Anti-Cancer Drugs, 3, pp. 481–484

Case report

Salvage cisplatin and adriamycin for advanced or recurrent basal or squamous cell carcinoma of the face

Ofer Merimsky,[CA] Meira Neudorfer, Edna Spitzer and Samario Chaitchik

O Merimsky, E Spitzer and S Chaitchik are at the Department of Oncology, and M Neudorfer is at the Department of Ophthalmology, Tel-Aviv Sourasky Medical Center and Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv 64239, Israel.
Fax: 03-5469580.

Is it justified to treat a small, localized and relatively indolent malignancy by systemic combined chemotherapy? Five patients with locally advanced skin tumors were treated by salvage cisplatin and adriamycin for three to five courses. Three achieved complete response, one achieved partial response and one succumbed to an unrelated cause. The rapid induction of response, high response rate, unmaintained complete remissions of long duration and relatively low rate of toxicity may justify the use of this combination for the treatment of small skin tumors when other treatment options are of no avail.

Key words: Adriamycin, cisplatin, basal cell carcinoma, salvage chemotherapy, skin cancer, squamous cell carcinoma.

Introduction

Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) of the skin are very common, but rarely fatal. SCC of the skin metastasizes in only 3% of cases, SCC of mucocutaneous areas metastasizes in 11% of cases and SCC arising in burn scars in 10–30% of cases.[1] BCC only rarely metastasizes.[1] BCC and SCC are usually localized and well controlled by limited surgery or radiotherapy, achieving cure rates over 90%.[2] However, if the initial or the recurrent tumor exceeds 5 cm in diameter, then radiotherapy has poor results.[3] In many cases the lesions are confined to the face, hence the surgical option is sometimes very limited in order to avoid contractures and severe cosmetic deformities.[4] Primary lesions along the embryonal fusion planes—the nasolabial fold, retroauricular sulcus and periorbital areas—infiltrate deeply.[4] Locally advanced lesions might deeply penetrate the fascia and bone, thus rendering surgical complete resection difficult and mutilating. Re-irradiation of the tumor area might be complicated by radionecrosis of the underlying tissues. Although it has been stated in the literature that systemic chemotherapy would probably never play a role in the treatment of any primary or recurrent BCC,[4] several encouraging reports have been published.[5,6] The use of cisplatin combined with adriamycin in such cases has achieved an overall response rate of 68%.[5,6] We present five patients with advanced skin tumors, where surgery or radiotherapy were of no avail, who were salvaged by cisplatin–adriamycin combination.

Patients and methods

Patients

Five patients whose age ranged from 64 to 78 years (median 75 years) were included in the study group. All the patients had a Karnofsky's performance status of at least 70%. The malignant lesions were either BCC or SCC on the facial area or behind the auricle. They were small, usually not larger than 5 × 5 cm. Previous treatments and the patients' clinical data are summarized in Table 1.

[CA] Corresponding Author.

Table 1. Patients' clinical data

No.	Sex/age	Histology	Site and size (cm)	Extension	Previous treatments
1	F\73	SCC	retro-auricular, 2.5 × 3.5	penetration of bone	wide excision, skin graft, radiation therapy
2	M\64	BCC	ala nasi, 3 × 4 × 4 cauliflower shape	destruction of septum and vomer	wide excision
3	F\75	BCC	eyelid, 1.3 × 3.2	invasion of orbit, ethmoid bone and nose	local excision
4	M\78	BCC	retro-auricular, 2.2 × 3.9	penetration of fascia, ulceration	wide excision, skin graft, radiation therapy
5	F\75	SCC	ala nasi, 0.5 × 1.0	perforation of the ala	local excision

Table 2. Chemotherapy and response

No.	Treatment[a] and no. of cycles	Toxicity	Results[b] and duration
1	ADR + CIS × 2 followed by ADR + CARBO × 3	alopecia, vomiting	CR, 8 months
2	ADR + CIS × 2	vomiting, sudden death[c]	NA
3	ADR + CIS × 4	alopecia, vomiting	CR, 58 months
4	ADR + CARBO × 3	alopecia, vomiting	CR, 8 months
5	NOV + CARBO × 1	neutropenia, sepsis	MR[d]

