

Pulmonary vascular involvement in neoplastic angioendotheliosis

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Abstract

Neoplastic angioendotheliosis has rarely been described as a respiratory disease. A patient is described with pulmonary vascular involvement induced by neoplastic angioendotheliosis in pulmonary vessels.

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Keywords: neoplastic angioendotheliosis, pulmonary symptoms.

Neoplastic angioendotheliosis (NAE)¹ or angiotrophic large cell lymphoma, is characterised by multifocal intravascular aggregates of tumour cells of B cell nature that have a predilection for small vessels, especially in the skin and central nervous system. Cutaneous and neurological symptoms induced by vascular occlusions are therefore a predominant clinical feature. Although respiratory symptoms have rarely been mentioned as a clinical manifestation of NAE, we describe a case in which lung involvement predominated.

Case report

A 65 year old man whose previous occupation was a policeman was admitted to Kurume University Hospital because of progressive dyspnoea and fever. He had noticed shortness of breath about two months earlier without any prodromal illnesses. Before being admitted he was treated with broad spectrum antibiotics at another hospital but did not improve. The patient had smoked one pack of cigarettes a day for 20 years. He and his family had no relevant medical histories.

On admission he was not dyspnoeic or cyanosed at rest, but complained of shortness of breath upon light physical exertion. His body temperature was 37.8°C; respiratory rate was 19/min; blood pressure was 100/70 mm Hg, and heart rate was 70 beats/min with a regular rhythm. There was no lymphadenopathy. Heart sounds, breath sounds, and neurological findings were normal. Haematological values on admission showed a white blood cell count of 4800/ μ l, haemoglobin of 11.5 g/dl, and platelet count of 60 000/ μ l. Blood chemistry revealed an elevated LDH level (2456 U/l) but other liver function test results were normal: GOT

21 U/l, GPT 8 U/l, ALP 8.2 U/l, total bilirubin 0.76 mg/dl. The test for autoantibodies was negative. No coagulopathies were found. Arterial blood gas determinations while the patient breathed room air at rest showed pH 7.4, Pco₂ 5.1 kPa, and Po₂ 9.6 kPa. Repeated blood cultures were consistently negative. There was no serological evidence of fungal, mycoplasmal, viral, or chlamydial infection. A tuberculin skin test (1/2000 Old tuberculin) result was negative. Pulmonary function test results expressed as percentage of predicted normal were: vital capacity 99.1%, FEV₁ 81.4%, and transfer factor for carbon monoxide (TLCO) 28.6%. An electrocardiogram disclosed right ventricular strain, although echocardiography was normal.

A plain chest radiograph showed increased markings in both the lower lung zones and bullae in the lower part of the right lung. A computed tomographic (CT) scan of the chest did not provide any additional information. A 67-gallium labelled scintiscan was also normal. A pulmonary perfusion scintiscan with ^{99m}Tc-macroaggregates of albumin (MAA) disclosed bilateral defects (fig 1). Ultrasonography and CT scanning of the abdomen demonstrated no abnormalities except splenomegaly.

The patient gradually became dyspnoeic at rest, with a lowered Po₂ of 6.4 kPa, despite the administration of O₂ by mask. Treatment with several antibiotics and antituberculous and antifungal agents was uniformly unsuccessful. Open lung biopsy was contemplated, but was postponed because of the patient's precarious condition. The administration of corticosteroids and anticoagulants was started as we suspected that his condition may have been due to pulmonary thromboembolism associated with pulmonary vasculitis. However, it did not produce a favourable outcome. About three months after admission clustered atypical cells were found in both the peripheral blood and in bone marrow aspirates. Immunohistochemical examination revealed positivity for leucocyte common antigen and L26, indicating a B cell phenotype. A diagnosis of malignant lymphoma was established and pulmonary vascular infiltration by the lymphoma was assumed to be the cause of the respiratory distress. Treatment with pirarubicin, vindesine,



Figure 1 A perfusion scintiscan with ^{99m}Tc-MAA showing a bilateral defect.

