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Short reports

Small cell and squamous cell lung carcinomas: sequential occurrence at a single site

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The detection of a second primary bronchogenic carcinoma after treatment for small cell lung carcinoma is a rare[1] and recently described[2] phenomenon. Nonetheless, at least 17 cases have been reported to date[1 3 4] and there is now evidence to suggest that such tumours are an important late complication of small cell lung carcinoma in remission.[4] In the present case the two tumours developed at the same site. To our knowledge this has not been reported before.

Case report

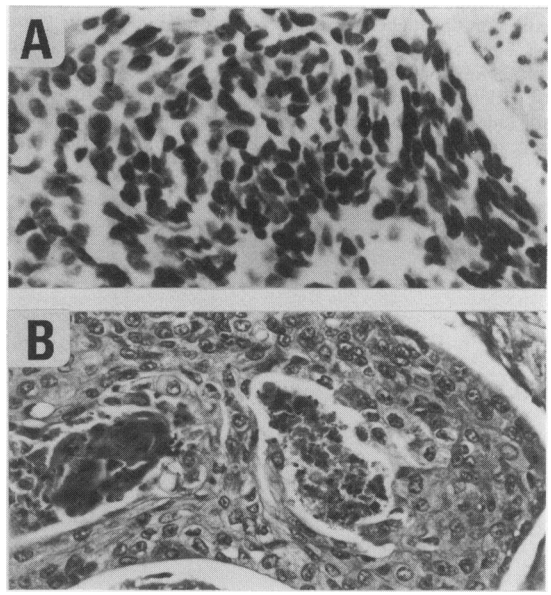
A 56 year old man, a cigarette smoker, presented with recent haemoptysis. Chest radiographs showed left hilar enlargement and fibreoptic bronchoscopy showed a tumour at the origin of the left upper lobe bronchus. Biopsy was performed and histological examination showed anaplastic small cell carcinoma (figure). There was no evidence of intrathoracic or extrathoracic metastatic spread.

Cytotoxic chemotherapy with cyclophosphamide, doxorubicin, and vincristine was given, with an excellent response. Repeat bronchoscopy with biopsy four months after presentation failed to show any evidence of residual tumour. A chest radiograph at this time showed a normal left hilar outline. The patient continued to smoke. Maintenance chemotherapy with cyclophosphamide and doxorubicin was continued for a further 15 months. Bronchoscopic review at this time showed a haemorrhagic area at the site of the original tumour. While the histological appearance of a biopsy specimen was normal cytological examination of brush specimens showed some dysplastic changes. Repeat biopsy two months later showed focal squamous metaplasia but no evidence of malignancy. Cytological examination of bronchial aspirates, however, showed definite malignant cells with squamoid characteristics. Finally, at a further bronchoscopy, 27 months after presentation, an endobronchial lesion was seen to have developed at the original tumour site, biopsy of which showed invasive squamous cell carcinoma. Repeat chest radiography at this time did not show any new lesion.

A full search for metastatic disease again having negative results, left pneumonectomy was performed. The resection specimen contained a 2 cm nodule of squamous carcinoma situated at the proximal end of the upper lobe bronchus (figure). Despite careful searching there was no evidence of the original small cell tumour or of local or metastatic spread. The patient made an excellent recovery and remains well three years after surgery.

Discussion

Several mechanisms may be postulated to explain the emergence of a second primary lung tumour in a patient who has received chemotherapy for small cell carcinoma. A second tumour may have developed that was independent of the first. This may have occurred spontaneously in a patient already prone to the development of bronchogenic neoplasia or may have been a carcinogenic effect of cytotoxic chemotherapy.[5] Another possibility, which is supported by



Photomicrographs of anaplastic small cell carcinoma in the original bronchial biopsy specimen (A) and a moderately differentiated area of squamous cell carcinoma at the same site in a pneumonectomy specimen 28 months later (B). Other areas of the resected squamous carcinoma were more poorly differentiated but none resembled the original small cell tumour. (Haematoxylin and eosin.)

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the well recognised phenomenon of heterogeneity in lung carcinomas,[6] is that elements of small and squamous cell differentiation may have been present from the outset, the second becoming clinically apparent only after the more rapidly proliferating small cell component had been suppressed by chemotherapy. Alternatively, the initial small cell tumour may have undergone further differentiation, either with time or as a result of treatment. This would be in keeping with the theory that all bronchogenic carcinomas arise from a common stem cell that possesses the capacity for various differentiations.[7]

An interesting feature of the case presented is the documented progression from histological and cytological metaplasia and dysplasia to the development of an endobronchial lesion composed of infiltrating squamous cell carcinoma. Such a progression has never before been described in these circumstances. This course of events suggests the emergence de novo of a second tumour.

There are no reports of second primary lung carcinomas occurring in patients previously diagnosed as having small cell carcinoma before 1975.[2] An obvious explanation is the poor prognosis of such patients before the advent of modern treatment. Current treatment regimens for small cell carcinoma can result in prolonged survival or even cure, particularly in limited stage disease.[8] Accordingly, the problem of second tumours may now be encountered more frequently. This is borne out by the work of Johnson *et al*,[4] who show that non-small cell lung carcinoma is more common than recurrent small cell carcinoma in those patients who survive beyond three years from the initial diagnosis of small cell carcinoma. These workers also suggest that there may be a considerably higher incidence of second tumours in those patients who continue to smoke. This therefore is an important complication to bear in mind in the management of patients who relapse after an initial response to treatment for small cell carcinoma. A second non-small cell tumour will often demand treatment quite different from that appropriate to recurrent small cell carcinoma. Histological or cytological "rediagnosis" should be sought in such circumstances, especially where surgical cure might be feasible. This point is exemplified by our case, where the patient remains well with no evidence of tumour recurrence three years after pneumonectomy for squamous carcinoma and five years after initial diagnosis of small cell carcinoma. Survival has been brief, however, in all previously reported cases (maximum 40 weeks after diagnosis of the second tumour).[4]

This case highlights a little known late complication of small cell carcinoma in remission and shows the importance of vigilant follow up of such patients. It also provides further evidence that patients being treated for small cell carcinoma should be strongly advised to discontinue smoking.

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