Online Case Report

Malignant eccrine poroma in breast cancer-related lymphoedema

MD Lynch, AE Jones, A Marker, JW Grant, AD Purushotham

Cambridge Breast Unit, Addenbrooke's Hospital, Cambridge, UK

We describe the first case of malignant eccrine poroma arising in a lymphoedematous site. The patient had long-standing lymphoedema of the upper limb following breast cancer treatment. Lymphoedema is a recognised complication of breast cancer treatment and a risk factor for the subsequent development of malignancy. Possible mechanisms for this are discussed.

Key words: Lymphoedema – Malignant eccrine poroma – Breast cancer

A 70-year-old woman presented with multiple purple-red ulcerating lesions distributed throughout the

right upper limb (Figs 1 and 2). Her past medical history included carcinoma of the breast in 1971, aged 38 years,

Figure 1 Malignant eccrine poroma on a background of lymphoedema.

Correspondence to: AD Purushotham, Cambridge Breast Unit, Box 97, Addenbrooke's NHS Trust, Hills Road, Cambridge CB2 2QQ, UK
Tel: +44 1223 586627; Fax: +44 1223 257219; E-mail: amybyrtus@addenbrookes.nhs.uk

Figure 2 Multiple epidermotropic metastases throughout right forearm.

treated by radical mastectomy, axillary clearance and adjuvant radiotherapy to the chest wall. The patient subsequently developed lymphoedema of the right upper limb but remained otherwise well. In 1991, she presented with a single skin lesion on the right upper limb which was initially considered clinically and histologically to be

squamous cell carcinoma and treated by wide, local excision with split skin grafting. Local recurrence occurred and a review of the pathology revealed the tumour to be a malignant eccrine poroma with squamous differentiation. Over the next decade, she developed multiple similar lesions and underwent further wide, local excision and skin

Figure 3 Histopathology: ulcerated infiltrating carcinoma with malignant basaloid cells (H&E taken with a x2 objective).

grafting as required. Staging investigations showed no evidence of metastasis. In the light of extensive local recurrence, she underwent a transhumeral amputation.

Histologically, the tumour was an ulcerated infiltrating carcinoma composed of malignant basaloid cells. There were foci of squamous differentiation and ductal lumina (Fig. 3). Cells were arranged in large islands and broad anastomosing trabeculae with central necrosis and infiltrated deeply into the reticular dermis and subcutaneous fat. There was evidence of lymphovascular invasion.

Discussion

Lymphoedema as a risk factor for malignancy

Lymphoedema is a common complication of treatment for breast cancer and can affect up to 25% of patients.¹ The development of lymphangiosarcoma in an arm rendered chronically lymphoedematous following treatment for breast cancer (Stewart-Treves syndrome) is well recognised^{2,3} and is estimated to affect up to 0.5% of these patients. Other tumours described in post-mastectomy lymphoedema include Kaposi's sarcoma,⁴ non-Hodgkin's lymphoma,⁵ and Merkel cell carcinoma.⁶ In addition, chronic lymphoedema of other aetiology promotes the development of these neoplasms and others, in particular squamous cell carcinoma.⁷

Lymphoedema could promote the development of tumour by a number of different mechanisms. It is possible that impaired immune surveillance in lymphoedematous regions is important.⁸ Surgical ablation of lymph nodes increases the survival of skin grafts⁹ and, in breast cancer-related lymphoedema, the cell-mediated response to dinitrochlorobenzene is selectively impaired in the lymphoedematous arm.¹⁰ The mechanism of impaired immune function is poorly understood but it may result from impaired circulation of lymphocytes from lymphatic fluid to local lymph nodes. In support of this hypothesis, in lymphoedematous regions there is a higher concentration of lymphocytes in peripheral lymph and of Langerhan's cells in skin. This was interpreted by Olzewski *et al.*¹¹ as evidence of impaired lymphocyte circulation, but has yet to be formally proven. There are a number of alternative explanations for the increased incidence of neoplasia in lymphoedema. Mutagenesis may be increased by the chronic inflammation present in lymphoedematous skin¹¹ in a similar manner to the occurrence of squamous cell carcinoma in chronic leg ulcers (Marjolin's ulcer) or by impaired clearance of mutagens normally eliminated by lymphatic drainage.

