Unusual association of diseases/symptoms

Metastasis of carcinoma of the lung to a carotid body paraganglioma

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Tumour-to-tumour metastasis is a rare phenomenon, but has been described in the literature in just over 100 cases. It can be particularly puzzling for the reporting pathologists, when encountered unexpectedly in a tumour showing abrupt transition from the usual morphology to another unusual pattern. The literature reports a variety of combinations with carcinoma-to-carcinoma being the most common; and renal cell carcinomas appear to the most common recipient tumours with common donor tumours being breast, lung and renal cell carcinomas. The authors report a case of poorly-differentiated lung carcinoma metastasising into a carotid body paraganglioma. Our case is unique and in our knowledge the first described case of carotid body paraganglioma with metastasis from a lung primary. To the best of our knowledge this is the first report of this interesting biological phenomenon in this combination.

BACKGROUND

Tumour-to-tumour metastasis is a rare phenomenon, but has been described in the literature in just over 100 cases.¹ It can be particularly puzzling for the reporting pathologists, when encountered unexpectedly in a tumour showing abrupt transition from the usual morphology to another unusual pattern. The literature reports a variety of combinations with carcinoma-to-carcinoma being the most common; and renal cell carcinomas appear to the most common recipient tumours with common donor tumours being breast, lung and renal cell carcinomas.² However, neuroendocrine, mesenchymal and even haematolymphoid neoplasms have been described recipients to carcinomas, melanomas and other haemato-lymphoid malignancies.

The recipient tumours are usually well vascularised, slowly growing and might be of similarly high-grade malignancy, low-grade malignancy or even benign. Most cases of lung carcinoma reported in the literature metastasising into other tumours have been to renal cell carcinoma³ and intracranial meningiomas.⁴ Many other benign or low-grade malignancies have been described as recipient tumours, such as pancreatic adenocarcinoma, pulmonary hamartoma,⁵ angiomyolipoma,⁶ testicular seminoma,⁷ follicular variant papillary thyroid carcinoma,⁸ renal oncocytoma,⁹ adrenal adenoma,¹⁰ follicular thyroid adenoma¹¹ and Warthin's tumour.¹² These reported cases include different types of donor pulmonary carcinoma such as small cell, squamous and adenocarcinomas.

In the literature there is only one report of recipient paraganglioma (an intracranial mass) with metastasis from oesophageal carcinoma.¹³ We report a case of poorly differentiated lung carcinoma metastasising into a carotid body paraganglioma. Our case is unique and in our knowledge the first described case of carotid body paraganglioma with metastasis from a lung primary. To the best of our

knowledge this is the first report of this interesting biological phenomenon in this combination.

CASE PRESENTATION

A 58-year-old gentleman presented to the ear, nose, throat outpatients department with a 6-week history of dysphonia following a lower respiratory tract infection. He was a smoker of approximately 40 pack years and suffered from asthma but no other complaints. On examination there was a smooth deep level II mass on the right side of his neck.

INVESTIGATIONS

Fibre-optic laryngoscopy showed left vocal cord palsy with no other abnormalities evident in the upper aero-digestive tract. Blood haematological and serum biochemistry investigations showed raised calcium at 2.72 mmol/l but no other abnormalities.

An ultrasound scan was performed showing a large deep right-sided neck mass, reported as a deep jugular lymph node measuring 19×32×39 mm and several non-enlarged left-sided jugular nodes with 'suspicious' ultra-sonographic appearances. Cytology from the right neck mass was reported as suspicious with atypical cells present but not diagnostic of malignancy. CT images from the skull base to the diaphragm were acquired and showed appearances suspicious of a left hilar bronchial tumour with extension into the upper lobe. Also, bilateral mediastinal lymphadenopathy was present and interpreted as possible cause of the left vocal cord palsy; in addition, a large right-sided cervical mass suggestive of metastatic disease with bilateral large nodes at the root of the neck was seen (figure 1).

The patient underwent bronchoscopy, which showed the left upper lobe blocked with tumour from which biopsies were taken. Pan-endoscopy of the upper aero-digestive tract was also performed, biopsies from which

Figure 1 (a) CT scan of the base of the skull showing a vividly enhancing nodule in the right vascular space displacing great vessels in keeping with a paraganglioma with a low attenuation nodule of 4 mm thought to be metastasis. (b) CT scan showing tumour around the left pulmonary artery with confluent mediastinal lymphadenopathy.

Figure 2 (a) Nests of islands of poorly differentiated carcinoma within a background of a typical paraganglioma (HE, x20). (b) Immunohistochemistry for cytokeratin highlighting the carcinoma of the lung (MNf116, x40). (c) Immunohistochemistry for CD 56 demonstrating the neuroendocrine differentiation of the recipient paraganglioma (x40). (d) Immunohistochemistry for synaptophysin highlighting the paraganglioma cells (x40).

failed to identify any additional primary tumour. An incisional biopsy of the right neck mass was subsequently undertaken.

Pathological features

From the right neck biopsy, a brown tissue nodule measuring 24×20×16 mm was received and showed a firm light cut surface containing a circumscribed pale nodule of 8 mm diameter. Microscopic examination showed a well-defined tumour nodule without lymphoid tissue.

