Metastatic Zosteriform Squamous Cell Carcinoma in an Immunocompetent Patient

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Abstract

Background: Although described in several reports of internal malignancies metastasizing to the skin, zosteriform metastases have been reported in only two cases of cutaneous squamous cell carcinoma (SCC). In both of these reports, the patients were immunosuppressed related to renal transplantation.

Objective: We present a case of an immunocompetent patient with zosteriform metastases originating from a recurrent cutaneous SCC. The lesions were present along the maxillary division of the trigeminal nerve.

Methods: Biopsies from eight lesions were studied using hematoxylin and eosin (H&E) and with immunohistochemistry.

Results: Neural involvement was detected in H&E preparations before and during excision of the metastatic nodules by Mohs micrographic surgery. The tumor cells reacted with antikeratin antibodies. The patient has had no evidence of recurrence or metastases 30 months following surgery.

Conclusion: To our knowledge, this is the first case of cutaneous SCC with zosteriform metastases in a patient with an intact immune system. SCC should be included in the differential diagnosis of lesions presenting in a dermatomal distribution.

Sommaire

Antécédents: Bien qu'elles aient été décrites dans plusieurs rapports sur les tumeurs malignes qui se métastasent au niveau de la peau, les métastases zostériformes n'ont été rapportées que dans deux cas de carcinomes squameux (CS). Dans ces deux cas, les patients étaient immunodépressifs à la suite d'une transplantation rénale.

Objectif: Nous présentons le cas d'un patient immunocompétent souffrant de métastases zostériformes provenant de CS récurrents. Les lésions se trouvaient dans la branche maxillaire du nerf trijumeau.

Méthodes: Des biopsies de huit lésions ont été étudiées au moyen d'une coloration à l'hématoxyline–eosine (HÉ) et par immunohistochimie.

Résultats: La lésion neuronale a été détectée grâce à la coloration HÉ avant et durant l'excision des nodules métastatiques au moyen de la chirurgie micrographique de Mohs. Les cellules tumorales ont interagi avec les anticorps anti-kératines. Trente mois après la chirurgie, le patient ne présentait aucune récurrence ni métastase.

Conclusion: À notre connaissance, il s'agit du premier cas de CS avec métastases zostèriformes chez un patient ayant un système immunitaire intact. Les CS doivent être inclus dans le diagnostic différentiel des lésions présentes dans les distributions dermatomales.

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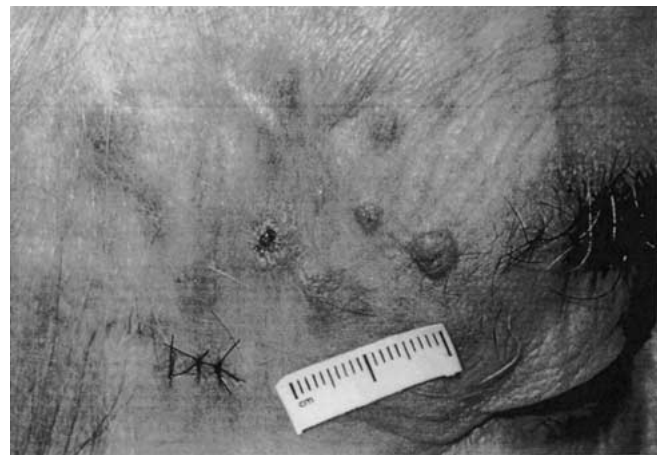
An 83-year-old Caucasian woman was referred for evaluation and treatment of a recurrent squamous cell carcinoma (SCC) on the right temple. Past medical history was significant for hypertension and hypothyroidism. There was no history of immunosuppression. In February 1998 the original 1.1 cm × 1.0-cm lesion had been excised by a dermatologist. The pathology report at that time indicated a moderately differentiated SCC with negative margins and no evidence of neural involvement.