The frequency of skin neoplasms occurring in lymphoedematous sites differs from those arising in non-lymphoedematous sites. In particular, tumours of the vascular endothelium such as angiosarcoma and Kaposi's sarcoma are greatly over-represented. It has been proposed that there is increased angiogenic drive in lymphoedematous limbs.¹²

This is consistent with the observations of Mellor *et al.*¹³ who compared the dermal microvessel density on the normal and lymphoedematous sides. Due to the increase in diameter and, therefore, skin surface area on the lymphoedematous side, a decrease in microvessel density would be expected; however, Mellor *et al.*¹³ found no difference implying that angiogenesis had occurred. Angiogenic drive would promote proliferation of vascular endothelial cells increasing the probability of neoplastic transformation.

Malignant eccrine poroma

Malignant eccrine poroma (porocarcinoma) is a rare cutaneous neoplasm first described by Pinkus and Mehregan in 1963.¹⁴ Since then more than 200 cases have been reported and several large series published.^{15–20} The diagnosis is based on the histological findings of cytological pleomorphism or invasive morphology in a tumour with eccrine differentiation (usually defined by the presence of ductal structures).¹⁷ The overall incidence of malignant eccrine poroma is unknown but they represent 0.005% of all cutaneous biopsy samples examined.¹⁹ These tumours are most common in adults aged 50–80 years^{17,19,20} and sex bias has not been consistent between the series. In most cases, the aetiology is unclear and no previous association with lymphoedema has been noted. Malignant eccrine poromas are found in order of frequency on the lower limb, trunk, head and upper limb^{19,21} and in many cases have been present for a number of years before coming to attention.²¹ Frequently, malignant spread presents as epidermotropic deposits.^{17–20}

The treatment of malignant eccrine poroma is primarily surgical – wide local excision with or without block dissection of local lymph nodes. Local recurrence rates are in the region of 11–25%.^{16,17} The management of metastatic malignant eccrine poroma is difficult. In general, there is a poor response to chemotherapy and radiotherapy, although several cases of complete remission have been reported with various chemotherapy regimens.²² Histological predictors of poor prognosis and lymph node metastasis are as follows: an increasing mitotic rate; lymphovascular invasion; tumour depth greater than 7 mm and an infiltrative morphology at the tumour margin.¹⁷ The role of sentinel node biopsy is as yet poorly defined but it is thought to be useful in tumours with adverse histological features.

The tumour in this patient was initially thought to be a squamous cell carcinoma. Squamous differentiation is a common feature of malignant eccrine poromas and in small specimens it may be impossible to distinguish the two.¹⁷ There have been a number of previous reports of cases of malignant eccrine poroma where the initial diagnosis was squamous cell carcinoma^{23,24} and it is important that malignant eccrine poroma is considered as an, albeit uncommon, differential diagnosis for squamous

cell carcinoma. We note that in this patient there is an extended history of epidermotropic metastases throughout the upper limb but no evidence of distal metastasis. This is in agreement with the larger series¹⁵⁻²⁰ which found that, in contrast to the bleak picture painted by early case reports, metastasis to draining lymph nodes and distant sites only occurs in a minority of cases. Furthermore, patients with multiple cutaneous malignant eccrine poromas do not appear to have a worse prognosis than those with a single lesion.¹⁷

There have been several reports of malignant eccrine poroma with other independent neoplasms. Cribier *et al.*²⁵ described a 75-year-old woman who developed, within a short period of time, malignant eccrine poroma, two independent squamous cell carcinomas and tricholemmal carcinoma. Roumen *et al.*²⁶ reported a young patient who presented with malignant eccrine poroma and subsequently developed multiple basal cell carcinomas. Bottles *et al.*²⁷ described a patient who developed villous adenoma of the colon and renal cell carcinoma in addition to malignant eccrine poroma. We note that our patient developed breast carcinoma at the relatively young age of 38 years. These reports, whilst anecdotal, suggest that some patients developing malignant eccrine poromas may have a susceptibility to the development of other neoplasms.

Conclusions

We have described the case of a 70-year-old woman who developed malignant eccrine poroma with extensive local spread in the setting of breast cancer related lymphoedema. This is the first report of an association between malignant eccrine poroma and lymphoedema and is further evidence for the concept that lymphoedema is a risk factor for malignancy.

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