

### Skin Acrometastases in Squamous Cell Carcinoma of the Tongue

From July 2003 to February 2004, a 66-year-old man with a diagnosis of squamous cell carcinoma of the tongue and concomitant lung metastases was submitted to locoregional radiotherapy and systemic chemotherapy with the combination of cisplatin and continuous infusion of fluorouracil for six cycles, obtaining a complete clinical response. On August 2006, because of a progression of disease in the lung, the patient started second-line chemotherapy with a combination of taxol and carboplatin for three cycles. On December 2006, the

computed tomography scan showed an increase in number and dimension of the lung lesions. Based on these data, on January 2007, we started a new systemic therapy with weekly methotrexate. After only 3 weeks of treatment, the patient was hospitalized for the rapid onset of two bleeding skin lesions—one in the left cheek (Fig 1A) and the other one on the fourth toe of the left foot (Fig 1B). Objective examination documented an exophytic and ulcerated skin lesion located at the bottom in the left cheek, with a diameter of  $3.0 \times 2.0$  cm, without pain and infiltrative signs of deeper tissues, and another lesion, with a bleeding ulcer of the superficial skin, located at the acral extremity of the fourth toe of the left foot. A few days after the hospitalization,

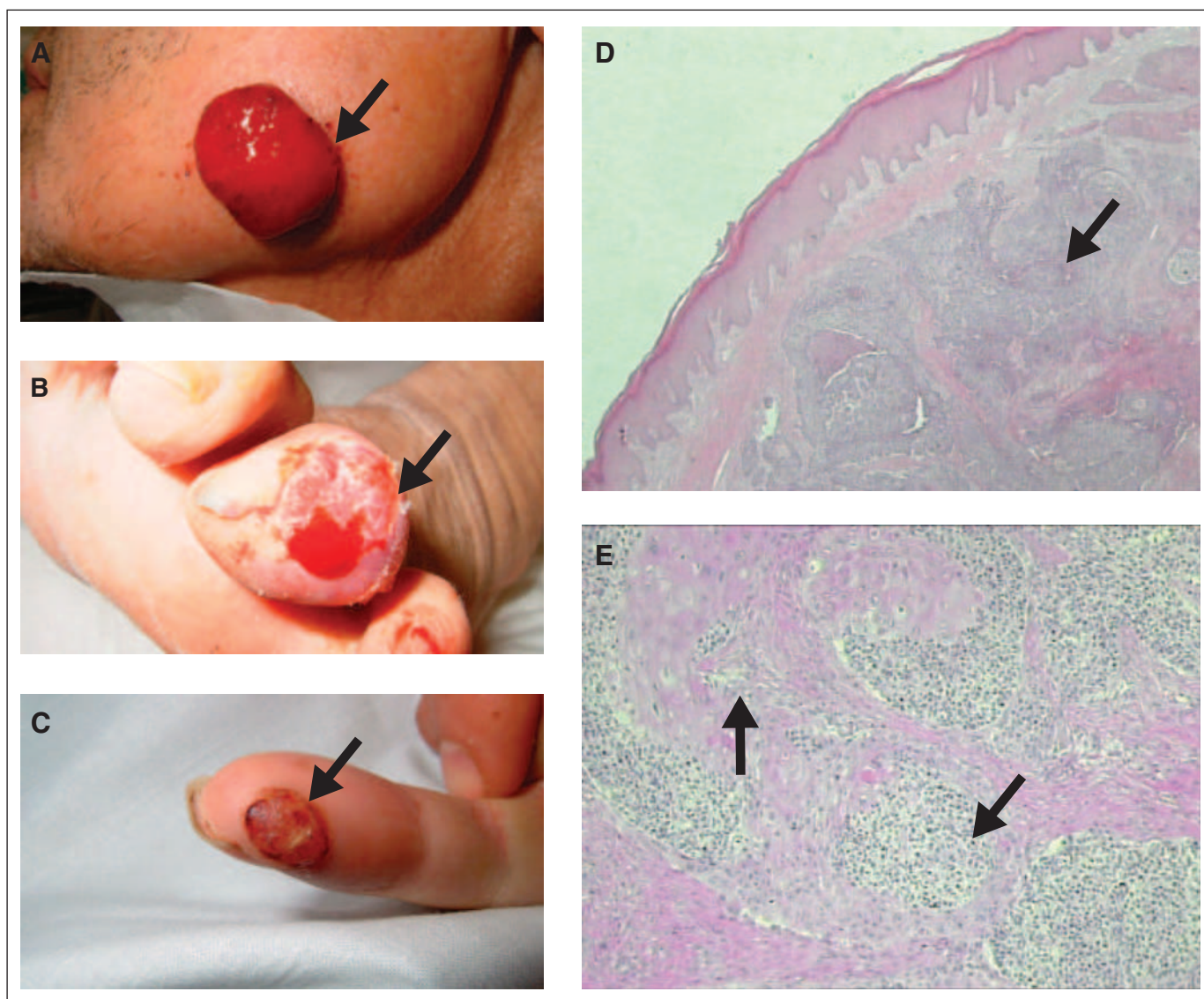


Fig 1.

another ulcerated skin lesion was observed at the fifth finger of the left hand (Fig 1C). Blood chemistry, leukocyte count, hematocrit, and ECG were in the normal ranges. Computed tomography scan documented disease stabilization in the lung without new metastases in other organs. Considering the continuous bleeding, the patient underwent surgical resection of the cheek and fifth finger lesions and amputation of the fourth toe. Histologic examination showed squamous tumor cells infiltrating the dermis and the subcutaneous tissue (Fig 1D,  $\times 10$ , arrow). At a major enlargement (Fig 1E,  $\times 40$ ), tumor cells presented two different components: one poorly differentiated (left arrow) and the other one well differentiated, with formation of structures similar to keratin pearls (right arrow). The patient was managed with antibiotics for 5 days and discharged.