When seen in early June 1998, there was an ill-defined linear scar, measuring approximately 2.5 cm × 0.2 cm, on the right temple which was surrounded by eight firm nodules (Fig. 1), with a ninth nodule on the right temporal-frontal scalp. The lesions varied in size from 4 to 6 mm. None of the nodules was contiguous with the scar. The distance between the scar and the nodules ranged from 0.5 to 2.5 cm. There was no complaint of pain, paresthesia, or dysesthesia in this area and no detectable clinical involvement of regional lymph nodes.

FIGURE 1 Ill-defined scar surrounded by seven satellite nodules (arrows) and a biopsy site from previous nodule.



Histopathology

Biopsies of the eight temple nodules and the scalp lesion show similar histologic features. Hematoxylin and eosin (H&E) of each lesion revealed a proliferation of pleomorphic spindle cells in the dermis (Fig. 2A and B). The tumor was present around cutaneous nerves in the largest temple lesion biopsied (Fig. 2C), as well as in the subsequent biopsies of the remaining lesions. In addition, significant perineural inflammation was present in several of these sections (Fig. 2D). A panel of immunohistochemical stains was performed. Cytokeratin stain was strongly positive (Fig. 2E). HMB-45, S-100, and vimentin stains were negative.

Clinical Course

The temple and scalp lesions were treated by excision of the involved area with Mohs micrographic surgery. Neural involvement was noted in a Mohs surgery section from the scalp lesion. Excision of three tissue layers was needed to reach a tumor-free level in the temple area, and the final defect was 7.0 cm × 6.6 cm (Fig. 3). The scalp lesion was cleared after excision of two layers, and the final defect was 2.6 cm × 2.1 cm (Fig. 4). An advancement flap was used to repair the temple defect (Fig. 4), and the scalp site was closed primarily. Despite potential benefits of adjuvant radiation therapy, after discussing logistical difficulty we decided against local radiation. She was last seen in December 2000, 30 months after first presenting to us without any signs or symptoms of local or regional recurrence.

