ALVEOLAR CELL CARCINOMA

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Alveolar cell carcinoma was first described by Malassez in 1876. Its aetiology, cell of orign and pathological characteristics remain as yet incompletely defined and in the past doubts have been cast on its very existence (Bennett & Sasser, 1969). Most authorities are now agreed that it is a valid clinico-pathological entity, and recent E/M studies have demonstrated that the neoplastic cell involved is derived from the alveolar type II cell (Adamson *et al.*, 1969; Coalson *et al.*, 1970).

The reported incidence varies between 0.4-8% of all the primary tumours of the lung. It has thus the lowest incidence of the primary malignant lesions of the lung, but remains the most controversial and probably the most interesting (Douglas, 1972). Such a wide range in incidence appears to indicate a need for greater uniformity and consistency in the diagnostic criteria that are applied. The tumour is commonest between the 50—70 year age group, is equally prevalent in both sexes and its incidence has markedly increased over the past twenty years (Colpinto and Joynt, 1970).

Case Report

The patient, a 55 year old female, was first admitted to hospital on 13/7/73 with a six months history of breathlessness on moderate exertion and a cough with a slight amount of whitish sputum. Her dyspnoea had been becoming progressively more severe 4 weeks prior to hospital admission. The patient had no other complaints, in particular there was no haemoptysis, anorexia or loss of weight.

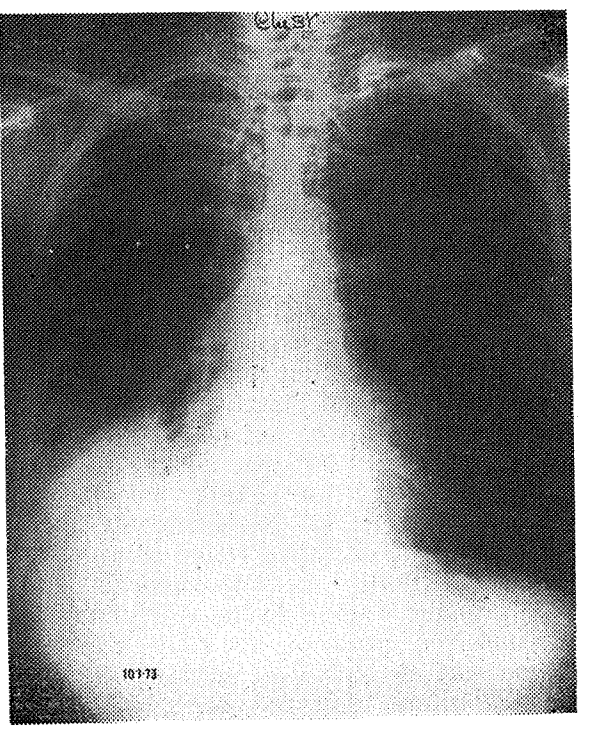


Fig. 1

Postero-anterior (PA) chest radiograph taken on 10/1/73 soon after onset of symptoms, showing an opacity in the lower zone right lung.

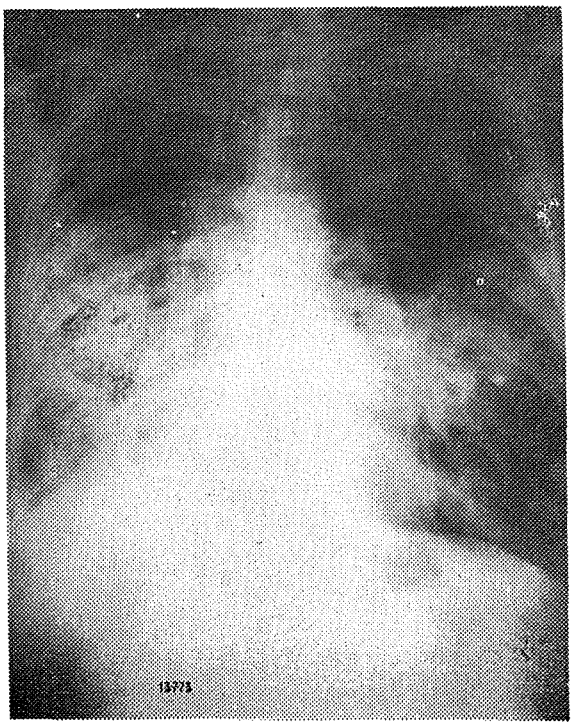


Fig. 2
PA radiograph taken on 13/7/73, on the day of admission to hospital, showing progression of the lesion on the right side with extension to the opposite side.