The tumour had a nested and organoid growth pattern with nests of rather monomorphic cells with abundant eosinophilic cytoplasm. Some of these cells showed mild pleomorphism and very occasional mitoses. Within this tumour, there was a tumour nodule of drastically different cell morphology with abundant central necrosis. The tumour cells in this area showed irregular islands. The cells showed focal intracytoplasmic vacuolation and prominent pleomorphism with prominent mitoses including atypical forms. No definite squamous differentiation

was identified in this nodule, although the cells had a more eosinophilic cytoplasm (figure 2).

Immunohistochemistry was performed and showed the nested background tumour cells to be negative for cytokeratin 7, whereas the small pleomorphic tumour nodule showed focal positivity with cytokeratin 7. Pancytokeratin MNF116 was absent in the nested variant, while the pleomorphic cells showed strong positivity. Cytokeratin 20 was negative in both tumour elements. Thyroid transcription factor 1 was negative in the nested background tumour cells while in the pleomorphic cells there was weak patchy positivity. S100 highlighted sustentacular cells in the periphery of the tumour nests in the background tumour while negative in the pleomorphic tumour. Monoclonal carcinoembryonic antigen was mainly negative in both tumours except for very occasional cell positivity within the pleomorphic tumour nodule. The nested areas were strongly positive for CD56, synaptophysin and chromogranin A but the pleomorphic tumour nodule was negative for these antigens. The tumour cells were negative for Melan A and HMB45. Ki67 showed a high proliferation index within the pleomorphic tumour nodule while the background nested tumour nodule proliferation activity was low with about 2% of positive cells. The findings confirmed the background-nested tumour to represent a carotid body paraganglioma with a deposit of poorly differentiated carcinoma within it. A review of the original bronchial biopsy performed at another hospital confirmed similar morphological appearances in keeping with origin from a lung primary.

TREATMENT, OUTCOME AND FOLLOW-UP

The patient was referred for palliative chemotherapy but quickly deteriorated and unfortunately passed away after a short time.

DISCUSSION

Carotid body paraganglioma has not previously been described in tumour-to-tumour metastasis, which may be related to its relative rarity and the fact that it usually occurs 10 years earlier than lung cancer. Metastases of carcinoma of the lung into hilar, mediastinal and supraclavicular lymph nodes are apparent in up to 50% at time of pathological staging and metastases are also commonly seen to adrenals, liver, brain and bone. Less common metastatic involvement is seen in the contralateral lung, pericardium and kidneys. Metastases of pulmonary adenocarcinoma into meningeoma^{14 15} and renal cell carcinoma have also been reported. The exact mechanism of this tumour-to-tumour phenomenon and the molecular and cellular basis of the tissue-specific metastasis remain elusive, although tumour vascularity as well as lipid and glycogen content have been suspected from a morphological point.¹⁶ Abou-Hamden *et al*¹⁷ have reported metastasis of renal cell carcinoma to a haemangioblastoma in von Hippel-Lindau (VHL) disease and have hypothesised that renal cell carcinoma and haemangioblastoma both represent attractive sites for metastasis on the basis of their common VHL gene mutations and associated high vascularity. Recent data suggest that distinct sets of genes regulate the colonisation of lung and bone tissue after breast tumour cells succeed in the early steps of metastasis and

reach blood circulation.¹⁸ A striking feature of these candidate genes for metastasis in breast cancer is that they mostly encode secreted cytokines or cell surface receptors. This is consistent with the century-old 'seed and soil' hypothesis, which metastasis formation depends on the pathological interactions between tumour cells and the stromal environment. However, even if pathologists will use gene expression profiles in their routine reporting practice to evaluate tumour origin and ability to metastasise, they still will need to consider the possibility of tumour-to-tumour metastasis, when encountering a tumour with a strikingly dimorphic appearance.

Learning points

- ▶ Tumour to tumour metastasis is a rare occurrence but has been described in the literature in just over 100 cases.
- ▶ The presence of abrupt transition of cell morphology within a tumour should prompt the reporting histopathologist to consider the possibility of tumour-to-tumour phenomenon to aid the correct diagnosis.
- ▶ The literature reports a variety of combinations with carcinoma-to-carcinoma being the most common; and renal cell carcinomas appear to be the most common recipient tumours with common donor tumours being breast, lung and renal cell carcinomas. However, neuroendocrine, mesenchymal and even haematolymphoid neoplasms have been described recipients to carcinomas, melanomas and other haemato-lymphoid malignancies.
- ▶ The recipient tumours may be similarly high-grade malignancy, low-grade malignancy or even benign.
- ▶ Most cases of lung carcinoma reported in the literature metastasising into other tumours have been to renal cell carcinoma, and intracranial meningiomas, but many other benign or low-grade malignancies have been described as recipient tumours. The reported cases include different types of donor pulmonary carcinoma such as small cell, squamous and adenocarcinomas.

Competing interests None.

Patient consent Obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Bury Y, Green R, Jain M, Moor J. Metastasis of carcinoma of the lung to a carotid body paraganglioma. *BMJ Case Reports* 2012; 10.1136/bcr.01.2012.5517, Published XXX

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