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Case report

Another possible primary carcinoid tumour of skin?

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Summary. A 62-year-old female patient presented with a skin nodule on the chest wall which histological and ultrastructural examination showed to be a carcinoid tumour. Subsequent clinical investigation and follow-up of the patient have revealed no evidence of a carcinoid tumour elsewhere in the body, suggesting that the skin nodule itself may be the primary lesion.

Key words: Carcinoid tumour – Skin neoplasms

Introduction

The metastasis of visceral carcinoid tumours to the skin is well documented (e.g. Willis (1940), Rudner et al. (1965), Bean and Fusaro (1968), Norman et al. (1971). We have found only one example in the literature of a cutaneous carcinoid with no apparent primary site elsewhere (van Dijk and ten Seldam 1975). This paper describes a similar case.

Clinical history

A 62-year-old caucasian lady presented with a ten year history of a tumour overlying the sternum. In the last 6 months it had increased in size and become tender to touch. There was no history of bleeding or pruritus. Hypertension was diagnosed three years before presentation, her blood pressure being well controlled. On examination the tumour was 1.5 cm in diameter, raised, blue and rounded, with no obvious ulceration. It was firm, smooth, non-fluctuant and fixed to the skin but not to deeper structures. No breast lump, lymphadenopathy or hepatomegaly was present. The tumour was excised under local anaesthetic and subsequent histological examination showed it to be a carcinoid tumour (see below).

Post-operatively, closer questioning revealed no history of flushing, bronchospasm or diarrhoea. Subsequent investigations have shown no evidence of a carcinoid tumour on barium meal and follow through, barium enema or chest x-ray. Full blood count, liver function tests, ultrasound of liver and 24 h urine collection for 5-hydroxyindoleacetic acid (5HIAA) were all within normal limits.

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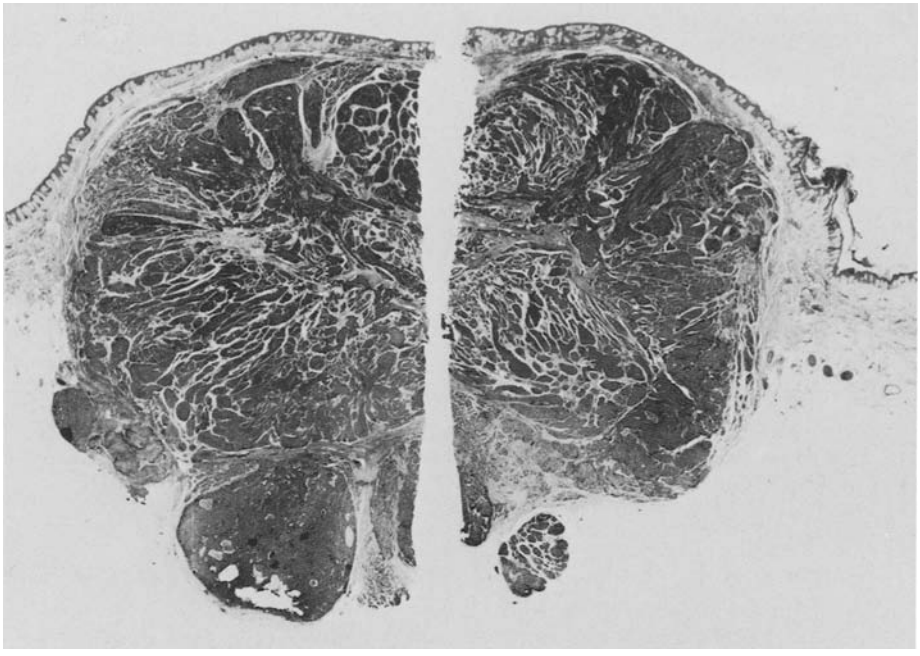