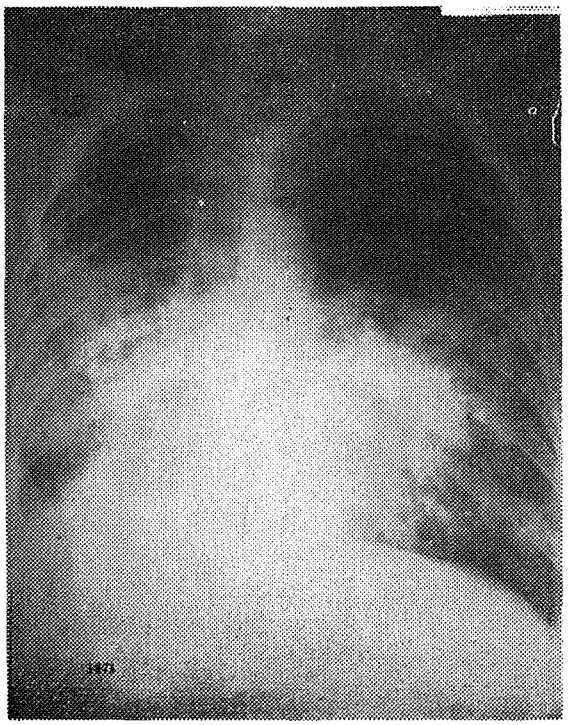
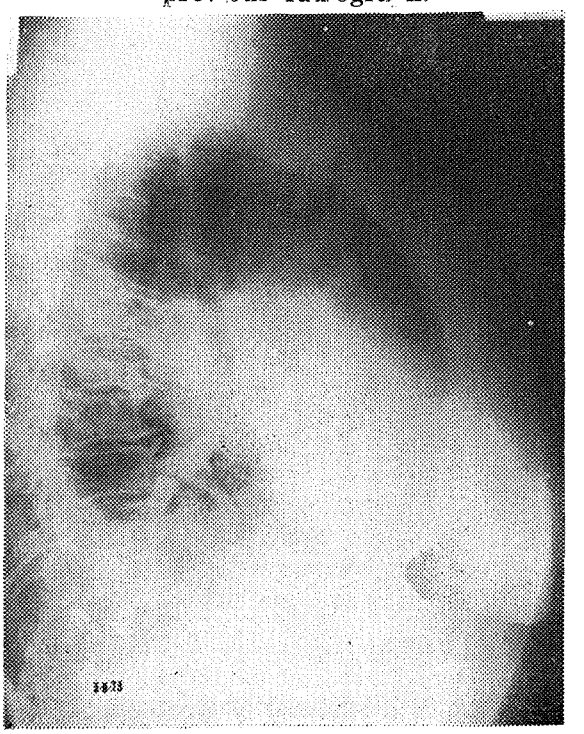


Fig. 3 & 4
PA and lateral chest radiographs taken on 3/8/73 a few days prior to her first discharge showing very little change from previous radiograph.



