Primary malignant lymphoma of lung

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Summary

Primary malignant lymphoma of the lung is a rare variety of lymphosarcoma, to be distinguished from secondary lung involvement in disseminated malignant lymphoma. The condition tends to remain localized to the lung, and lymph nodes are not involved. The prognosis is better than in disseminated malignant lymphoma, and in the case described here a 35-year-old woman was treated by radiotherapy and chemotherapy and survived 20 years.

Introduction

Malignant lymphoma is usually a disseminated disease involving lymphoid tissue at the time of diagnosis, but the condition does occasionally arise in and remain localized to one organ, e.g. stomach intestine or lung (Willis, 1960; Sternberg, Sidransky and Ochsner, 1959; Havard, Nichols and Stansfield, 1962). Primary malignant lymphoma of the lung is rare, approximately one hundred cases having been reported (Saltzstein, 1963). Although the disease is malignant, its course with or without treatment may be prolonged. In the case described here, the progress of the disease was only partially controlled by therapy, but 20 years elapsed from diagnosis to death.

Case report

The patient was aged 35 years when first seen. She had given birth to her third child in January 1955, and an abscess in the right breast was drained in March 1955. Two weeks later, because her husband had been found to have active pulmonary tuberculosis, she had her first chest radiograph which revealed an opacity with hazy outline in the right lower zone (Fig. 1). She had no respiratory symptoms at the time, and was tuberculin negative. Tomographs confirmed that the radiological opacity was not in the breast but situated in the lower lobe of the right lung. She remained under observation, and in 1956 a similar opacity developed in the lower lobe of the left lung. By 1957 the right lower lobe lesion was more prominent, and in 1959 a small opacity appeared in the left mid zone. There was no mediastinal lymph node enlargement. Clinically she was symptomless and there were no abnormal

FIG. 1. Chest radiograph (PA) 1955. Opacity in right lower zone.

physical signs. She remained tuberculin negative, and blood count, sedimentation rate and liver function tests were normal.

The patient had been reluctant to undergo any invasive investigation, but by January 1961 she was more easily dyspnoeic and she agreed to have a lung biopsy. Percutaneous needle biopsy failed, and an open biopsy of the right lower lobe lesion was performed through a small thoracotomy. The histology of this showed massive infiltration of the lung tissue by well differentiated small lymphocytes spreading into the interalveolar septa (Fig. 2). The diagnosis of small-cell lymphocytic lymphosarcoma was independently confirmed by several pathologists.

Initial treatment in April 1961 consisted of telecaesium irradiation of the right lower lobe to a total dose of 3340 rad given over a period of 30 days. This was followed by oral prednisone 40 mg daily

FIG. 2. Photomicrograph of lung biopsy, showing infiltration of lung by small cell lymphocytes ($\times 500$).

FIG. 3. Chest radiograph (PA) 1961. Opacity in right lower zone more extensive. Opacity in left lower zone. Small opacity appearing in left mid zone.

for one month, and 30 mg daily for a further month, but both lower lobe lesions continued to progress (Fig. 3). In August 1961, intravenous chlorambucil 20 mg weekly for 4 weeks failed to produce any clinical

or radiological improvement. However, in 1962, treatment with oral cyclophosphamide 100 mg twice daily for a period of 6 weeks led to regression of the lesion in the right lower lobe (Fig. 4). In 1963, she developed a left pleural effusion which responded to treatment with antibiotics and was presumably due to infection.

By 1965, the lung disease had stabilized radiologically, and the patient managed to live a normal life, although she developed dyspnoea and tachycardia more easily on effort. In the ensuing 5 years, the opacities in the left lung and pleura extended slowly (Fig. 5). Clinically, there were crepitations and rhonchi in both lungs, but finger clubbing did not develop. There was no sign of extrathoracic disease at any time: no lymph nodes were palpable, the liver and spleen were never enlarged and blood count and liver function tests remained normal.

In 1970, she was more dyspnoeic, and radiotherapy to the left lung was given by linear accelerator to a total dose of 3000 rad. Although this did not produce significant radiological change, her clinical condition improved for a time, but by 1971 she was again more dyspnoeic, and she was treated for one month by combination chemotherapy, with a regime of vincristine, nitrogen mustard, procarbazine and prednisone. This produced little benefit, she continued to suffer from respiratory insufficiency, and in June 1974 she died at home of a respiratory infection.

It was not possible to arrange a post-mortem.

Discussion

Primary malignant lymphoma of lung must be distinguished from the more common secondary pulmonary involvement in disseminated malignant lymphoma which has been reported as occurring in 25–40% of these cases (Vieta and Craver, 1941; Robbins, 1953; Rosenberg *et al.*, 1961).

FIG. 4. Chest radiograph (PA) 1962. Right lower zone opacity resolving.

The normal lung parenchyma contains a lymphatic network, and it is in this that primary malignant lymphoma of lung arises as a proliferation of well differentiated small lymphocytes (and, less commonly, cells of reticulum-cell or Hodgkins' type) which extend by direct spread into the interalveolar septa. This mass replacement by lymphocytes of a limited area of lung may traverse interlobar fissures or even spread to the contralateral lung. Although there is usually little destruction of lung tissue, cavitation occasionally results (Cooley, McDonald and Clagett, 1956; Berghuis, Clagett and Harrison, 1961). The pleura and bronchial wall may be infiltrated but, unlike bronchial carcinoma, broncho-stenosis does not result. Mediastinal lymph nodes are not involved, and there is little tendency to distant spread by blood-stream or lymphatics.

The condition usually occurs in middle age, in either sex, and is frequently symptomless when diagnosed by routine radiography, but later cough, dyspnoea and chest pain develop. Diagnosis often proves to be difficult, although a persistent homogeneous lung opacity with hazy margins may lead one to suspect the disease, but conditions such as

tuberculosis, alveolar cell carcinoma, lipoid pneumonia, etc. will enter into the differential diagnosis. Tomography has occasionally shown patent bronchus traversing the opaque lesion, producing the appearance of an air-bronchogram (Baron and Whitehouse, 1961). Sputum cytology has been reported as diagnostic on one occasion (Jackson, Bertoli and Ackerman, 1951) and bronchoscopic biopsy may also be positive (Rose, 1957). However, the diagnosis usually rests on lung biopsy, performed by percutaneous needle technique or by thoracotomy. Hurt and Kennedy (1974) have described an abnormal immunoglobulin (IgM) in a patient with primary malignant lymphoma of lung.

Treatment should aim at cure by surgical excision of the diseased lobe or lobes. Since the tumour is radiosensitive, the alternative treatment is radiotherapy, which should be given in curative rather than palliative dosage. If these measures do not control the disease, a combination chemotherapy regime should be persevered with.

The prognosis is better than in disseminated malignant lymphoma, because the disease remains indolent, spreading by direct extension, and tending to remain confined to the lung without lymph node involvement (Papaioannou and Watson, 1965; Rees, 1973). Of the 4 cases described by Jenkins and Salm (1971), 2 survived with therapy for 15 and 25 years, and of 2 who died, one survived 10 years without therapy. In the case described here, the patient lived for nearly 20 years following diagnosis.

The aetiology of the condition – like that of all

FIG. 5. Chest radiograph (PA) 1969. Left lower zone opacity. Consolidation with pleural reaction.

lymphomas – remains unknown, and although it has been reported in association with lipoid pneumonia resulting from oily nasal drops (Hall and Blades, 1959) there is no reason to believe that this is the cause.

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