Clinical case

Metastatic eccrine porocarcinoma: Response to docetaxel (Taxotere) chemotherapy

T. A. Plunkett,1 A. M. Hanby,2 D. W. Miles1 & R. D. Rubens1

1Academic Oncology Unit 2Hedley Atkins Breast Pathology Unit Guy’s & St. Thomas’ Hospitals NHS Trust, Guy’s Hospital, London, UK

Summary

Background: Eccrine porocarcinoma is an uncommon neoplasm of the intra-epidermal sweat gland duct.

Patients and methods: A case of eccrine porocarcinoma in a female renal transplant patient aged 45 years is described with a review of pertinent literature.

Results: The primary tumour was highly pleomorphic. In places large and small cells merged and focally the former component infiltrated the epidermis in a manner akin to Paget’s disease of the breast. The majority of the tumour was high grade; using the modified Bloom and Richardson grading system, usually applied to mammary ductal carcinomas, the tumour graded as 3. Metastatic disease developed nine months following primary surgical treatment. The metastatic eccrine porocarcinoma was resistant to epirubicin but responded to docetaxel chemotherapy.

Conclusions: There are no data to support the use of adjuvant therapy in the management of eccrine porocarcinoma. The use of the modified Bloom and Richardson grading system may define cases at high risk of relapse in which adjuvant therapy might be considered. Metastatic eccrine porocarcinoma has proven resistant to many chemotherapeutic agents. We report the first use of docetaxel in the management of this disease. The treatment was well tolerated and resulted in marked symptomatic and radiological responses. Treatment with docetaxel should be considered in future cases of this rare tumour.

Key words: eccrine porocarcinoma, sweat gland tumours, Taxotere

Introduction

Sweat gland adenocarcinomas are rare and represent approximately 0.005% of cutaneous epithelial tumours. Eccrine porocarcinoma (EPC) is the most common variant and arises from the intra-epidermal portion of the eccrine sweat gland [1]. Pinkus and Mehregan described the first definite case in 1963 [2], and since then about 150 cases have been reported in the literature, but there have been few large series [3–6]. Ours is the first report of a case in a renal transplant patient and the first reported use of the cytotoxic agent docetaxel in the management of metastatic EPC.

Case report

In April 1998 a 45-year-old woman presented with a three years history of a scaly erythematous patch on the left shoulder. In the few weeks prior to her presentation an exophytic lesion measuring 1 cm had developed on the scaly area.

She had a complex past medical history. In 1978 she had Hodgkin’s disease presenting in her left cervical lymph nodes (stage IIa) and treatment comprised splenectomy, chemotherapy and local radiotherapy. In 1985 she developed chronic failure secondary to acute tubular necrosis complicating pneumococcal septicaemia. She commenced continuous ambulatory peritoneal dialysis in 1991, and later that year received her first cadaveric renal transplant. The graft was removed after three weeks due to primary non-function. She received a second cadaveric renal transplant in December 1991, which proceeded uneventfully. The transplant kidney was functioning normally and she was taking triple-agent immunosuppressive therapy (cyclosporine, azathioprine and prednisolone) at the time of presentation.

The initial clinical diagnosis was of a squamous-cell carcinoma arising in Bowen’s disease. The lesion was outside of the previous radiotherapy field. An excision biopsy was performed and histological examination unexpectedly demonstrated eccrine porocarcinoma (Figure 1). Although much of the tumour was a highly pleomorphic large cell lesion, a peripheral population of distinctly smaller cells was also seen. In places the large and small cells merged and focally the former component infiltrated the epidermis in a manner akin to Paget’s disease of the breast. The lesion was estrogen receptor (ER) negative, progesterone receptor (PR) negative and c-erbB2/HER2 negative.

A further wide excision was undertaken to ensure adequate clearance and histological examination revealed no residual tumour. There was no clinical evidence of local lymph node involvement and a CT scan of the
neck, chest and abdomen showed no evidence of metastatic disease. Triple-agent immunosuppression was converted to single-agent therapy using cyclosporine alone.

