Extensive bone metastases from basal cell carcinoma of the eye

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ABSTRACT

The incidence of metastases from basal cell carcinoma is rare. We report a 66-year-old woman who had basal cell carcinoma of the outer canthus of the left eye. Six months following radical radiotherapy, she developed local recurrence for which an orbital exenteration was done. Four months later, she developed rapidly-progressive multiple skeletal metastases and died soon after.

Keywords: basal cell carcinoma, bone metastases, distant metastases, eye tumour

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INTRODUCTION

Basal cell carcinoma (BCC) of the skin is the most common malignancy in humans[1]. The biological behaviour is usually benign and cure is almost always achieved by electrodessication and curettage, cryosurgery, excision, or irradiation. Rarely, however, the clinical course may be aggressive and regional, or distant metastases can develop, especially in patients who have had multiple local recurrences. Once distant metastases develop, cure is no longer possible. We report a case of BCC of the outer canthus of the left eye, which developed widespread skeletal metastases following a local recurrence.

CASE REPORT

A 66-year-old woman presented to the Department of Radiotherapy and Oncology in November 2003 with a lesion in the outer canthus of the left eye. The lesion was first noticed two years previously, and it had been growing slowly since that time. This lesion had become friable and ulcerated in the two months prior to presentation. Physical examination revealed a 3 × 3 cm sized ulcer on the outer canthus of the left eye. The ulcer had a slough-covered floor with a purulent discharge, an inflamed base and beaded margins. There was no lymphadenopathy. The rest of the physical examination was unremarkable. Biopsy from the lesion revealed an adenoid variant of BCC.

She was treated with radical radiotherapy to 60 Gy/30 fractions/6 weeks till January 2004. The lesion disappeared completely after radiotherapy (RT), and she was placed on a two-monthly follow-up. Six months after completing RT, she developed a local recurrence, for which she underwent a left orbital exenteration in July 2004. Histopathology showed BCC with negative margins of resection. In November 2004, the patient complained of pain in the right shoulder and left hip. On examination, there was tenderness at these sites. There was no evidence of local recurrence or lymphadenopathy.

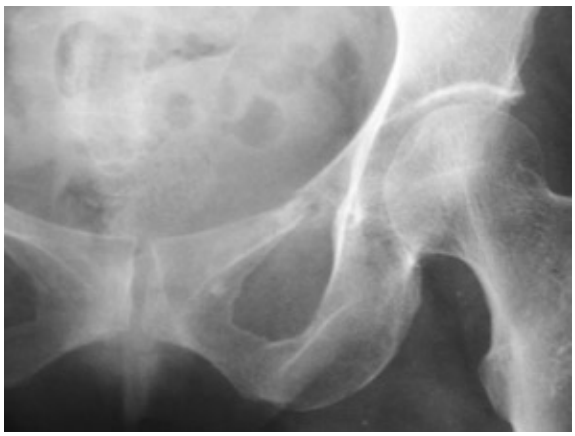

Fig. 1 Radiograph of the pelvis shows a destructive osteolytic lesion involving the left superior ilio-pubic ramus.

A radiographical skeletal survey showed osteolytic lesions in the lateral one-third of the right clavicle and left superior pubic ramus (Fig. 1). A radionuclide bone scan (Fig. 2) showed extensive areas of uptake of radiotracer in the skull, right clavicle, left scapula, ribs, dorsolumbar spine, sacrum and the left pubic rami, which was consistent with skeletal metastases. β_2-microglobulin and serum electrophoresis were normal. Chest radiograph and ultrasonography of the abdomen were normal.

