the left upper lobe with an air bronchogram.

*Immunocytoma is synonymous with malignant lymphoplasmacytoid B lymphoma with production and secretion of monoclonal immunoglobulins (Kiel classification); well differentiated lymphocytic lymphoma with plasmacytoid differentiations (Rappaport nomenclature); and lymphoplasmacytoid non-Hodgkin's lymphoma (Lukes and Collins and International formulation).

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Accepted 16 September 1983

against the heavy chains of IgG, IgM, and IgA as well as against K, L and joining chains. All sera were purchased from Nordic and pretested on lymphomas and plasmocytomas of known monoclonality. Specificity controls included replacement of the specific layer by PBS.

Microscopic examination showed a dense infiltration of the perivascular and peribronchiolar connective tissue with lymphoid cells, which extended into alveolar septa (fig 2) and the walls of some venules. The infiltrate comprised nearly the entire range of lymphoid cells from small lymphocytes to mature plasma cells and included some immunoblasts. The nuclei of some plasmacytoid cells contained periodic acid Schiff (PAS) positive inclusions. The alveoli were stuffed with an eosinophilic PAS positive and Congo red negative protein like material. The bronchial resection line and the paratracheal lymph nodes were infiltrated by tumour.

Immunohistological examination showed that there were only a few IgG and IgM producing cells scattered through the pulmonary tissue, whereas many of the lymphoplasmacytoid cells showed monoclonal IgA (λ) inclusions within their nuclei (fig 3). The same cells were positive for J chains, which take part in the synthesis of IgA dimers. The immunoblasts were completely negative for immunoglobulins.

Electron microscopic examination The infiltrate was dominated by plasmacytoid cells with activated endoplasm. Endoplasmic cisterns and intercellular spaces contained a mass of fine grained, nearly homogeneous material. This material is consistent with atypical immunoglobulin and was also found within the nuclear inclusions (fig 4). In addition, small lymphocytes with lymphocytic differentiation, lymphoblasts, and immunoblasts with prominent nucleoli and cytoplasmic polyribosomes were found.

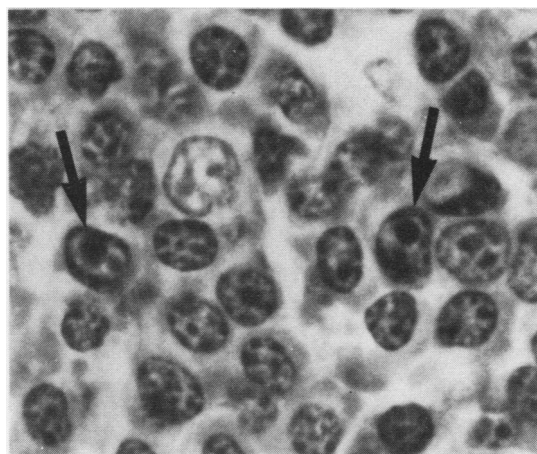


Fig 3 Cells from pulmonary infiltration immunostained for light chains. Arrows show nuclear inclusions. ($\times 815$.)

After resection of the upper lobe the patient recovered slowly. He continued coughing and had blood stained sputum. On the 22nd postoperative day and 18 months after the onset of the disease he suddenly died from massive haemoptysis. Necropsy could not be performed and bone marrow had not been examined so staging of the malignant lymphoma remained incomplete. Swelling of peripheral lymph nodes, however, had never been observed during the whole course of the disease. Computed tomography of thorax and abdomen in combination with abdominal lymphangiography gave no evidence of

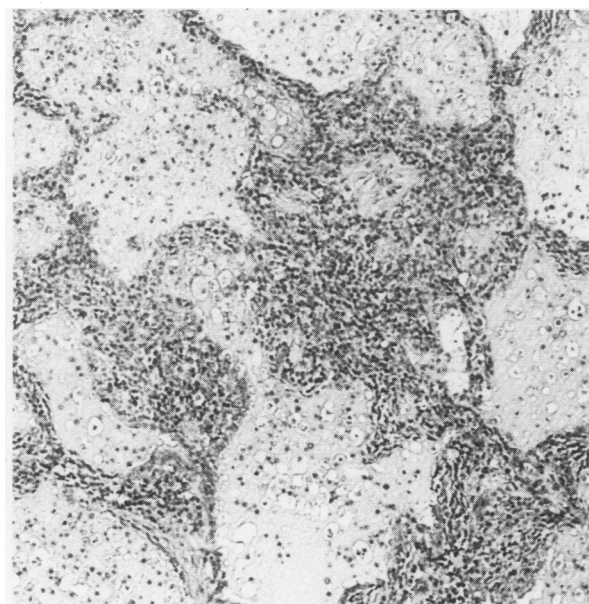


Fig 2 Interstitial infiltration of the lung by lymphoma cells.

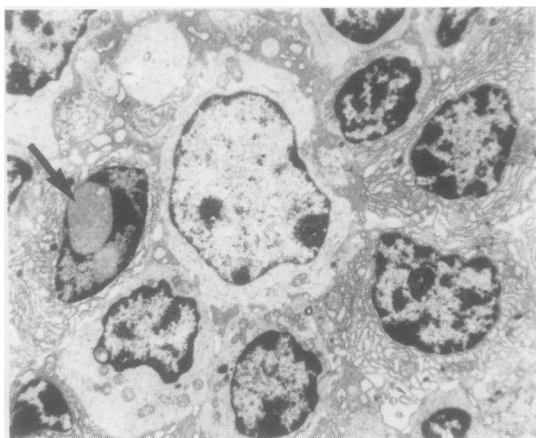


Fig 4 Electron microscopic appearance of cells from the infiltration. The nuclear inclusions (arrow) consist of finely granular material (immunoglobulin) that can also be seen between the plasmacytoid cells. ($\times 4200$.)

any tumour in liver, spleen, abdominal lymph nodes, or any other organ.

Discussion

The immunohistological and serological examinations show that this non-Hodgkin's lymphoma of the lung corresponds to the polymorphous subtype of an IgA(λ) producing immunocytoma.⁷

Though the bone marrow was not checked and necropsy could not be carried out, there are compelling reasons for the lung being the primary site of the lymphoma. The disease began with respiratory symptoms, the mediastinal lymph nodes were initially free of tumour at mediastinoscopy, the peripheral blood gave no evidence of disease of the bone marrow during the whole course of the illness, and computed tomography carried out shortly before death did not show any tumour in liver, spleen, or abdominal or thoracic lymph nodes.

The monoclonality of the immunoglobulin production provides convincing evidence for the malignancy of the lymphoma. The malignant nature of the lesion could not be proved by the usual cytological criteria but the histological features of malignant pulmonary lymphoma as defined by Saltzstein⁸ could easily be demonstrated in our case (invasion of vascular walls and regional lymph nodes). Further-

more, there were no lymph follicles, which are almost invariably seen in pseudolymphomas.⁹

Pulmonary lymphomas are sometimes misdiagnosed as chronic pneumonia because of non-specific symptoms, a relatively benign course, temporary remission during treatment with corticosteroids, an unusual radiographic presentation, and the lack of tumour cells in sputum and bronchial secretions. In other cases bronchial carcinoma has been diagnosed.¹⁰ The malignant lymphomas of the lung seem to have a better prognosis than other extranodal lymphomas.⁸ Some patients have survived as long as 25 years after removal of the tumour. But in these cases lymphocytic lymphomas without monoclonal immunoglobulin production were found.

We thank Professor K Lennert of the University of Kiel for verifying the diagnosis.

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