[a] ADR, adriamycin (50 mg/m^2); CIS, cisplatin (50 mg/m^2); CARBO, carboplatin (200 mg/m^2); NOV, novantrone (10 mg/m^2).
[b] CR, complete response; MR, minimal response; NA, not assessed.
[c] Possible toxicity: the patient refused to continue after the second course and expired 2 months later.
[d] CR was achieved by electron beam irradiation. Cosmetic results were poor.

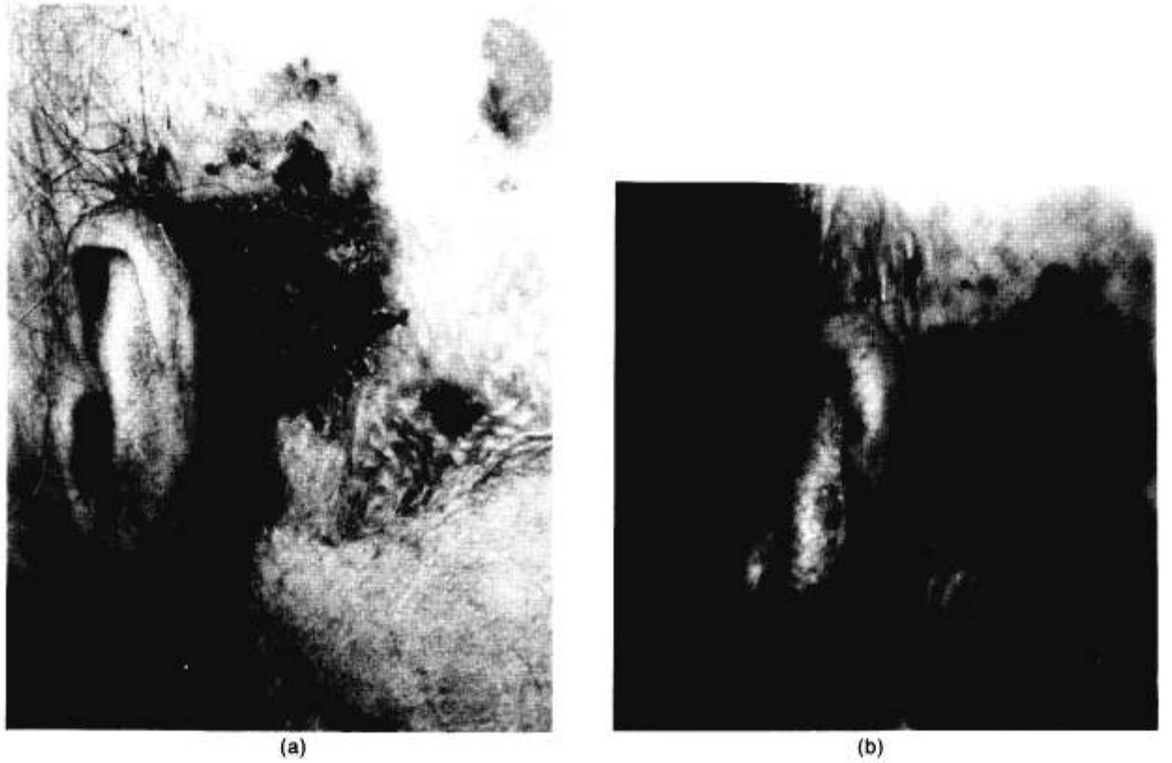

Figure 1. Patient no. 1, recurrent SCC in a skin graft (a). State after two courses of chemotherapy (partial response) (b) before complete disappearance was observed.

