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SHORT COMMUNICATION

Metastatic pulmonary ameloblastoma. An unusual case

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SUMMARY. **We present a patient who had a large metastatic pulmonary ameloblastoma resected 25 years after removal of an apparently benign primary ameloblastoma of the jaw. It highlights three areas: problems with the histopathological diagnosis of pulmonary metastases using fine needle aspiration; a noted radiological improvement after a 5-year course of oral cyclophosphamide, in keeping with occasional patients who have responded to chemotherapy; and the technical difficulties of resection of a large pulmonary metastasis, particularly when it is adherent to the mediastinum.**

INTRODUCTION

Ameloblastomas are rare odontogenic neoplasms, which account for about 1% of all oral tumours. They arise from the epithelium of the dental lamina, particularly in the mandible (80%), but also the maxilla (20%).[1] They are usually benign, but are locally aggressive with a high incidence of local recurrence. Malignant variants are usually reported as either ameloblastoma with metastases or widely infiltrating lesions with histological features of carcinoma. Metastases are rare, but can be found in lung (75%), bone (25%), cervical nodes (18%), liver (11%), and brain (10%).[2] Spread is thought to occur through lymphatics and blood, but lung metastases may theoretically arise from aspiration of cells at the time of oral surgery.

CASE REPORT

A 46-year-old white man, who was a lifelong cigarette smoker, presented to the respiratory physicians at his local district general hospital with evidence of clubbing, purulent sputum and an abnormal sensation over his right chest. The chest radiograph showed a 1.5-cm opacity at the base the of the left lung. Computed tomogram (CT) scan showed mediastinal lymphadenopathy with an additional 7 cm mass in the right lower lobe that was indenting the left atrium, which had not been visible on the chest film. Fluid obtained for fine needle aspiration cytology of the left-sided lesion was reported as being unequivocally malignant. Although the precise histogenesis was uncertain, a provisional diagnosis of squamous cell carcinoma was made. The patient was a poor historian and a history of removal of a left-sided mandibular ameloblastoma with subsequent rib bone graft, performed in a distant dental hospital 19 years previously was not elicited.

A cardiothoracic surgeon considered that the lung tumour was inoperable because of extensive mediastinal lymphadenopathy and adherence to the left atrium.

As the patient had no symptoms referable to his tumour radiotherapy was not indicated, and he was given a course of cytotoxic monotherapy with cyclophosphamide, 50 mg three times a day. This was reduced to 50 mg twice a day because of neutropenia 2 years later. In 1996 (5 years after the start of cyclophosphamide) he complained of right-sided chest pain, but was otherwise in good physical condition. Further CT showed no change in the right-sided lesion but the mediastinal lymphadenopathy was less prominent and the lesion in the left lower lobe lesion had decreased in size.

The original diagnosis was now questioned and the history of resection of an ameloblastoma was discovered. The cyclophosphamide was discontinued and he was referred to our cardiothoracic centre for review and further

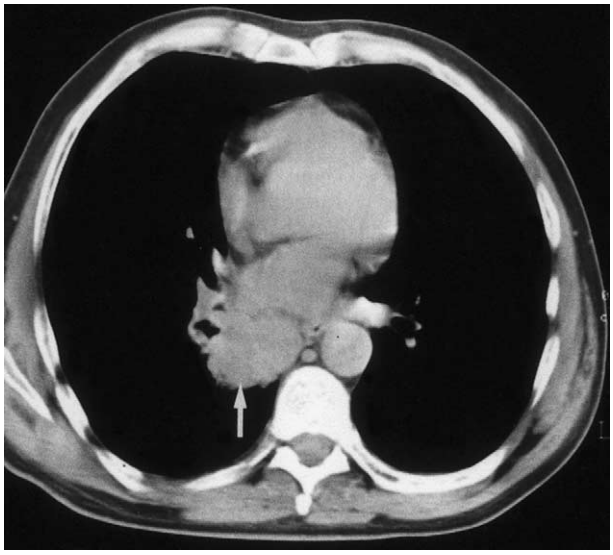

Fig. 1 Computed tomogram showing a mass in the right lower lobe.

investigation. A repeat thoracic CT confirmed a mass in the right lower lobe (Fig. 1) with a peripheral left-sided nodule (Fig. 2). Further fine needle aspiration cytology was inconclusive, so the left-sided lesion was excised to secure a tissue diagnosis. This lesion was a metastatic ameloblastoma with squamous differentiation. There was no clinical evidence of local mandibular recurrence and both liver ultrasound and bone scans were within normal limits.

The chest pain that had precipitated his re-investigation was not well controlled even by morphine sulphate so, after much discussion the tumour was excised 7 years after it had first been found. At operation, the tumour was adherent to the mediastinum, oesophagus, and pericardium. It did not penetrate the pericardium and there was no mediastinal lymphadenopathy. The right lower lobe was mobilised and the lower lobe bronchus ligated. There was difficulty in ligating the inferior pulmonary vein because of extensive bulky haemorrhagic tumour in the inferior hilar area. After removal of the specimen, a bleeding point caused by a traction tear in the inferior pulmonary vein across the left atrium required repair. Postoperatively, the patient required substantial transfusion of blood and blood products and ventilation for several days in the intensive care unit. He made a good recovery and after treatment of a resistant supraventricular tachycardia with flecainide and atenolol, he was discharged home on the fourteenth postoperative day. He initially noted improvement in his pain, but by the following year it returned.