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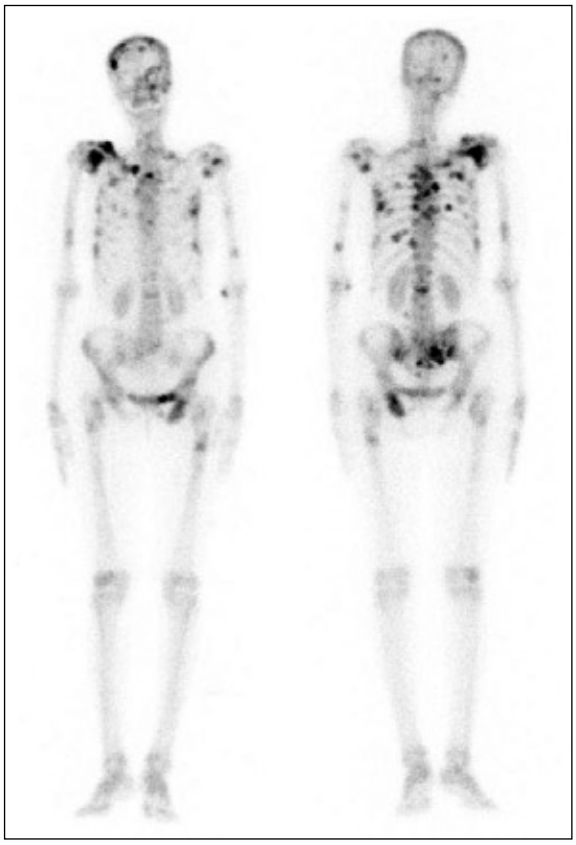

Fig. 2 Radionuclide bone scan shows multiple foci of radiotracer uptake in the skull, right clavicle, left scapula, ribs, dorsolumbar spine, sacrum and the left pubic rami, typical of extensive skeletal metastases.

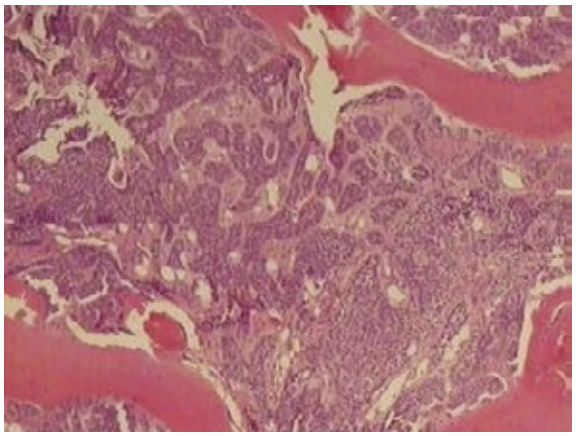

Fig. 3 Photomicrograph of iliac crest biopsy specimen shows islands of basaloid cells with palisading at periphery and a haphazard arrangement, suggestive of basal cell carcinoma (Haematoxylin & eosin, ×40).

Biopsy from the iliac crest (Fig. 3) revealed clusters of malignant cells that were similar in morphology to the primary and recurrent tumour. A diagnosis of extensive skeletal metastases from BCC was made. Single fraction palliative RT was given to the right shoulder and left hemipelvis. However, the patient's clinical condition deteriorated rapidly before any systemic treatment could be planned, and she died soon after.

DISCUSSION

BCC is the most common malignancy in humans, accounting for almost one-quarter of all cancers[1]. Despite its high incidence, metastases are rare, with the reported frequency being 0.0028-0.1%[1]. In one review of 67 patients of metastatic BCC[2], metastases were most commonly seen to involve the regional lymph nodes (64.6%) and lungs (33.9%), and less commonly the bone, skin and other sites (18.5% each). Isolated bone metastases are rare. They are usually observed in conjunction with metastases at other sites[3]. Although the median time interval between onset of the primary tumour and metastases is nine years, once metastases have occurred, median life expectancy is only eight months[2].

The risk factors for the development of metastatic BCC include a large tumour size (>5 cm), increased depth of invasion[2], a history of persistent BCC for many years[4], refractoriness to treatment, defective cellular immunity[5], and exposure to radiation[6]. BCC originating on the face is believed to metastasise more commonly than that at other sites. This is possibly related to the thin skin and increased concentration of blood vessels in the face[7]. Further, trisomy of chromosome 6 has also been shown to be predictive of metastatic potential[8].

