Metastatic Pulmonary Adenocarcinoma Deposit Arising Within a Cutaneous Basal Cell Carcinoma: A Case Report

Elinor Carey · Simon D. Jones · Paul Griffiths ·
Prue Baxter

Received: 23 November 2010 / Accepted: 7 April 2011 / Published online: 20 May 2011
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Abstract Skin metastases are rare complications of internal malignancies, and most commonly arise from primary lung carcinoma (Brownstein and Helwig in *Arch Dermatol* 105:82–68, 1972). Metastatic cutaneous lesions have not previously been documented to arise within other skin tumours. We report our experience of a solitary pulmonary adenocarcinoma metastasis that arose within a pre-existing basal cell carcinoma in a patient with undiagnosed lung cancer. Immunohistochemistry was invaluable in confirming both the metastatic nature of the secondary skin lesion and its site of origin.

Keywords Adenocarcinoma · Basal cell carcinoma · Skin · Metastasis · Thyroid transcription factor-1 · Tumour-to-tumour metastasis

Case Presentation

An 83-year-old male was referred by his general practitioner (GP) to the maxillofacial department at Morriston

Hospital, Swansea, UK complaining of a slow growing, painless skin nodule on the left neck present for several months. The GP also wrote to inform the department that the patient was concurrently being investigated for chest pain and shortness of breath on exertion.

On examination, there was a 2 cm fleshy lesion over the left posterior triangle (Fig. 1). There was no associated ulceration, induration, or surrounding erythema, and no cervical lymphadenopathy or other cutaneous lesions were noted. The treatment, from a surgical point of view, was a wide elliptical excision with 5 mm margins, and the specimen was sent for histopathological examination.

Hematoxylin and eosin (H&E) stained sections revealed nests and lobules of hyperchromatic, uniform, basaloid cells with peripheral palisading and loose stroma, consistent with basal cell carcinoma (BCC). In between these classic areas of BCC were irregular nests of highly atypical cells characterized by abundant eosinophilic cytoplasm, irregular nuclei, fine chromatin, and one or more prominent nucleoli. Mitotic figures were readily identified. Similar cells were identified in lymph-vascular spaces (Fig. 2). This pleomorphic population had features suggestive of squamous cells. In fact, the lesion was initially reported as a BCC with co-existent squamous cell carcinoma, the latter most likely derived from the former, i.e. a baso-squamous carcinoma. Immunohistochemical staining of the skin tumour confirmed the dimorphic nature of the lesion, with strong EMA positivity in the pleomorphic squamoid dermal and intra-lymphatic deposits. In contrast, the basal cell component was EMA negative.

A chest X-ray, performed for his concurrent respiratory symptoms, was highly suggestive of a primary lung cancer with nodal and distant metastases, with a provisional radiologic staging of T4 N3 M1. A CT-guided core needle biopsy was reported as a non-small cell carcinoma of the

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Electronic supplementary material The online version of this article (doi:10.1007/s12105-011-0263-1) contains supplementary material, which is available to authorized users.

E. Carey
Royal Gwent Hospital, Newport, Wales, UK

S. D. Jones · P. Griffiths · P. Baxter
ABM University NHS Trust, Morriston Hospital, Swansea,
Wales, UK

E. Carey (✉)
2 Vicarage Mews, Conway Road, Pontcanna, Cardiff CF11 9PD,
UK
e-mail: ellecarey@doctors.org.uk

Fig. 1 A 2 cm, pink, fleshy skin lesion on the left posterior triangle of the neck

Fig. 2 HE, original magnification $\times 100$. Islands of nodular basal cell carcinoma (bcc) and adenocarcinoma (adenoca). Arrows show intra-lymphatic tumour emboli of adenocarcinoma

lung. The patient was referred for palliative care and no further tissue samples were taken.

Subsequent immunohistochemical studies showed that both the lung tumour and the pleomorphic eosinophilic squamous-like component of the cutaneous lesion were strongly positive for Cytokeratin 7 and TTF-1 (Thyroid Transcription Factor-1) (Fig. 3). Interestingly, this squamoid population was negative for Cytokeratin 5/6 and nuclear p63. Moreover, scanty intra-cytoplasmic mucin droplets were demonstrable in both lesions by diastase resistant PAS staining. Therefore, the combined morphologic features and immunophenotype best supported a diagnosis of poorly-differentiated adenocarcinoma of the lung with cutaneous metastasis.

TTF-1 is a nuclear transcription factor normally expressed in lung and thyroid tissue. In lung tumours,

Fig. 3 Consecutive section. Immunoperoxidase for TTF-1, original magnification $\times 100$. The adenocarcinoma shows intense nuclear staining for TTF-1 with no staining in surrounding basal cell carcinoma

TTF-1 is positive in 53–96% of small cell carcinomas, up to 100% of adenocarcinomas, and up to 4% of squamous cell carcinomas, depending on the author and the antibody used [2]. Whilst TTF-1 was originally thought to be highly specific for pulmonary and thyroid tissues, more recent reports have appeared of TTF-1 being expressed in other normal tissues [3] and in a few non-pulmonary, non-thyroid tumours [4]. However, these primarily include benign tissues of gynecologic origin and ovarian neoplasms, respectively. Despite this, it remains one of the most useful antibodies for investigating the primary source of a metastasis (i.e., lung, thyroid) when interpreted in full clinical context [2].

Discussion

Lung cancer is the commonest cause of skin metastases in men, and is second only to breast cancer in women. This cutaneous involvement generally arises in the head, neck, and trunk region [1]. Among patients with bronchogenic carcinoma, 2.8–7.5% will develop cutaneous metastases (via haematogenous spread), particularly in tumours of the upper lobes [5].

The presence of two distinct morphologies in any given lesion can be explained most commonly by either (1) two or more lines of differentiation within one tumour, or (2) a “collision tumor.” Bilineal neoplasms are usually attributed to neoplastic stem cells within the tumour activating divergent pathways of differentiation within their normal repertoire. BCCs often display squamous differentiation, the so-called metatypical BCC or basosquamous carcinoma, which may behave more aggressively than typical

BCC. In the second mechanism, two distinct tumours have arisen independently in the same vicinity and have grown or collided into each other due to their proximity.

In this case report, a poorly differentiated, pulmonary adenocarcinoma metastasized to a BCC. Since the metastases had squamous features, the lesion was originally interpreted as two co-existent cutaneous neoplasms: BCC and squamous cell carcinoma. The clinical history combined with the presence of intra-lymphatic emboli suggested the possibility that the poorly differentiated component was metastatic, and this was confirmed by immunohistochemistry.

It is known that tumours have a selective ability to metastasize to specific sites [6, 7]. Moreover, the co-existence of two or more primary neoplasms in the same patient is not uncommon. However, a tumour-to-tumour metastasis is a rare phenomenon. In these cases, the most frequent donor tumour is from the lung [8]. Nonetheless, no previous cases have been reported of lung to skin tumour-to-tumour metastasis, and this is probably a rare event. Whether our case is simply a rare coincidence or the result of alterations in the vasculature of the recipient tumour, is not entirely clear.

In summary, the presence of dual morphology in a skin neoplasm and intra-lymphatic involvement by one histologic component on routine H&E staining suggested the possibility of a metastasis. Immunohistochemistry of this unusual skin tumour was invaluable in confirming both the

metastatic nature of the poorly-differentiated component and its site of origin. We are not aware of previous reports of lung cancer metastasizing to pre-existing skin tumours.

Conflict of Interest There are no conflicts of interests.

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