Contralateral haemorrhagic pulmonary metastases ("choriocarcinoma syndrome") after pneumonectomy for primary pulmonary choriocarcinoma

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Abstract

The case history is presented of a patient which illustrates both the diagnostic difficulties of an extremely rare tumour (choriocarcinoma of the lung) and its associated haemorrhagic metastases ("choriocarcinoma syndrome").

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Choriocarcinoma is a germ cell tumour containing syncytiotrophoblastic cells and secreting human β-chorionic gonadotropin (hCG). It occurs in women, principally as a gestational trophoblastic neoplasm, and in men as a testicular non-seminomatous tumour. The less common extragonadal choriocarcinomas generally arise in midline locations (mediastinal, retroperitoneal, intracranial). Even rarer are the primary choriocarcinomas of the lung which can be confused with giant cell carcinomas of the lung which they resemble morphologically and which may produce β-hCG.[1,2]

Haemorrhagic metastases, most often pulmonary, are the hallmark of the "choriocarcinoma syndrome" which is associated with advanced germ cell tumours having large choriocarcinoma elements, significant elevation of serum levels of β-hCG, and a poor prognosis.[3–5]

Case report

A 61 year old man with a 48 pack/year history of smoking presented with haemoptysis and upper left chest pain. The chest radiograph and computed tomographic scan showed a 5 × 6 cm solitary mass in the left upper lobe. There was no evidence of mediastinal involvement or pleural effusion. Fibreoptic bronchoscopy was normal, as was abdominal ultrasonography and the computed tomographic brain scan. The patient underwent left pneumonectomy. The tumour was haemorrhagic and microscopically diagnosed as giant cell carcinoma. Because of involvement of the contiguous parietal pleura, the patient received postoperative radiotherapy (50 Gy).

One month later the patient presented with daily and increasing haemoptysis, together with malaise and a 2·5 kg weight loss. The chest radiographs showed multiple rapidly growing nodules in the right lung. The computed tomographic scan revealed typical tumour nodules surrounded by groundglass opacities suggestive of haemorrhage.

This unusual sequence prompted us to ask for a review of the pathology of the previously resected tumour. Microscopically the tumour was extremely necrotic and haemorrhagic, containing large blood filled cavities. It consisted of a dual population of cells: (1) giant multinucleated cells with ill defined borders, pleomorphic nuclei, and an abundant cytoplasm (syncytiotrophoblastic cells), and (2) small cells with distinct borders and clear cytoplasm (cytotrophoblastic cells). Immunoperoxidase staining was positive for β-hCG using the polyclonal antibody DakoR which labelled only the syncytiotrophoblastic cells bordering the vascular cavities (fig 1).

Clinical and ultrasonographic testicular examinations were entirely normal (the patient did not have gynaecomastia), and the computed tomographic brain scan was normal. Abdominal ultrasonography revealed a right adrenal or renal mass not present at preoperative evaluation. The serum α-fetoprotein level was less than 5 mg/l ($n < 10$) and the serum β-hCG level was 137 221 IU/l ($n < 5$), increasing to 151 398 within five days (fig 2).

A chemotherapy regimen with cisplatin, etoposide, vinblastine, and bleomycin was started as soon as the results of the pathological evaluation and biological markers were known. The serum β-hCG level fell rapidly (fig 2), together with a decrease in haemoptysis. However, the patient died suddenly 11 days after starting chemotherapy whilst aplastic. Blood cultures grew *Enterococcus faecium* and there was no clinical evidence of cerebral bleeding. Permission for necropsy was not obtained.

Discussion

A definite diagnosis of choriocarcinomatous neoplasia was made in this patient only when the unusual postoperative course led to the revision of the initial histological findings. We cannot entirely exclude the possibility that the lung tumour was metastatic, but imaging before surgery was negative as was testicular examination at the time of relapse. There remains the theoretical possibility of a giant cell carcinoma with ectopic production of β-hCG.[1] However, the serum β-hCG level was very high, and the histological and immunocytochemical findings in the resected primary tumour were characteristic of the dual cell population of choriocarcinoma.

