

## Dramatic Response of a Case of Recurrent Basal Cell Carcinoma to Systemic Chemotherapy

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### Abstract

Basal cell carcinoma (BCC) is the most common cancer among humans, and the standard treatment is surgery. Other modalities are reserved as a second line of treatment. Topical chemotherapy may be used in primary BCC. Systemic chemotherapy has no role in the primary treatment of BCC, although it may be efficacious in metastatic cases. We report the case of a patient with persistent recurrent BCC following multiple surgeries and radiotherapy, who achieved a dramatic response with a cisplatin and 5-flourouracil chemotherapy regimen.

**Keywords:** Basal cell carcinoma, Recurrence, Chemotherapy, Cisplatin, 5-Flourouracil

### Introduction

Basal cell carcinoma (BCC) is the most frequent malignancy worldwide, and its incidence is increasing by 3%-10% annually.<sup>1,2</sup> It is a slow-growing tumor that has a low metastatic tendency.<sup>3-5</sup> At presentation, BCC is almost always localized.<sup>6</sup> The main risk factors for developing BCC are ultraviolet exposure, increasing age (>40 years), male sex and genetic predisposition.<sup>7</sup> Treatment is usually restricted to

local modalities of which the main treatment is surgery. The gold standard is Mohs microsurgery, particularly in patients with an aggressive tumor.<sup>7,8</sup> Other modalities such as radiotherapy, cryotherapy and topical chemotherapy may be used in cases for which surgery fails or cannot be performed.<sup>8</sup> Systemic chemotherapy has no proven role in the treatment of BCC.

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## Case Report

The patient was a 74-year-old man who developed a 3.5×1 cm lesion in his lower abdomen (suprapubic) in September 2002. He underwent surgery and histological examination revealed a pigmented BCC. After the initial surgery, the tumor recurred twice and each time he underwent additional surgery. The third recurrence was in September 2007. At that time, he received radiotherapy with a superficial X-ray machine (Siemens Stabilipan: 120 KV, 10 mA, 4 mm Al half-value layer) up to 60 Gy in 2-Gy fractions, which were well tolerated. In March 2010, the lesions recurred. The last recurrence presented as widespread ulcerative lesions that involved the suprapubic area and base of the penis (Figure 1). The patient was referred for plastic surgery and urology consultations, but due to the risk of penile necrosis, surgery was not performed. He received chemotherapy consisting of cisplatin 100 mg/m<sup>2</sup> on day one and 5-flourouracil 1000 mg/m<sup>2</sup> for three days. The tumor decreased in size following each chemotherapy cycle and after the fourth cycle, the ulcerative lesions disappeared completely (Figure 2). Chemotherapy continued for a total of six cycles. The major chemotherapy side effects consisted of nausea, vomiting and anorexia, which were controlled with support measures. Five months after the last cycle of chemotherapy, the patient was well and free of ulcerative lesions.

## Discussion

BCC is the most common cancer worldwide in Caucasians, and comprises one-sixth of all cancers;<sup>9</sup> however, the incidence varies in different areas. In some areas of Australia, the rate of BCC is as high as 1 per 100.<sup>10,11</sup> The most frequent site of BCC is the head and neck region, where 85% of the cases are located,<sup>10,12</sup> followed by the limbs and trunk.<sup>13</sup> This neoplasm grows slowly and causes local destruction. Consequently, the usual treatment modalities are local and consist of surgical excision, cryosurgery, Mohs microsurgery, curettage, electrodesiccation or radiotherapy.<sup>10</sup> Topical forms of 5-flourouracil and imiquimod



Figure 1. Before treatment.



Figure 2. After treatment.

may be recommended for small tumors in low-risk areas.<sup>14</sup> Immunologic status seems to be important in BCC pathology, and some patients with diffuse metastatic BCC have been reported to have immunodeficiency.<sup>12,15</sup>

Although the mortality rate due to BCC is low, the high incidence of this neoplasm in Caucasians<sup>2,16</sup> signifies the need for a treatment when conventional therapies (surgery and radiotherapy) fail or cannot be performed, as in metastases or multiple local recurrences. Most relapses (two-thirds) occur during the first three years;<sup>7</sup> however, they may occur between 6 months to 10 years after treatment. The location, histological subtype and size of lesions have prognostic effects on the recurrence rate. In spite of the high incidence of BCC, the exact rate of its recurrence is not known.<sup>10</sup> Aggressive forms

(recurrent or invading underlying tissue, which occur most often in the nasolabial fold), flat lesions, lesions that are not well circumscribed and perineural invasion are associated with a greater likelihood of local recurrence.<sup>9,17</sup> Infiltrating and micronodular subtypes of BCC, especially if located on the face, have a higher risk of recurrence.<sup>13</sup> This problem is of particular concern for patients if surgery or radiotherapy is not feasible. Therefore, the search for an effective option is important.

Metastasis in BCC, although rare, has a poor prognosis with only an 8-month median survival.<sup>4</sup> Its incidence rate is 0.0028% to 0.1%.<sup>5</sup> At the time of metastasis, the primary lesion is often active.<sup>12</sup> The most frequent site of metastasis is the lymph nodes (66-70%), but the lungs, skin and bone have also been reported.<sup>4,12,15</sup>

BCC is usually considered to be nonresponsive to chemotherapy; however, sometimes this modality is the last available choice.<sup>6</sup> When there are metastases, or when neither radiotherapy nor surgery is feasible, chemotherapy is an option. Pfeifer et al. reviewed reports of 55 patients with BCC who received chemotherapy between 1960 and 1983. Twenty-eight patients received varying combinations of non-cisplatin-containing regimens (methotrexate, bleomycin, vinblastin, 5-fluorouracil and adriamycin). Non-cisplatin-based combination regimens produced incomplete remission and only few partial responses, with no complete responses observed. Of 27 patients who received cisplatin-based chemotherapy, 22 had evaluable disease. Ten (45%) showed complete disappearance of the disease. Therefore, Pfeiffer et al. suggested four to six cycles of cisplatin-based chemotherapy for metastatic or locally advanced cases.<sup>6</sup>

Fabrizio et al. reported a case with multiple local recurrences. They used a combination of cisplatin and 5-fluorouracil; however, treatment response was not satisfactory.<sup>4</sup> Bason et al. observed a brief response in a case of metastatic BCC when the patient was treated with metotrexate, bleomycin, cisplatin and 5-fluorouracil.<sup>18</sup> Jefford et al. used a combination of

cisplatin and paclitaxel chemotherapy in a case with metastatic pulmonary BCC. An incomplete response was observed and the patient relapsed after 3 months.<sup>5</sup> The combination of carboplatin and paclitaxel was effective in a case with metastatic BCC, according to Benediti et al., who used this combination in a patient with pulmonary metastasis. However, the patient developed pure red cell aplasia.<sup>3</sup>

Our patient was a high-risk case because he had undergone multiple surgeries, received previous radiotherapy and had widespread lesions. Therefore, he was treated with six cycles of cisplatin plus 5-fluorouracil, and after the fourth cycle he showed a dramatic response. Although systemic chemotherapy may not be an ideal primary treatment for BCC, there is some evidence in favor of its efficacy in metastatic and recurrent diseases. Novel chemotherapeutic agents such as taxanes or gemcitabine, alone or in combination with cisplatin, should be evaluated in future trials.

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