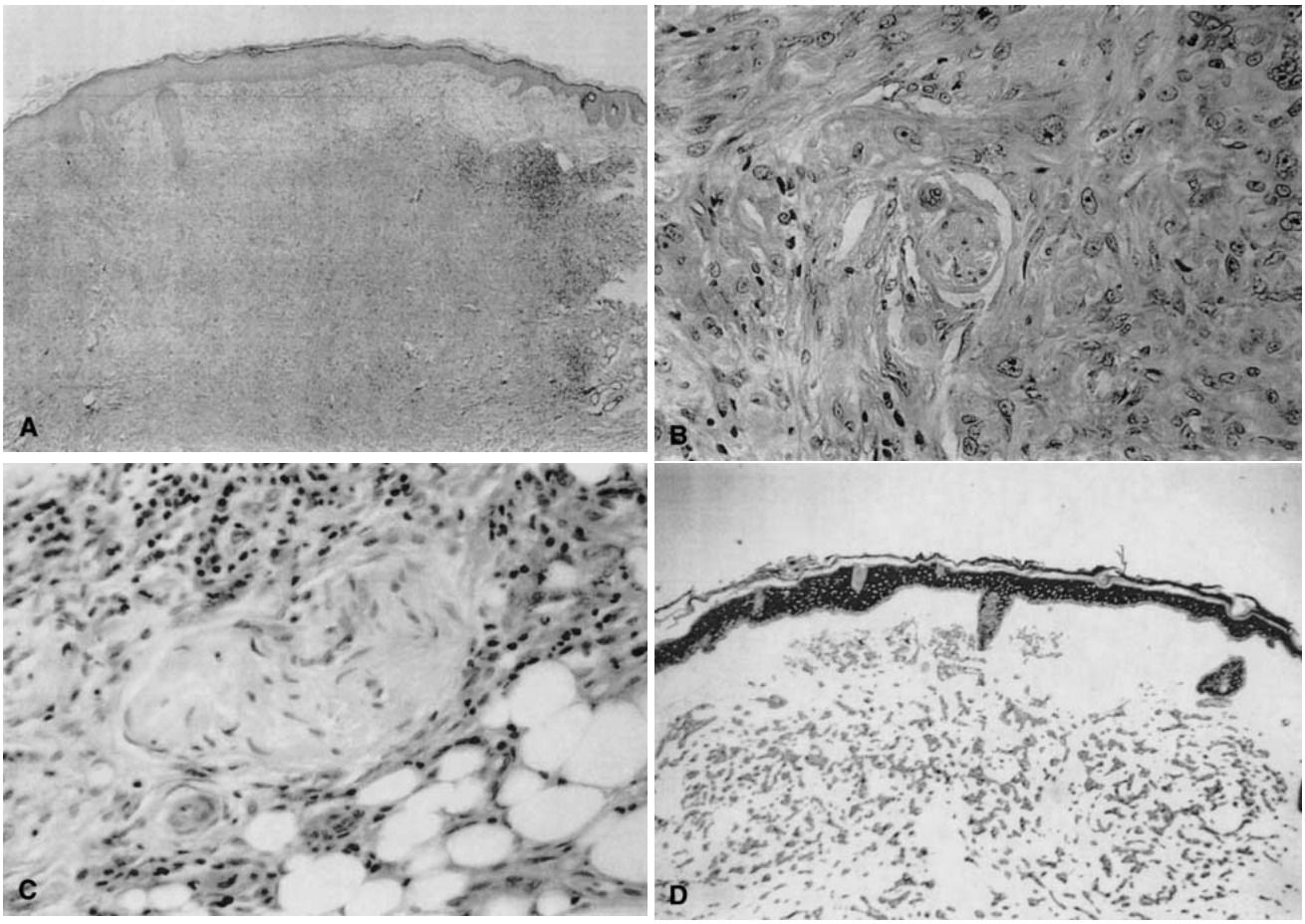
Discussion

A zosteriform distribution of cutaneous metastases has been described in cutaneous SCC only twice[1,2] In both instances, the patients were immunosuppressed due to renal transplantation. This pattern, though still rare, has been described in several reports of internal malignancies metastasizing to the skin, including adenocarcinomas of the breast[3], prostate[4], and lung[5,6] as well as transitional cell carcinoma of the bladder[7].

In our patient, given this zosteriform distribution and the histologic evidence of perineural invasion, it appears that the spread took place via neural extension. The presence of metastases along the distribution of the zygomaticotemporal branch of the maxillary division of the trigeminal nerve is in accordance with this likely mode of spread. In the two previous reports of primary cutaneous SCC with this distribution occurring in immunosuppressed patients, the presence or absence of perineural invasion was not documented. In at least three of the reports of zosteriform occuring in patients with primary internal malignancies [3,6,7], tumoral invasion of a dorsal root ganglion or nerve was suspected.

Perineural invasion in cutaneous SCC has been reported to have an incidence of 2% – 14%,[8–10] with recurrent tumors having incidences at the higher end of these figures[11] Based on several large studies, Rowe et al.[12] believe the overall incidence of neurotropism in cutaneous SCC is 3.7%. Reports have shown a worse prognosis with a lower 5-year survival rate in these neurotropic cases [8,13]. The nerves with the highest rates of involvement are the peripheral branches of the trigeminal and facial nerves, with one study specifying the maxillary division of the trigeminal nerve to account for 47.2% of cases[8]. It is noteworthy that this study by Goepfert et al[8] also reported a higher incidence of neural invasion in spindle cell SCC (and a high number of patients with lymph node and distal metastases), the subtype present in our patient. However, Lawrence and Cottell[16] had 44 patients with no cases exhibiting the spindle cell variant. The two reports[1,2] of metastatic

FIGURE 2 (**A**) Low-power view (H&E) of tumor showing diffuse infiltrate of atypical epithelioid cells. (**B**) Atypical squamous cells (H&E) are present around small cutaneous nerves. (**C**) Perineural lymphoplasmocellular inflammation (H&E) is also identified. (**D**) Cytokeratin stain is strongly positive.



