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Synchronous double primary lung cancers of squamous and neuroendocrine type associated with cryptogenic fibrosing alveolitis

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Abstract

A 72 year old man with simultaneously occurring squamous cell and neuroendocrine carcinomas in association with cryptogenic fibrosing alveolitis is reported. The tumours were separate and both were in the fibrotic area of the right lower lobe.

We report a case of two synchronous cancers developing in a 72 year old man with cryptogenic fibrosing alveolitis. The histological types were squamous cell carcinoma and neuroendocrine carcinoma, a combination that has not been reported previously.

Case report

A 72 year old Korean merchant visiting a hospital for a routine check was found to have a nodular density associated with diffuse infiltrates on his chest radiograph. He had smoked 20 cigarettes daily for 50 years. Cough, sputum, and mild dyspnoea were present. Physical examination disclosed end inspiratory crackles at both lung bases. The chest radiograph and high resolution computed tomogram of his chest showed diffuse, irregular, and bilateral reticulonodular densities in the lung, which were more pronounced in the lower lung fields and subpleural areas in keeping with cryptogenic fibrosing alveolitis. Two intrapulmonary masses, 2 and 3 cm in diameter, were also seen in the right lower lobe in association with the reticulonodular densities. Ventilatory function was normal; transfer factor for carbon monoxide was 63% predicted.

A right lateral thoracotomy disclosed a serosanguinous effusion and diffuse pleural fibrosis and nodularity. A right lower lobectomy was performed.

Gross examination of the resected lobe showed diffuse honeycombing, especially in the subpleural areas of the lung. There were also two separate masses within the honeycomb area, measuring when fixed 3·0 × 1·5 × 1·5 cm and 1·2 × 1·0 × 0·5 cm. The larger one had a granular cut surface and

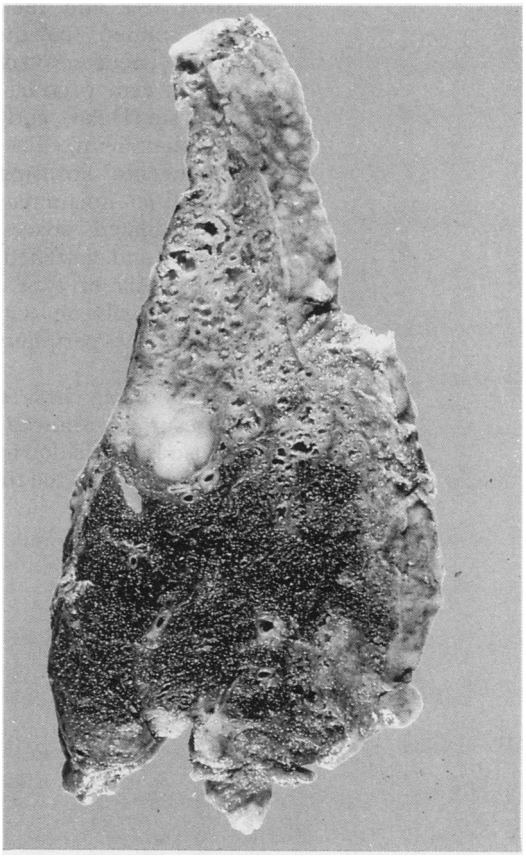

Figure 1 Slice of the right lower lobe showing subpleural honeycombing and a fleshy mass arising in it.

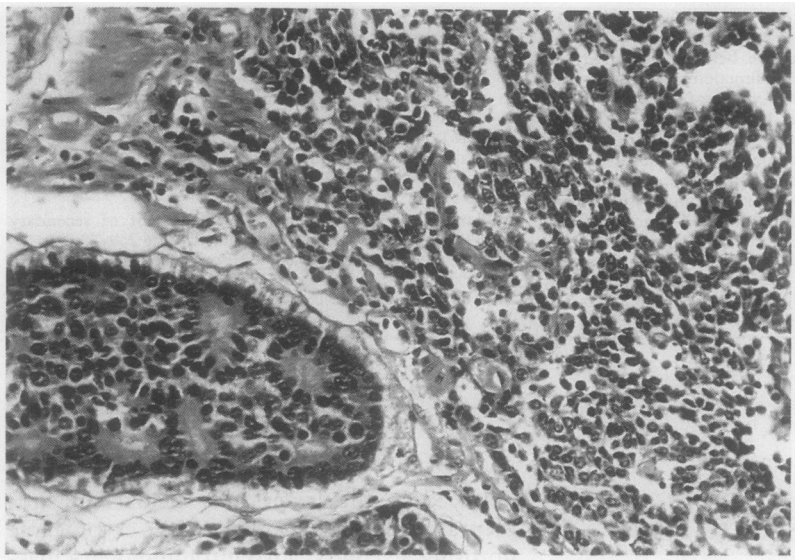

Figure 2 Section of the lesion seen in figure 1 showing a well differentiated insular carcinoid merging into a small cell carcinoma of intermediate type.

extended out into normal lung; the other tumour was a white fleshy lesion (fig 1). Neither lesion connected directly with the bronchus. Histological examination of the lesions showed the larger one to be a keratinising squamous cell carcinoma and the smaller a well differentiated neuroendocrine carcinoma (atypical carcinoid) with direct transition to intermediate type small cell carcinoma (fig 2). Immunohistochemical staining of the lesions showed keratin (CAM 5·2, Beckton Dickinson) positivity in both tumours. The neuroendocrine carcinoma in both the well differentiated area and the intermediate small cell area stained for the neuroendocrine antibodies neurone specific enolase (Dako), protein gene product 9·5 (Ultraclone), synaptophysin (Dako), and chromogranin (Boehringer-Mannheim). The remaining lung showed cryptogenic fibrosing alveolitis with dense interstitial inflammation and fibrosis. There were dilated spaces lined by respiratory ciliated and flattened epithelium. There was hyperplasia of type II pneumocytes in the surviving alveoli with mild atypia of these cells at the periphery of the squamous cell carcinoma.

A follow up chest radiography three months after surgery showed a slight increase in the diffuse lung shadowing without any evidence of recurrence of the tumours.

Discussion

Several conditions resulting in chronic interstitial fibrosis of the lungs are associated with the later development of cancer. Progressive systemic sclerosis,[1] rheumatoid interstitial lung fibrosis,[2] and cryptogenic fibrosing alveolitis[4] are examples. The incidence of lung cancers varies from 9·8%[3] to 17%.[4] The distribution of the histological types of carcinoma is similar to that in patients without fibrosis,[3 5] though some authors have claimed an increased frequency of adenocarcinoma, including bronchioalveolar cell carcinoma and small cell carcinoma.[4 6 7]

Only one previous report details the presence of synchronous primary lung tumours associated with diffuse interstitial pulmonary fibrosis.[9] These were a squamous cell carcinoma and a bronchioalveolar cell carcinoma. Synchronous tumours of different histological type have been reported rarely and the most common combination has been squamous cell carcinoma and adenocarcinoma.[9] This is the first report of a squamous cell carcinoma associated with a neuroendocrine tumour in diffuse lung fibrosis. The neuroendocrine tumour was unusual in displaying a well differentiated area merging into the more aggressive small cell carcinoma of intermediate type.[10]

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