She was a non-smoker and her past medical history was unremarkable. On examination the patient was found to be slightly dyspnoeic at rest, becoming increasingly so on exercise. There was no cyanosis and no finger clubbing. Her pulse was 74 per minute, regular, good volume and her blood pressure was 140/90 mm Hg. Coarse crepitations and occasional high-pitched expiratory rhonchi could be heard over both lung fields but were most marked over the mid-zone of the left lung posteriorly. No other clinical signs could be elicited The following investigations were carried out: E.S.R. 73 mm (1 hour, Westergren) Hb. 16.8 g/100 ml, W.B.C. 12,800/cmm with a normal differential count; Tine test was negative; urea 33 mg/100 ml, Serum Calcium 5mEq/l, Serum alkaline phosphatase 4 K-A units/100 ml; urinalysis was normal. The Kveim test was repeatedly ne-

gative. Bacteriological examination of the sputum for pathogens, including tubercle bacilli, was negative, as was the cytological examination for malignant cells. The electrocardiogram was normal. Drill lung biopsy showed the presence of pulmonary fibrosis. Her FEV_1 was 1.35l (2.2l), FVC 1.85l (2.8l), showing a typical 'restrictive pattern' with a normal FEV_1/FVC ratio of 73% but a markedly reduced FEV_1 and FVC, in keeping with a diagnosis of pulmonary fibrosis. Predicted values are shown in brackets. She was put on Salbutamol 4mg q.i.d. and Prednisone 5mg q.i.d. and improved on this therapy. She was discharged on 15/8/73 from hospital on this treatment with an FEV_1 of 1.60l and an FVC of 2.05l. The patient attended the medical outpatient department regularly. Her condition was noticed to be getting progressively worse. On 2/11/73 she had to be re-admitted because of severe dyspnoea on slight exertion. She was noted to be bringing up copious amounts of whitish sputum. Coarse crepitations could be heard over both lungs. The patient was not cyanosed but was hyperpnoeic; she had a shallow respiratory rate of 36/min. Her FEV_1 was down to 1.05l and her FVC was 1.65l. She was treated with oxygen, prednisone 30mg/dy and Salbutamol 4mg. q.i.d. There was some slight improvement on this regime and she was discharged home on 22/12/73. She was admitted once again on 18/1/74 with the same complaints, but on this occasion, showed marked central cyanosis. Soon after admission she developed respiratory failure and died on 25/1/74. Figures 1-6 show the radiological progression of her condition, the first X-ray film being taken at the onset of symptoms, six months prior to her first admission to hospital. The last chest X-ray was taken a day before she died. A post-mortem was performed and histological

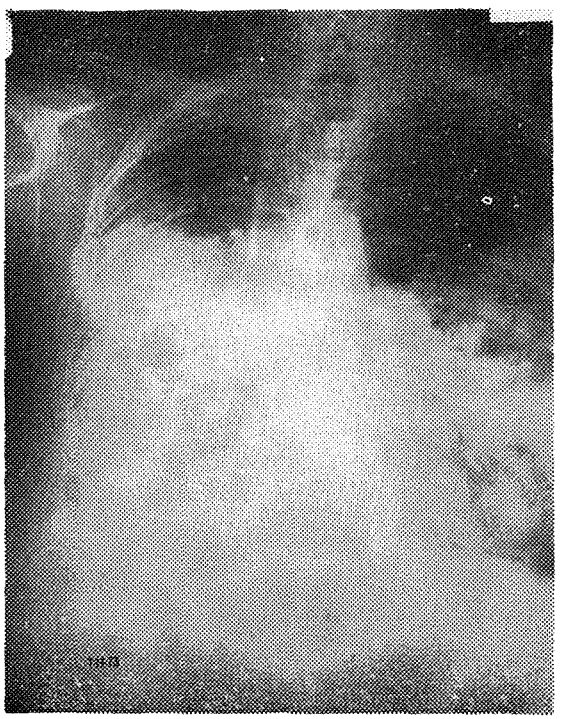


Fig. 5
PA radiograph taken on 7/11/73 some time after her second admittance showing marked bilateral progression.