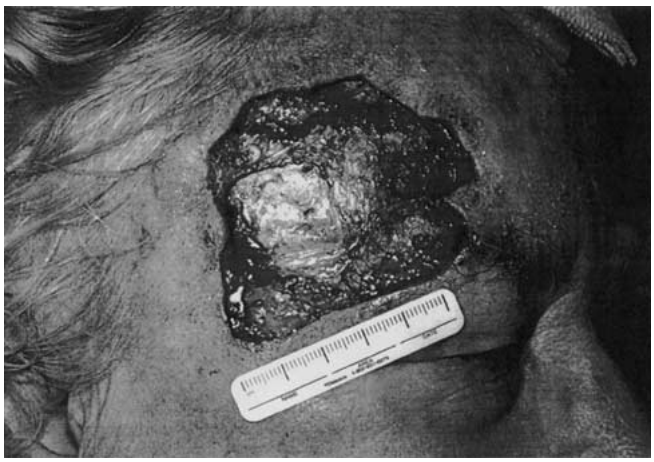
zosteriform SCC in transplant recipients did not document the subtype of SCC, although the report by Buecker and Ratz shows an H&E picture of well-differentiated keratinizing SCC.

As there are only two cases noted in the English-language literature with zosteriform metastases from cutaneous SCC, minimal data exist as to the most effective treatment. The first immunosuppressed patient died several weeks after diagnosis, prior to any treatment of these specific lesions, and autopsy revealed metastasis of SCC in the right lung[2]. In the more recent report[1], neither the treatment nor outcome of the patient was described. Extrapolating our case to cases of SCC with perineural invasion, a report by Lawrence and Cottel[16] suggests Mohs surgery is the treatment of choice for SCC with perineural involvement, finding an 88.7% survival rate. Reports employing conventional surgical excision have previously documented less than 30% survival[8] and cure rates[13]. A report from the head and neck oncology literature of combining surgical excision with radiotherapy for SCC with perineural invasion found a recurrence rate as high as 60%[17]. The SCCs in the study had additional risk factors for recurrence including invasion of cartilage or bone.

As Bernstein et al[18] point out in their review, many tumors with perineural invasion display other risk factors such as greater tumor size, depth, recurrence, or high-grade histology. Johnson et al[19]. report that recurrent tumors are often larger and deeper than the primary SCC, and such recurrent neurotropic tumors can carry a 25% overall metastatic rate.

In the study by Lawrence and Cottel[16], 44 patients (70% with lesions greater than 2 cm) with neurotropic SCC (56% of which had recurrent lesions) underwent Mohs surgery with three patients manifesting recurrences within 3–6 years. Rowe et al.[12] reviewed several reports comparing surgical excision versus Mohs surgery for these neurotropic cases of SCC, finding Mohs to be far superior—acknowledging, however, that these results are confounded by the fact that radiation was used in combination with each modality in several cases. Mohs surgery in combination with radiotherapy was used in a study of seven patients with neurotropic SCC, with report of a 100% cure in three patients with primary dis-

FIGURE 3 Temple area after Mohs micrographic surgery.



ease and a 50% cure in four patients with recurrent disease 18–28 months following treatment.[20]

Taking the results of both the Lawrence and Cottel[16] and Barrett et al.[20] studies into account, a controlled study (stratifying the variables that Bernstein et al.[18] highlight) comparing Mohs surgery alone to Mohs. surgery with adjuvant radiotherapy is needed to determine the most effective treatment for SCC with perineural invasion.

In summary, to our knowledge this case represents the first report of a cutaneous SCC with zosteriform metastases in a patient with an intact immune system. It appears that the spread took place via neural extension. The presence of metastases along the distribution of the zygomaticotemporal branch of the maxillary division of the trigeminal nerve is in accordance with this likely mode of spread. Our patient's 30-month recurrence-free postoperative course thus far following Mohs surgery is in accordance with the findings of the most recent report on the management of patients with cutaneous SCC demonstrating perineural involvement of peripheral nerves.[16] It is felt that SCC should be included in the differential diagnosis of lesions presenting in a dermatomal distribution.

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