Fig. 1. Low power view of the tumour nodule. H and E, × 25

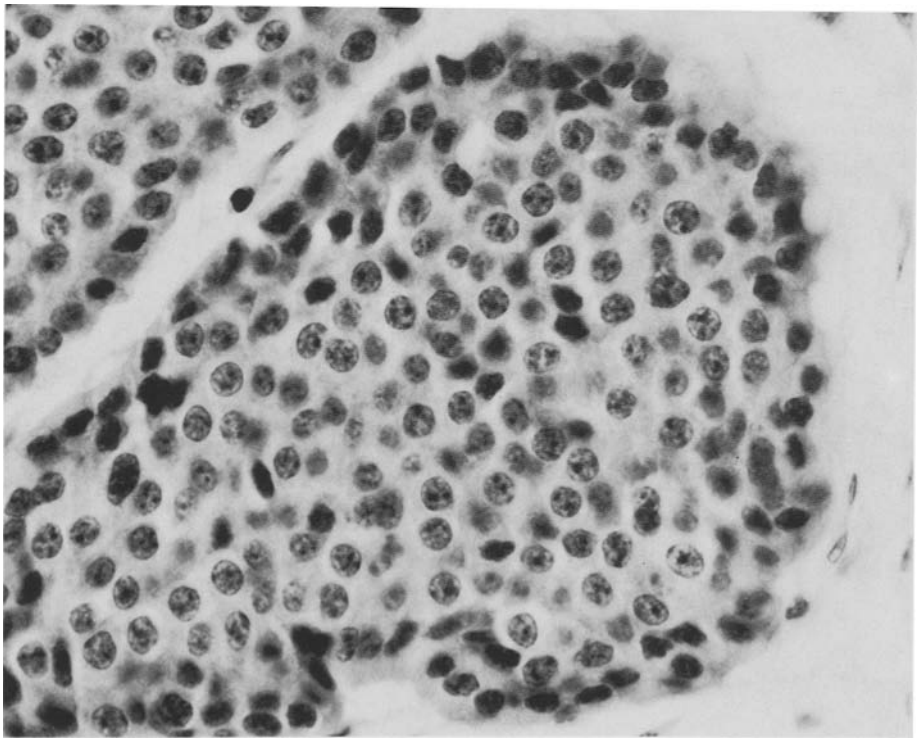

Fig. 2. Solid sheets of tumour cells subdivided by a fibrous stroma. H and E, × 800

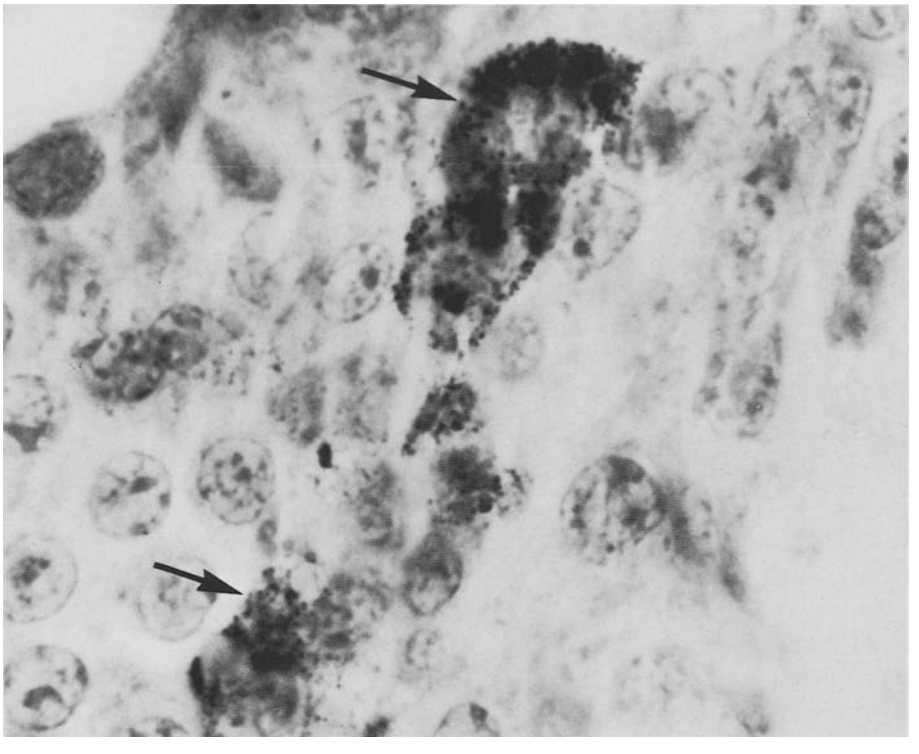

Fig. 3. Argentaffin granules within tumour cells (*arrows*). Masson-Fontana ×1,500

Post-operative follow-up has totalled 11 months. No local recurrence has occurred and no primary site elsewhere has become apparent. Repeated screening of 24 h urine samples for 5HIAA has been normal.

Pathological findings

Gross appearance. The tumour consisted of a firm, roughly spherical nodule within the skin, covered by intact epidermis on its superficial aspect. It protruded up to 0.5 cm above the normal skin contour and was blue-grey in colour. On section (after formalin fixation) the cut tumour surfaces were greyish-yellow in colour and homogeneous in texture. The maximum diameter was 1.6 cm.

Histological findings

Light microscopy. Routinely prepared, formalin-fixed and paraffin-embedded sections stained with haematoxylin and eosin (H and E) were examined. The tumour was within the dermis and extended into the subcutaneous fat, and was well circumscribed but unencapsulated. It reached the papillary dermis, and in places the overlying dermis and epidermis were partly atrophic (Fig. 1).