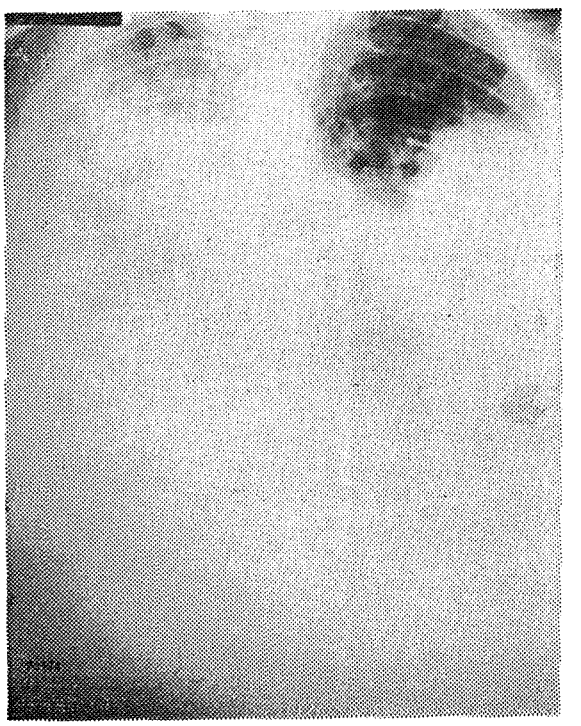


Fig. 6
PA radiograph taken on 24/1/74 a day before the patient died showing almost total bilateral pulmonary involvement.

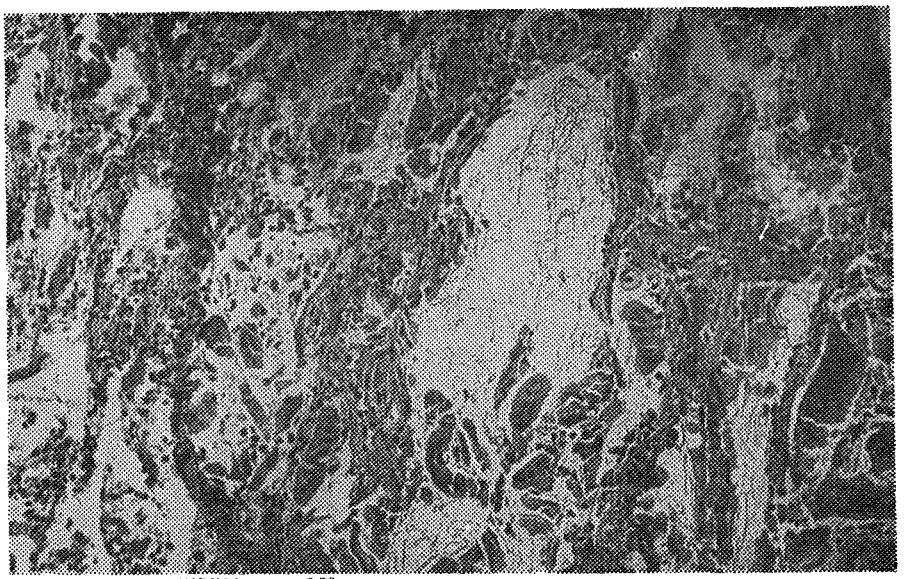


Fig. 7
Well differentiated alveolar cell carconima with preservation of alveolar architecture (x100).

