Brain metastasis from cutaneous squamous cell carcinoma of the dorsum

Case report

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Central nervous system metastases involve common lesions that originate, in order of frequency, from lung carcinoma, breast carcinoma, melanoma, and lymphoproliferative disease.11,18,19,23 Brain metastasis from cutaneous SCC is extremely rare. Cutaneous SCC tends to invade regional structures, so that secondary brain involvement has always been described as the result of a head or face SCC dissemination.1,3,15,20,21,25 To our knowledge, the case described here is the first of distant brain metastasis from skin SCC. Although cutaneous SCC rarely spreads to the brain, its incidence is increasing. This fact prompted us to describe this particular case.

Case Report

History. In December 2002 this 54-year-old man presented to a dermatologist for a recent ulcerated skin lesion in his dorsum (Fig. 1A). His medical history was negative. The lesion was excised completely. Results of a histopathological examination of the lesion were positive for moderately differentiated SCC and demonstrated a tumor size and thickness of 50 mm and 8.5 mm, respectively (Fig. 1B–D). There was no perineural or vascular invasion. A sentinel lymph node biopsy and imaging studies (ultrasonography and CT scanning) revealed no evidence of metastatic disease. The tumor stage was T2N0M0. Follow-up examinations displayed no local recurrence of the dorsum tumor.

Examination and Treatment. In November 2003 the patient presented to our institution with headache, vomiting, and ataxia. A Gd-enhanced magnetic resonance image documented a cerebellar lesion, which was totally removed. Results of histological studies revealed SCC. The patient received whole-brain radiotherapy (30 Gy over 2 weeks using a linear accelerator). A metastatic work-up showed enlarged inguinal and para-aortic lymph nodes that were histologically examined using excisional biopsy. Inguinal lymph nodes were tumor-positive and were dissected. The patient was subjected to two cycles of chemotherapy with cisplatin (75 mg/m²). After 3 months, a significant reduction in the size of the para-aortic lymph nodes was documented on control computerized tomography studies. Although the described case is unique, knowledge of the potential for this uncommon behavior in cutaneous SCC may be useful, especially because of its increasing incidence.

Discussion

Primary SCC is a malignant tumor arising from the kera-
tinizing cells of the epidermis or its appendages.1,16 This lesion is the second most common skin tumor. In European countries, the annual incidence of SCC is approximately 25 cases/100,000 people.3 Australia has the highest incidence in the world: more than 300 cases/100,000 population.22 Although most patients with primary skin SCC have a good prognosis, survival in patients with metastatic disease is poor.27 Tavin and Persky24 analyzed 31 patients with metastatic disease from cutaneous SCC. During the mean follow-up period of 49 months, 11 (35%) of these 31 patients died of the disease. Recurrence of the primary tumor appeared to increase the risk for nodal and distant metastases. The most common sites of metastasis from cutaneous SCC are regional lymph nodes.26 Some Australian studies have indicated a nodal metastatic rate of approximately 5%.7,13 Metastatic brain SCC from cutaneous lesions is extremely rare, with very few reported cases.1,2,4,5,8,10,15,20,21,24,25 To our knowledge, cerebral metastasis from cutaneous SCC has been described only in cases with primary localization in the skin of the head or face.1,2,4,5,8,10,15,20,21,24,25 The present report represents the first case with a distant primary SCC. Perhaps patients affected by SCC die of the primary disease before cerebral metastasis manifests itself given that SCC typically involves elderly patients. This hypothesis may be a plausible explanation for the rarity of brain metastasis from SCC. Nevertheless, perhaps physician awareness of this complication and the rising incidence of SCC will increase the number of reported cases of distant cerebral metastasis from SCC. This concept should prompt physicians to consider distant brain metastasis from SCC in the planning of future therapeutic protocols and campaigns against excessive exposure to ultraviolet rays.

Factors affecting the metastatic potential of cutaneous SCC include site of origin, size, rate of growth, origin, degree of histological differentiation, host immunosuppression, and previous treatment.1,16 Motley, et al.,16 recommend caution in interpreting data on treated SCC from reported series because the aforementioned details are often omitted. In a histopathological evaluation of SCC, Khanna, et al.,14 described the results of a survey among 120 dermatopathologists in the US and Canada. These authors concluded that histopathological reporting of SCC was not uniform and that there were different opinions on the use of some histopathological features in predicting prognosis, such as the importance of perineuronal, vascular, and lymphatic invasion; histological grade; and tumor depth. Several authors6,17 have reported a cumulative metastasis/recurrence–free survival of 98% at 3 years in patients with tumors 3.5 mm or thinner and 84% in those with tumors thicker than 3.5 mm. The patient in our study presented with all parameters indicative of a poor prognosis: moderately differentiated and infiltrative SCC, tumor thickness of 8.5 mm, and tumor ulceration. Cutaneous SCC usually shows its invasiveness with direct extension or local metastases. In the latter condition, the tumor spreads by the lymphatic, perineural, or vascular route. In the patient in our case, cerebral metastasis was distant from the primary tumor. Distant metastases to the central nervous system are usually associated with widespread dissemination of the disease. In our case, brain and inguinal and para-aortic lymph node involvement were the only
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Fig. 2. Axial (A), coronal (B), and sagittal (C) magnetic resonance imaging sections revealing a cerebellar lesion with ring enhancement. D: Photomicrograph of a cerebellar lesion with features typical of SCC. Original magnification × 20.

known metastatic locations. Thus, it is evident that the cerebral metastasis was the result of a direct hematogeneous spread without seeding in the lungs, liver, or bones. Exclusion of these organs can be explained by the hypothesis that the neoplastic cells have more affinity for some tissues rather than others. Researchers who have focused on the mechanisms of tumor metastases posit that distant metastases are site-specific lesions that occur when the appropriate series of growth and inhibitory factors at distant sites favor tumor migration and implantation.

There are no randomized, controlled trials for the treatment of primary and metastatic SCC. Patients with aggressive SCC should be followed by a multiprofessional oncological team including an oncologist, a dermatologist, and an appropriate surgeon. Complete removal of the primary tumor and any metastases is the goal of treatment. In a study on treatment results of regional metastasis from cutaneous head and neck SCC, Jol, et al., found no survival difference between patients treated using surgery alone and those receiving adjuvant radiotherapy. De Bree, et al., conducted a retrospective analysis of 13 patients with intracranial metastasis from SCC of the head and neck. These authors concluded that radiotherapy may improve survival time, but prognosis remains poor. Our choice to treat cerebral SCC metastasis with radiotherapy has been dictated by general indications of treatment of brain metastases. Chemotherapeutic protocol for SCC remains to be defined. The oncologist treated the patient in the present case with cisplatin given the aggressive behavior of the tumor.

Conclusions

This report should alert the physician to the possibility of cerebral metastasis in patients with distant primary cutaneous SCC. Although the incidence of cerebral metastasis from cutaneous SCC is very low, its occurrence should be remembered because of the increasing incidence of skin SCC.

References

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