The tumour consisted of sheets, cords and trabeculae of fairly uniform, polygonal or columnar cells, most areas of which were solid (Fig. 2) but some small, cystic or gland-like spaces were present. Many of the cells had finely granular, eosinophilic cytoplasm. Nuclei were also fairly uniform in size and shape with finely stippled chromatin and one or more nucleoli. Occasional mitotic figures were present. The tumour was subdivided by a fibrovascular

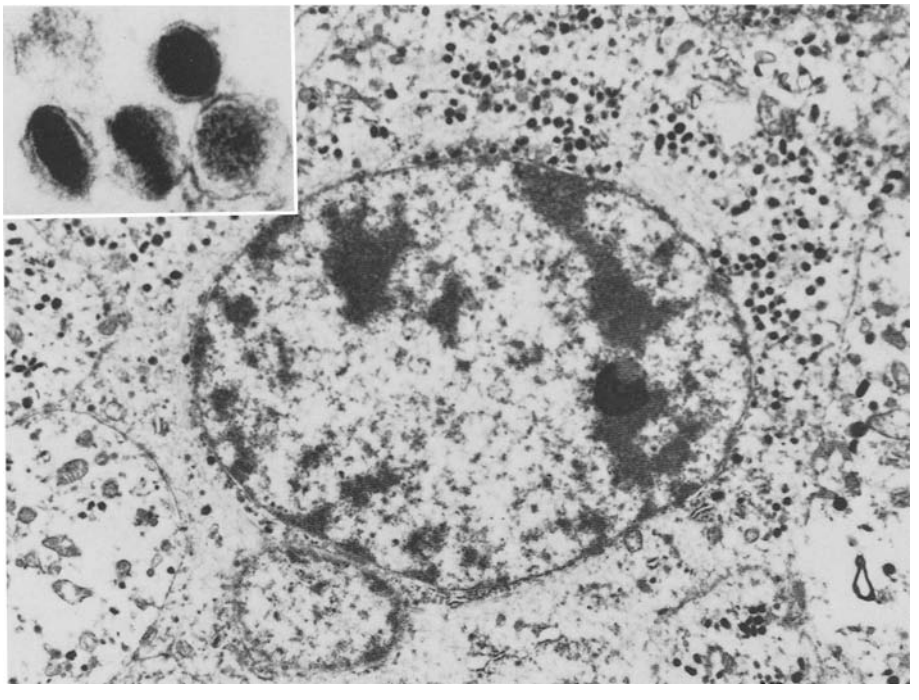

Fig. 4. Electron micrograph, formalin-fixed material. Tumour cell with cytoplasmic granules (Main field, ×8,100). *Inset* shows granules are membrane-bound with an electron-dense core (×56,570)

connective tissue stroma. No connections with the surface epidermis or any skin adnexal structures were noted.

Stains for argyrophil (Grimelius method) and argentaffin (Diazo and Masson-Fontana methods) granules were positive in many of the tumour cells (Fig. 3).

Electron microscopy. Formalin-fixed material was processed for electron microscopy and the presence of membrane-bound, dense-core cytoplasmic granules was demonstrated (Fig. 4).

Discussion

The diagnosis of carcinoid tumour in this case is established, and doubt remains only regarding its site of origin. If the tumour is metastatic rather than primary, then the positive argentaffin reaction of the granules is most suggestive of a carcinoid of mid-gut origin. However, the ten-year history of the lesion and negative clinical investigations strongly support the possibility that the lesion described above is indeed a primary carcinoid tumour of skin.

The only other case of possible primary carcinoid tumour of skin known to us is that of van Dijk and ten Seldam (1975). We note certain similarities between the cases. Both patients were female of similar age group and duration of history. Both tumours had simlar clinical characteristics. Histochemically, both tumours gave a positive argentaffin reaction suggesting

the presence of 5-hydroxytryptamine within the secretory granules. However, there is no suggestion in our case that the patient had a carcinoid syndrome.

Our observations included no histological features suggesting a particular structure or cell of origin within the skin. Neuroendocrine cells (Merkel cells) are present in the normal epidermis but the tumour we describe has the appearances of a carcinoid rather than a Merkel cell tumour. We know of no descriptions of endocrine cells with dense-core, membrane-bound secretory granules within the normal dermal appendages. There is evidence that endocrine cells of the amine precursor uptake and decarboxylation (APUD) series in some sites may be epithelial and not neuroectodermal in origin. To explain the occurrence of carcinoid tumours in organs in which APUD-type endocrine granules are not known to occur normally (e.g. kidney, cervix uteri) it has been suggested that neoplastic transformation is accompanied by "switching-on" of genes coding for endocrine differentiation (DeLellis et al. 1984). It seems possible that a similar mechanism might occur in the skin.

Clearly, careful long-term follow-up of the patient, including eventual necropsy, are required to establish that the above case is a primary carcinoid tumour of the skin.

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