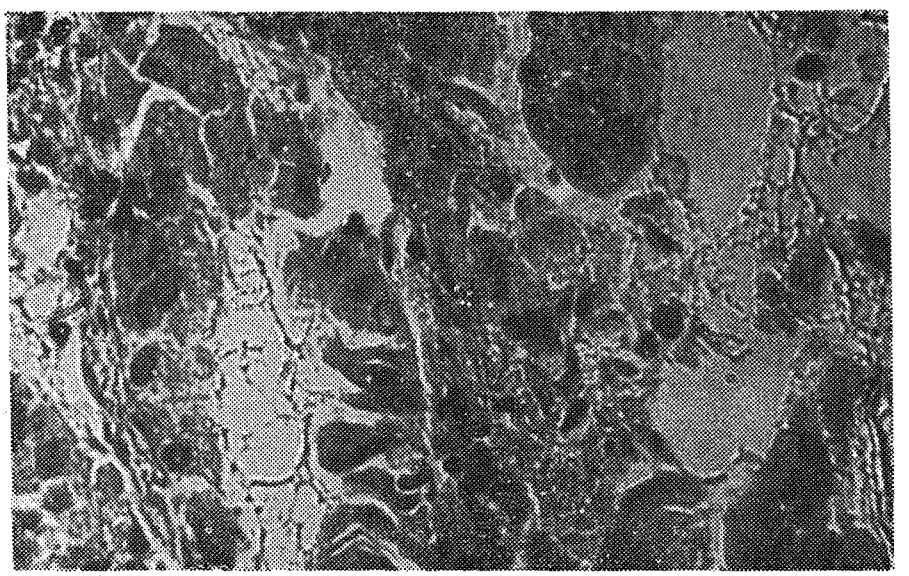


Fig. 8
Higher power view (x400) showing hyperchromatic basally situated nuclei. An occasional tumour cell may be seen lying free in alveolar lumen.

examination revealed the presence of an alveolar cell carcinoma (Fig. 7 & 8).

Discussion

Pathological evidence suggests that there is a correlation between pre-existing pulmonary disease and alveolar cell carcinoma, although there is little epidemiological evidence that previous lung disease predisposes the patient to this type of tumour. A large number of reports have been published in which the tumour has occurred in association with diffuse interstitial pulmonary fibrosis, as it appears to have done in our case. Progressive systemic sclerosis appears to be particularly liable to this complication (Caplan, 1959; Hollosi & Szam, 1960; Montgomery *et al.*, 1964; Szymczyk & Klott, 1967); but the tumour has also been reported in cases of cryptogenic fibrosing alveolitis (Jones, 1970) as well as in 'rheumatoid lung' (Fox & Ridson, 1968). Some workers have related the increasing incidence of this tumour to the increased lung scars developing as a consequence of the use of

antibiotic therapy for bacterial pneumonia (Beaver & Shapiro, 1956).

Pathologically alveolar cell carcinoma may present in 3 ways: (i) as a single nodule, (ii) as diffuse multinodular lesions, frequently bilateral, or (iii) as a diffuse pneumonic infiltration involving a single lobe, a lung or both lungs. The histological pattern of all forms is similar. The neoplastic cells are cuboidal or cylindrical, with faintly acidophilic cytoplasm, basally situated nuclei and few mitotic figures. The degree of differentation varies. In the well-differentiated tumour there is a uniform cellular pattern with preservation of the alveolar architecture which serves as a scaffolding for the growth. In the less differentiated forms the cells are more irregular, may be multi-layered and may sometimes form solid clumps. Mucin production is usually prominent although it is well known that this feature may be focal and distributed irregularly throughout the tumour. It is now generally believed that the tumour arises from a single focus and spreads mainly via the airways, to other parts of the lung (Munnell *et al.*, 1966) and less commonly by the lymphatics and blood stream.

Symptoms usually tend to occur rather late due to the slow progression of the tumour. The tumour may remain localized for long periods, even for years. The incidence of symptoms increases with extension of the lesion. Productive cough, breathlessness, chest pain and weight loss are common complaints, occasionally patients may present with haemoptysis, pyrexia or joint pains. One feature that is often stressed is the production of copious watery sputum, but this is in fact an inconstant finding and when it is present the carcinoma is usually advanced beyond surgical treatment. Physical signs depend on the extent of the carcinoma and whether or not there is an associated pleural effusion, which may at times be the initial finding (Hewlett *et al.*, 1964). Finger clubbing may be an early sign. Death occurs from respiratory failure due to the sheer extent of pulmonary involvement.

50% of patients with alveolar cell carcinoma are free of extrapulmonary metastases at the time of death (Colapinto *et al.* 1970). This justifies an aggressive surgical approach to the management of this form of malignancy. In most reported series the resectability rates have been of the order of 70% (Le Roux, 1968, McNamara *et al.*, 1969). The tumour is not susceptible to chemotherapy or radiotherapy (Douglas, 1972). This type of lung cancer has a much better prognosis than other forms if the diagnosis is made early when the lesion may be resectable.

Acknowledgements

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