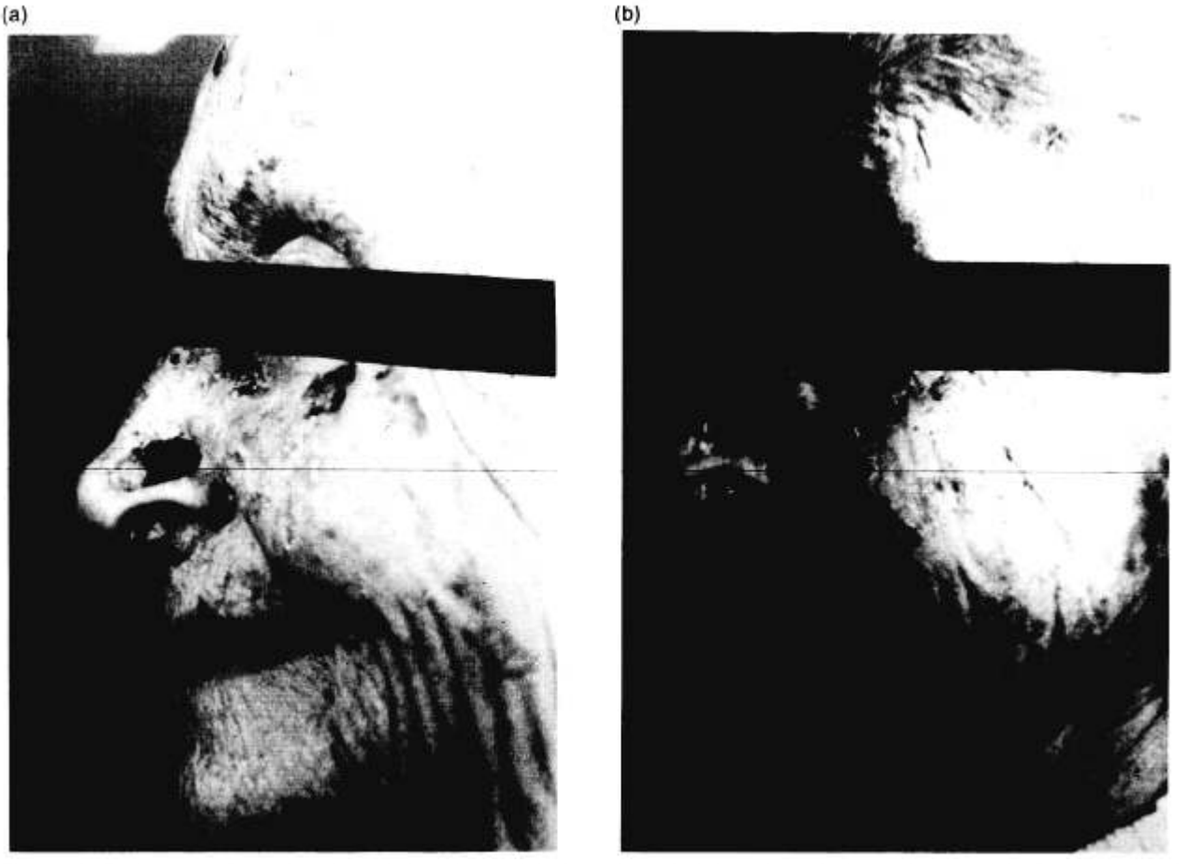

Figure 2. Patient no. 5, perforation of the ala nasi before the administration of chemotherapy (a). One course of chemotherapy achieved minimal response and grade IV toxicity. Electron beam irradiation was advocated, resulting in a complete response and an unavoidable radiation-induced permanent cosmetic deformity (b).

Treatment protocol

Adriamycin (50 mg/m^2) and cisplatin (50 mg/m^2) were administered i.v. once every 21 days on an inpatient schedule, because of the patients' advanced age. In cases of borderline–low cardiac ejection fraction, novantrone (10 mg/m^2) replaced the adriamycin. A creatinine clearance test below 50 ml/min was an indication for replacing the cisplatin by carboplatin 200 mg/m^2. Response and toxicity were evaluated according to the WHO criteria.