She remained well for five months until swelling of the left breast developed. On examination there was generalised swelling of the breast with palpable left axillary lymphadenopathy. Excision biopsy of the axillary node was performed. Histological examination demonstrated replacement by eccrine porocarcinoma identical in appearance to the primary tumour. Consequently, a complete axillary node dissection was performed; none of the nodes showed evidence of metastases, however, two small extra-nodal deposits of tumour were found in the axillary fat. Following the axillary dissection, the breast swelling resolved. A CT scan of the neck, chest and abdomen showed no evidence of metastatic spread.

She remained well for four months until a non-productive cough and intermittent left-sided chest pain developed. A CT scan demonstrated numerous pulmonary metastases and left-sided rib metastases. She was initially treated with epirubicin 90 mg/m² i.v. three-weekly. After three cycles of treatment there was evidence of progressive disease with an increase in size and number of pulmonary metastases; docetaxel (Taxotere) 100 mg/m² i.v. three-weekly was commenced as second-line palliative chemotherapy. After the first cycle of therapy there was a marked symptomatic improvement with a corresponding radiological improvement. There was no significant toxicity from the treatment. A total of six cycles of treatment was given (Figure 2) and she remained well for three months until there was progression in the pulmonary disease. She was re-treated with six further cycles of docetaxel and once again a partial response was observed. Painful rib metastases were treated with a single fraction of external beam radiotherapy. She is currently asymptomatic five months after completing the second course of docetaxel.

Discussion

Pathology

Eccrine porocarcinomas arise in the acrosyringium and in their early manifestations are composed of small, dark poroid cells which may form tubules and commonly infiltrate the dermis [7]. A Pagetoid growth pattern may be seen, as in this case, and is characterized by small, intra-epidermal nested or individual Pagetoid cells infiltrating the epidermis [2]. True Paget's disease of the breast typically shows evidence of amplification of the c-erbB2 gene, however the Paget-like areas in this lesion showed no evidence of this. This tumour was ER and PR negative. Whilst some sweat gland carcinomas are ER or PR positive [8], expression often relates to differentiation. It is therefore unsurprising that this high-grade lesion was hormone receptor-negative.

There does not appear to be a clear way to define 'aggressive' and assessment of the three components used for grading ductal carcinomas of the breast seems a rational way to proceed. The majority of the tumour was high grade; using the modified Bloom and Richardson grading system [9], usually applied to mammary ductal carcinomas, the tumour graded as III (tubule score 3, mitotic count 3, pleomorphism 3). If sufficient cases could be gathered, a retrospective analysis could be performed using these grading criteria and clinical outcome.

Clinical

EPC usually presents with a solitary slowly growing lesion. There is no characteristic macroscopic appearance. Although often red and papular, the lesion can be flesh-coloured or appear as a plaque, polypoid or verrucous lesion or as an ulcer. The rarity and variable appearance of EPC has led to them being mistaken clinically for basal cell carcinoma, seborrhoeic keratosis, wart, pyogenic granuloma, squamous-cell carcinoma, amelanotic melanoma, Bowen's disease or fibroma [10].

EPC generally affects individuals in their seventh decade, although a range of 19–94 years has been reported [11]. There is no definite association with gender. The natural history is variable and ranges from months to years. There is no reported association with immunosuppression and this is the first report of EPC in a renal transplant patient. The influence of immunosuppression on the outcome in this patient is uncertain.