Further CT showed recurrence in the posterior mediastinum, for which he was given palliative radiotherapy. An upper gastrointestinal endoscopy after a small haematemesis showed reflux inflammation but no tumour. He died in January 2001 of a myocardial infarction, 10 years after presentation with pulmonary metastases. Necroscopy showed recurrence of the tumour in the posterior mediastinum from the carina down to the oesophageal hiatus.

HISTOPATHOLOGY

The original lesion in the jaw showed typical features of well-differentiated follicular ameloblastoma. The lesion from the left lung and three separate nodules in the right lower lobe all showed a similar histological picture except that the pulmonary disease was less well-differentiated

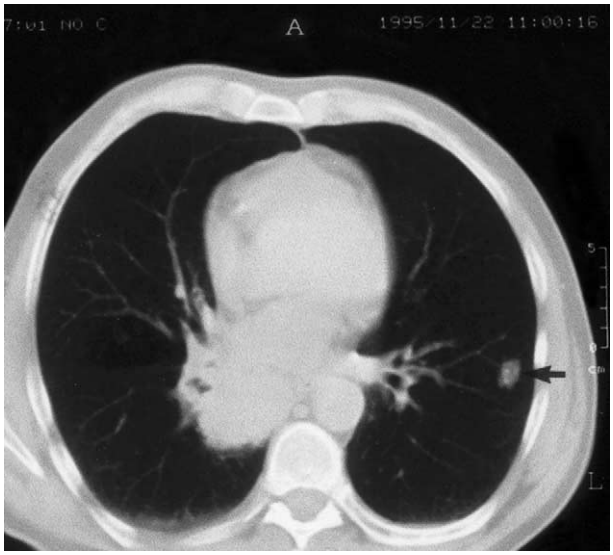

Fig. 2 Computed tomogram showing an additional nodule in the left lung.

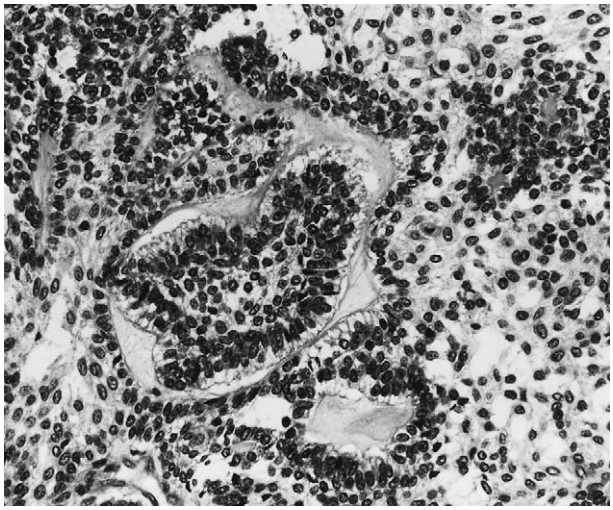

Fig. 3 Photomicrograph showing histological features of ameloblastoma (haematoxylin and eosin, original magnification × 200).

with more basaloid areas. The tumour, although lacking the high grade malignant cytological features of a carcinoma, was clearly invasive, and had destroyed airway cartilage and adjacent lymph nodes. In some areas it retained typical histological features of ameloblastoma (Fig. 3), while other areas were relatively undifferentiated, with sheets of basaloid cells showing peripheral pallisading and some squamous differentiation. No discrete nodal metastases were present, however, and the resection lines with pleura and pericardium were free of tumour.

DISCUSSION

Ameloblastomas are rare and only about 2% metastasise.[3] They are usually treated adequately by local excision. Local recurrence is common (50–72%).[1] The mean age at presentation with ameloblastoma is 33 years, but malignant and metastasising ameloblastomas usually present about 10 years later.

Of the several varieties of ameloblastoma described, those most likely to metastasise are the plexiform and follicular types,[3] otherwise the histopathological appearances have little ability to predict the risk of metastases.[4]

There is strong evidence, from both clinical and post mortem studies[3] to suggest that metastases are blood and lymph-borne. Aspiration of cells at the time of oral surgery has been considered as a possible mechanism of spread, and it has also been suggested that ameloblastoma may arise from heterotopic concealed odontogenic epithelial cell rests scattered during embryological development. A recent study reported human papilloma virus DNA in 8 out of 18 samples, but concluded that this was unlikely to have an aetiological role.

There are other reports of patients who presented late with pulmonary metastases (similar to the 19-year interval in this case), without evidence of local recurrence. Ramadas *et al.*[5] described a case of ameloblastoma that metastasised to the lung after 20 years, with no evidence of active disease at the primary site.

It is not surprising that histological diagnosis of this tumour may be difficult. Parts of these tumours may resemble basal cell carcinoma, and some lesions also show squamous differentiation.

Treatment of pulmonary metastases has been disappointing. Perhaps the best results are from surgical removal of operable lesions, particularly in the lung periphery where wedge excision is possible.[1] Resection can, however, be technically difficult because of the haemorrhagic nature of the tumour, particularly when it is adherent to the mediastinum. Chemotherapy has had variable results. However, a case with radiological and symptomatic improvement after treatment with cisplatin, Adriamycin and cyclophosphamide was encouraging.[5] Current views suggest cytotoxic monotherapy is probably not ideal, but otherwise it is difficult to say what the ideal management should be, given the rarity of the disease.

Virtually all the literature is in the form of case reports and reviews, with sometimes conflicting anecdotal evidence. This emphasises the need for managing such rare diseases in specialised centres, perhaps enabling multicentre trials to be established to find effective combined chemotherapeutic regimens to manage inoperable metastatic disease.

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