Results

Results are reported in Table 2. Four patients were evaluable. A fifth patient, poorly complying, had a history of myocardial infarction. Although his cardiac function was preserved prior to the administration of chemotherapy, he succumbed to a cardiac arrest 2 months after interruption of treatment on his request. Time to response was 2–3 weeks. Response was complete in two cases with BCC for 8 and 52 months, and in one case with SCC for 8 months (Figure 1a and b), after three, four and five courses, respectively. Patient no. 5 achieved partial response after a single course, but treatment was interrupted because of grade IV neutropenia and sepsis. Electron beam irradiation (8 MeV, 200 cGy × 5/week for 4 weeks) was required to achieve complete disappearance of the tumor. Cosmetic results were nevertheless poor: wide perforation of the ala nasi (Figure 2a and b). Toxic manifestations in the three complete responders included vomiting (grade II) and hair loss.

Discussion

Is it justified to treat a small, localized and relatively indolent malignancy by systemic combined chemotherapy? Except for neo-adjuvant schedules for aggressive tumors, this approach is only seldom used. A systemic regime is usually reserved for the treatment or prevention of systemic spread. Most skin tumors will not kill the patient unless they are neglected or invade vital structures. Most of the tumors occur in elderly patients, who usually suffer from other diseases such as cardiovascular disorders and diabetes mellitus, and whose bone marrow reserve is rather small. They are at high risk of developing severe treatment-related myelosuppression, sepsis, and impairment of renal and cardiac function. Chemotherapy in our patients was used as a systemic salvage treatment for locally advanced or problematic lesions. Cosmetic results are sometimes as important as complete resection of the tumor when treating facial lesions. In patients nos 1 and 4 excessive radiation dose might have resulted in radionecrosis of the skin and the underlying bone. Patient no. 2 had a locally advanced necrotic tumor, most probably radioresistant. In patient no. 3 irradiation was not delivered in order to spare the anterior optic system, and to avoid cosmetic deformity and functional impariment of the adjacent eyelid. In patient no. 5 chemotherapy was aimed at avoiding radiation induced cosmetic deformity to the ala nasi. Since toxicity was more severe than expected, radiation therapy was at last added, and the residual deformity was unavoidable.

To conclude, literature data[5,6] and our experience of rapid induction of response, high response rate and complete remissions of relatively long duration may justify the use of this method for the treatment of localized skin tumors. In many cases chemotherapy is a salvage, after other modalities have been unsuccessfully used. Selective or isolated intra-arterial perfusion of cisplatin and adriamycin may further minimize the side effects. However, this might be difficult to perform because of pre-existing arteriosclerosis, especially in distal arterial branches which supply the local lesions.

References

1. Moller R, Reymann F, Hou-Jensen K. Metastases in dermatological patients with squamous cell carcinoma. *Arch Dermatol* 1979; **115**: 703–6.
2. Chernosky ME. Squamous cell and basal cell carcinoma: preliminary study of 3817 skin cancers. *South Med J* 1978; **71**: 801–5.
3. Fisleback AJ, Sause NT, Plenk HT. Radiation therapy for skin cancers. *West J Med* 1980; **133**: 379–82.
4. Patterson JAK, Geronemus RG. Cancers of the skin. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer principles and practice of oncology*, 3rd edn. Philadelphia: Lippincott 1989: 1469–98.
5. Guthrie TH, McElveen LJ, Porubsky ES, *et al.* Cisplatin and doxorubicin. An effective chemotherapy combination in the treatment of advanced basal cell and squamous carcinoma of the skin. *Cancer* 1985; **55**: 1629–32.
6. Guthrie TH, Porubsky ES, Luxenberg NM, *et al.* Cisplatin-based chemotherapy in advanced basal and squamous cell carcinomas of the skin: results in 28 patients including 13 patients receiving multimodality therapy. *J Clin Oncol* 1990; **8**: 342–6.

(Received 30 June 1992; accepted 14 July 1992)