Lattes and Kessler[9] defined three criteria for establishing metastatic BCC, namely: (1) the primary tumour must originate from the skin and not the mucous membrane; (2) metastases must be at a site distant from the primary tumour and not by simple extension; and (3) the primary tumour and metastatic lesion must have similar histological subtypes. Our case meets all three criteria. The low incidence of metastases in BCC is believed to be due to the stromal dependence of tumour cells[10]. This theory presupposes that only large tumour emboli with attached stroma are successful in implanting at a metastatic site. Further, it has been hypothesised that history of repeated therapy in the primary tumour could be linked to the development of independence of ectodermal from mesodermal elements, which could, in turn lead to highly malignant behaviour[11].

Metastases from BCC occur most commonly via lymphatics, and then through the haematogenous route. The absence of lymphadenopathy in the present case suggests a direct haematogenous route of metastases. In rare instances, bone metastases may be extensive enough to produce myelophthisic

anaemia[12,13]. Given the rarity of metastases in BCC, no protocols exist regarding chemotherapy in widespread disease. Hartman et al reported a durable response of 36 months with surgery, radiation and cisplatin-based chemotherapy for a BCC with metastases to the cervical spine[14]. Further, a combination of cisplatin and paclitaxel has been recently shown to provide a symptomatic response[15]. In the present case, the patient's general condition deteriorated rapidly prior to the institution of systemic chemotherapy.

In summary, we have reported a case of a 66-year-old woman who developed extensive skeletal metastases from a BCC. Though skeletal metastases are rare in BCC, the possibility must be included in the differentials in a BCC patient who complains of bone pain.

REFERENCES

1. Aasi SZ, Leffell DJ. Cancer of the skin. In: DeVita VT, Hellman S, Rosenberg SA, eds. Cancer: Principles and Practice of Oncology. 7th ed. Philadelphia: Lippincott Williams & Wilkins, 2005: 1717-45.
2. Snow SN, Sahl W, Lo JS, et al. Metastatic basal cell carcinoma. Report of five cases. Cancer 1994; 73:328-35.
3. Kleinberg C, Penetrante RB, Milgrom H, Pickren JW. Metastatic basal cell carcinoma of the skin. Metastasis to the skeletal system producing myelophthistic anemia. J Am Acad Dermatol 1982; 7:655-9.
4. Conway H, Hugo NE. Metastatic basal cell carcinoma. Am J Surg 1965; 110:620-4.
5. Safai B, Good RA. Basal cell carcinoma with metastasis. Review of literature. Arch Pathol Lab Med 1977; 101:327-31.
6. Randle HW. Basal cell carcinoma. Identification and treatment of the high-risk patient. Dermatol Surg 1996; 22:255-61.
7. Cotran RS. Metastasizing basal cell carcinomas. Cancer 1961; 14:1036-40.
8. Nangia R, Sait SN, Block AW, Zhang PJ. Trisomy 6 in basal cell carcinomas correlates with metastatic potential: a dual color fluorescence in situ hybridization study on paraffin sections. Cancer 2001; 91:1927-32.
9. Lattes R, Kessler RW. Metastasizing basal-cell epithelioma of the skin: report of two cases. Cancer 1951; 4:866-78.
10. Blewitt RW. Why does basal cell carcinoma metastasize so rarely? Int J Dermatol 1980; 19:144-6.
11. Cornelius CE 3rd. Bone. A site of metastatic basal cell carcinoma. Arch Surg 1972; 104:848-50.
12. Jager RM, Weiner LJ, Howell RS. Basal cell carcinoma with bony metastases producing myelofibrosis. Arch Dermatol 1977; 113:1288-9.
13. Coletta DF, Haentze FE, Thomas CC. Metastasizing basal cell carcinoma of the skin with myelophthisic anemia. Cancer 1968; 22:879-84.
14. Hartman R, Hartman S, Green N. Long-term survival following bony metastases from basal cell carcinoma. Report of a case. Arch Dermatol 1986; 122:912-4.
15. Jefford M, Kiffer JD, Somers G, Daniel FJ, Davis ID. Metastatic basal cell carcinoma: rapid symptomatic response to cisplatin and paclitaxel. ANZ J Surg 2004; 74:704-5.

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