In contrast with benign eccrine poroma, the location of EPC does not correlate with the highest concentration of eccrine sweat glands (palmo-plantar areas). Instead it is found mainly on the lower limbs, and less commonly face and scalp, upper limbs or abdomen. The primary treatment of choice is surgical wide local excision of the tumour with histological confirmation of tumour-free margins [3, 4, 8], although Mohs micrographic surgery has been used in a series of five patients from one centre [12]. Prophylactic lymph node dissection has been recommended if regional lymphadenopathy is present, or in cases of recurrent or poorly differentiated tumour with intra-lymphatic permeation [8].
Prognosis is difficult to determine because of the rarity of EPC and the variations in natural history. There are no data to support the use of adjuvant chemotherapy or radiotherapy and there are currently no agreed criteria to define patients at high risk of relapse. There was no obvious benefit from chemotherapy given to a small series of patients clinically disease-free following surgical treatment of local or distant recurrence [13]. Similarly, there is no evidence of benefit from radiotherapy in these circumstances; in this case there would have been a considerable risk of lymphoedema in the arm from radiotherapy following axillary lymph node dissection.

The management of patients with metastatic EPC is difficult. Multiple cutaneous metastases may develop or less commonly metastases occur in lung, retro-peritoneum, bone, liver, breast, bladder, peritoneum or ovary [10]. Radiotherapy has not generally been effective [14], and EPC has proven resistant to many cytotoxic agents.

Anthracycline-based combination chemotherapy resulted in partial responses in two patients from one reported series, but the lack of detail on dosage and schedule make comparisons between trials difficult [13].

Briscoe et al. reported a complete response to melphalan and intra-arterial infusions of 5-fluorouracil (5-FU) combined with regional hyperthermia [15]. The patient had a primary tumour in the foot with metastatic nodules in the lower limb and metastatic abdominal lymphadenopathy. Mitts et al. reported a partial response to combined radiotherapy and i.v. 5-FU in a patient with an axillary metastasis [16]. In our patient, the extent of metastatic spread precluded concurrent chemo-radiotherapy. Swanson et al. reported a response to continuous infusion 5-FU for 4 days every 28 days [17]; the response was maintained for 3 months. In the case we report we wished to avoid long-term i.v. catheters given the patient's long-term immunosuppression and previous splenectomy.

Piedbois et al. report a prolonged complete remission in response to doxorubicin, mitomycin C, vincristine and 5-FU alternating with cisplatin and bleomycin every two weeks [18]. There were no reported toxicity data, but the treatment was modified after nine cycles as the limits of haematological, pulmonary and renal tolerance had been reached.

Single-agent isotretinoin caused necrosis in cutaneous deposits of a patient with metastatic EPC previously resistant to chemotherapy [19], but was ineffective in another patient [20]. Others have reported benefit from peri-lesional injection of cutaneous metastases with interferon-alpha (IFN-α) and interleukin-2 (IL-2) [21]. A combination of both isotretinoin and IFN-α has been reported to stabilise metastatic cutaneous disease. In the first case, the isotretinoin (2 mg/kg daily) was stopped after two months because of intolerance, but the IFN-α (9 MU three days per week) was continued and stabilised disease [10]. In the second case, isotretinoin (120 mg/day) and IFN-α (6 MU 3 days per week) stabilised cutaneous metastases for 10 months. The treatment was apparently well-tolerated [22]. This regimen was not utilised in our patient because of the risk of nephrotoxicity and the need to reduce rather than stabilise symptomatic pulmonary metastases.

We report the first use of docetaxel in metastatic eccrine porocarcinoma. Docetaxel, along with paclitaxel, is a member of the taxoid group. These agents stabilise microtubule assembly, and have cytotoxic activity against a wide variety of tumours. The treatment was well-tolerated and induced symptomatic and radiological responses lasting several months. Treatment with docetaxel chemotherapy, either alone or perhaps in combination with 5-FU (as a continuous infusion), should be considered for future patients with metastatic EPC. In patients with cutaneous or asymptomatic visceral disease treatment with IFN-α and isotretinoin could be considered.
References


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Correspondence to: Dr T. A. Plunkett Academic Oncology Unit Guy's Hospital London, SE1 9RT UK E-mail: blunkett@icrf.icnet.uk