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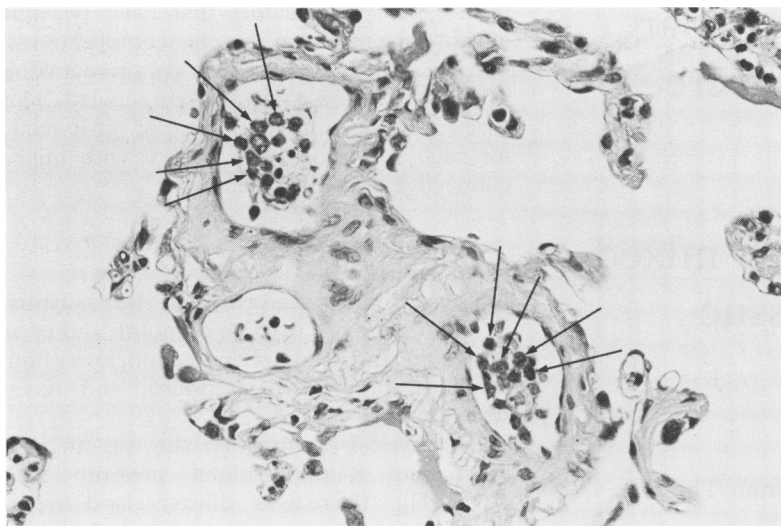


Figure 2 Photomicrograph of the lung at post mortem examination showed a proliferation of atypical cells (arrows) in the small vessels. On histochemical staining these blastic cells were positive for leucocyte common antigen and L26, a marker for B cells, and negative for UCHL1, a marker for T cells. Original magnification $\times 200$ reduced to 65% in origination.

cyclophosphamide, etoposide and prednisolone was therefore initiated. The breathlessness and hypoxia gradually decreased in parallel with the improvement in the %TLCO and reduction of the defects on pulmonary perfusion scintiscan.

The patient was discharged after completing four courses of chemotherapy, with his PaO_2 above 9.3 kPa on room air. Eleven months later he was readmitted in relapse despite maintenance chemotherapy and died of respiratory and renal failure. Post mortem examination of the lungs (fig 2) revealed a proliferation of large blastic cells in the middle sized arteries and particularly in the small vessels in the subpleural areas, which showed B cell phenotype on immunohistochemical staining. The lung parenchyma and alveolar septae were nearly normal. Although clinical features were atypical, a diagnosis of NAE was considered probable.

Discussion

Our case is not typical of NAE in that neurological and cutaneous symptoms were not observed. Instead, respiratory symptoms predominated although the plain radiographs and conventional examination of the chest disclosed

little abnormality relative to the degree of respiratory distress. The results of the pulmonary function tests and the ventilation-perfusion mismatch in the lung scans disclosed pulmonary vascular occlusion as the cause of the breathlessness and hypoxia. Although pulmonary thromboembolism, vasculitides, veno-occlusive disease,² and capillary haemangiomatosis³ may present with these physiological and radiological findings, identification of tumour cells with markers for B cells in the bone marrow and the efficacy of antineoplastic chemotherapy on the pulmonary vascular occlusion strongly suggested lymphoma. The diagnosis was eventually established at post mortem examination by finding lymphoma cells in the pulmonary vessel walls.

The lungs have rarely been mentioned as a clinically recognisable site of involvement in NAE. However, three cases have been previously reported in which pulmonary manifestations predominated.⁴⁻⁶ Interestingly, all three presented with progressive dyspnoea without cutaneous or neurological symptoms. Furthermore, two cases were shown to have a defect in the pulmonary perfusion scintigram with only minor changes on plain chest radiographs.^{4,5}

Diagnosis of NAE during life is difficult and depends on a biopsy of the skin, brain,⁷ or lung when these are involved.^{4,8} Early diagnosis is critical because of the excellent response to cytotoxic treatment reported in some cases.⁷

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