Cutaneous metastases are infrequent with an overall incidence of 5.3%<sup>1</sup> and, in some cases, represent the first manifestation of an unknown neoplasm. The most frequently observed cutaneous metastatic cancers are breast, colon, and melanoma in women and lung, colon, and melanoma in men. Cutaneous metastatic disease as the first sign of internal cancer is most commonly seen with cancer of the lung, kidney, and ovary. Cutaneous involvement is also seen in the leukemias, with a wide variation in morphology of lesions.<sup>2</sup> Acral located metastases are particularly rare, and the prognosis is very poor, with a survival time of only a few months. Although the clinical presentation varies, they are generally confused with an infectious or inflammatory process, which delays the diagnosis. When they are located on the fingers, the most frequent cause is lung carcinoma, whereas those of the toes are usually due to genitourinary tumors. In most acrometastases, first the bone and then the skin are affected. Treatment is palliative and includes surgical resection or amputation.<sup>3</sup> The incidence of distant metastases in squamous cell carcinoma of the tongue is relatively small as compared with other malignancies, and it is influenced by location of the primary tumor, initial stage, and the presence or absence of locoregional control. The most frequent metastatic sites include lung (66%), bone (22%), and liver (10%).<sup>4-6</sup> Skin metastases are exceedingly rare, with only a few cases reported in the literature. They present as solitary or multiple, discrete or confluent, and dermal or subcutaneous nodules discontinuous from the epidermis. They may also be ulcerated or necrotic and can spread by three modalities: direct spread, local spread via dermal lymphatics, and distant spread via the hematogenous route. The principal sites include neck, chest,

scalp, face, lips, axilla, areolas, back, arms, and digits—the most common being the neck and chest.<sup>7</sup> Skin metastases may represent the first clinical evidence of impending locoregional recurrence, suggest distant metastatic spread, or rarely, be the first sign of a silent tumor. They are usually associated with a poor prognosis and most often affect the supradiaphragmatic area. Treatment for skin metastases is inconclusive. Surgical treatment is not the norm and should only be considered in a few highly selective cases. In general, the treatment, irrespective of the form, is only palliative. Our case presents at least two interesting and unusual clinical aspects, the first being the very rapid cutaneous spread of metastases, in less than 1 month. The other one is the observation of a selective tumor spreading to skin tissues, compared with a documented stable disease in the lung, suggesting a particular and very infrequent dermatotropism of this tumor.

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#### AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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## Glioblastoma in a Patient With Early-Stage Tonsil Cancer

A 58-year-old man was referred to the multidisciplinary head and neck clinic with a right tonsil squamous cell carcinoma diagnosed after routine dental examination revealed right tonsillar ulceration. The patient was a lifelong nonsmoker and drank alcohol sparingly. There was no family history of cancer. Physical examination was notable for a right upper tonsil mass infiltrating into the soft palate. There was no trismus, and palate movement was normal. There was no palpable adenopathy. Biopsy showed a well-to-moderately differentiated squamous cell carcinoma. Polymerase chain reaction was positive for human papilloma virus (HPV16), and immunohistochemistry was negative for p16. Chromogenic in situ hybridization (CISH) demonstrated four to six epidermal growth factor receptor (EGFR) copies per nucleus in tumor cells. Evaluation of the oropharynx by neck com-

puted tomography was limited by dental artifact, and small, bilateral cervical lymph nodes smaller than 6 mm in size were present. Positron emission tomography/computed tomography demonstrated intense fluorodeoxyglucose uptake in the right tonsillar region only. Magnetic resonance imaging (MRI), performed to evaluate the extent of the primary or oropharyngeal tumor, showed a 2.4  $\times$  1.6  $\times$  2.0 cm-enhancing mass arising from the right tonsil (Fig 1A). Incidentally, a 1.4-cm ring-enhancing lesion in the anterior left temporal subcortical white matter was noted (Fig 1B). A dedicated brain MRI was performed, confirming the presence of a solitary left temporal mass.

A left craniotomy for gross total resection of the left temporal mass was performed. Microscopically, the mass had atypical, pleomorphic cells with hyperchromatic nuclei, scattered mitoses, vascular proliferation, and pseudopalisading necrosis, consistent with glioblastoma multiforme (GBM), WHO grade 4/4 (Fig 2). CISH for EGFR demonstrated high-level amplification ( $> 10$  signals per nucleus) in rare cells. Next, the patient underwent resection of