Primary pulmonary lung choriocarcinoma is extremely rare (we have found only 13 cases in the literature), and they have few distinctive clinical features discriminating them from the

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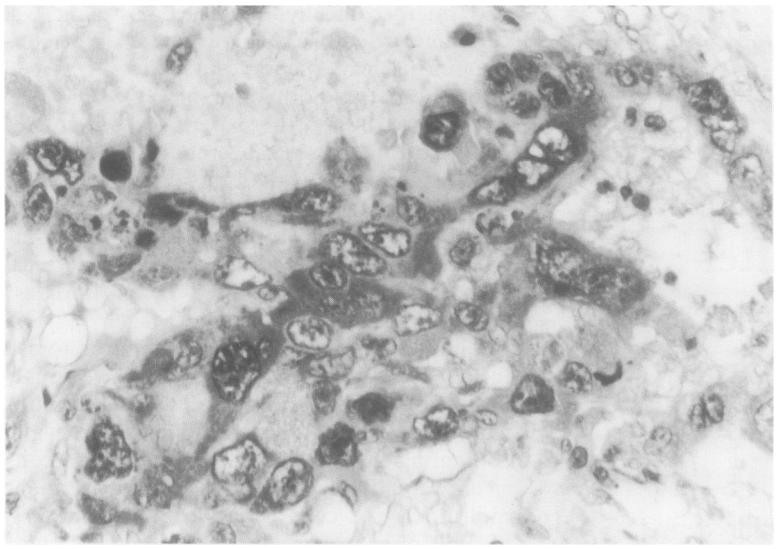

Figure 1 Syncytiotrophoblastic cells staining dark with β-hCG antibody. Stain: immunoperoxidase; original magnification × 400, reduced to 80% in origination.

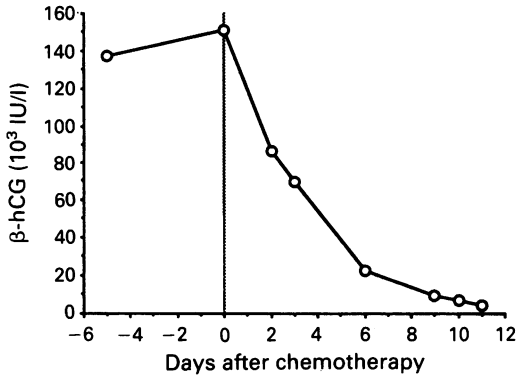

Figure 2 Change in serum β-hCG levels before and after chemotherapy.

usual lung carcinomas, except that gynaecomastia may be present in some cases.[6 7] Macroscopically the tumour is remarkable for necrosis and haemorrhage. The course of primary choriocarcinoma of the lung is not well established. Some patients have no recurrence of tumour after surgical resection, while others develop pulmonary metastases which may be single[2] or multiple,[6 8] as in the present patient.

Logothetis[4] first described the "choriocarcinoma syndrome" and additional cases have since been reported.[3 5] This distinctive clinical syndrome is characterised by life threatening bleeding at the sites of metastases from choriocarcinoma (pulmonary, intracranial, peritoneal). The syndrome may be responsible for the poor prognosis of patients with very elevated serum levels of β-hCG (above 50 000 IU/l).[5] Since pulmonary metastases occur frequently during the course of gonadal choriocarcinomas in men, haemorrhagic "choriocarcinoma syndrome" of the lung has been well described. The chest radiograph is rather characteristic with typical metastatic sharply defined nodules progressively obscured by the ill defined infiltrates corresponding to pulmonary haemorrhage. The computed tomographic findings in our patient, together with haemoptysis, were highly suggestive of haemorrhage surrounding the neoplastic nodules. Chemotherapy regimens including cisplatin are sometimes effective, but the overall prognosis in this subgroup remains poor, despite frequently dramatic falls in biomarkers.[5]

Although other tumours may give rise to haemorrhagic metastases, the "choriocarcinoma syndrome" merits special attention since its recognition can hasten the diagnosis and treatment of this presentation of metastatic germ cell tumours.

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