Cutaneous squamous cell carcinoma responding serially to single-agent cetuximab

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Cetuximab (Erbitux®) is a recombinant, chimeric monoclonal antibody that binds with high affinity to the extracellular ligand-binding domain of human epidermal growth factor receptor. We report a case of repeated responses to cetuximab in a patient with nonresectable squamous cell skin cancer having strong human epidermal growth factor receptor expression. Nonmelanoma skin cancer is the most common cancer in the US, with more than 1 million new cases detected annually, of which 20–25% are squamous cell carcinomas. Although most primary cutaneous squamous cell carcinomas have a high clinical cure rate and are easily treated, the small subset of cancers that recur or metastasize has a poor prognosis, and accounts for approximately 2000 deaths per year. Treatment with cetuximab should be considered for human epidermal growth factor receptor expressing tumors in a palliative setting. *Anti-Cancer Drugs* **18:827–829 © 2007 Lippincott Williams & Wilkins.**

Anti-Cancer Drugs 2007, **18**:827–829

Keywords: cetuximab, cutaneous, human epidermal growth factor, skin cancer, squamous cancer

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Received 12 December 2006 **accepted** 12 January 2007

Introduction

We report a case of successive significant responses to cetuximab in a patient with nonresectable squamous cell skin cancer.

An 87-year-old man with numerous medical comorbidities including peripheral vascular disease and chronic renal insufficiency was referred to our clinic for a recurrent cutaneous squamous cell carcinoma (SCC) in the sternal chest. Four years before presentation to our clinic, he had surgical removal of a $7 \times 6 \times 2\,cm^3$ left temporal cutaneous mass with positive margins. Pathology demonstrated poorly differentiated SCC (Fig. 1a) and a lymph node with a focus of small lymphocytic lymphoma. He received postoperative radiotherapy of 45 Gy to the left temporal lesion with concurrent treatment of 36 Gy directed at the left preauricular lymph node.

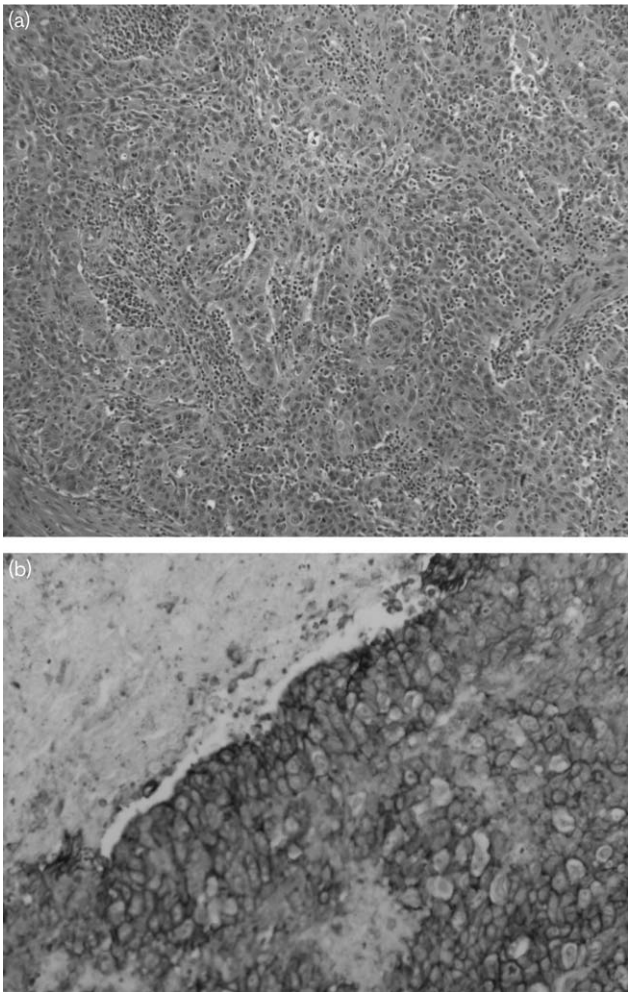
Seven months after radiotherapy, he presented with a new localized 1.5-cm left submandibular mass. Biopsy of this new lesion demonstrated poorly differentiated SCC. The patient received 70 Gy using intensity-modulated radiation therapy to the left submandibular mass and neck. Following intensity-modulated radiation therapy, surgical exploration and biopsies demonstrated no residual malignancy.

One and a half years later, the patient presented with a new $5.5 \times 5\text{-}cm^2$ mass extending from the left clavicular head to the base of the neck. The mass was fixed and tender with no associated lymphadenopathy. He completed a course of palliative intensity-modulated radiation therapy at a dose of 35 Gy, resulting in reduction of the mass.

Six months later, the patient presented to our clinic with an inoperable, rapidly growing $5.5 \times 6\text{-}cm^2$ cutaneous bilobular midline mass over the sternum. Treatment was limited to palliative therapy and we initiated treatment with single-agent cetuximab, based on recent evidence of epidermal growth factor receptor (EGFR) expression in primary cutaneous SCC [1,2]. EGFR testing on our patient's original tumor demonstrated strong 3+ membranous expression (Fig. 1b). No EGFR testing was performed on recurrent tumor owing to the use of fine-needle aspiration as the method of diagnosis and lack of sufficient tissue for further studies. Cetuximab was administered at a loading dose of $400\,mg/m^2$IV, followed by weekly infusions of $250\,mg/m^2$IV. He tolerated cetuximab therapy well without adverse events, including acneiform rash. After the seventh weekly dose, a complete clinical response was achieved. Cetuximab therapy was discontinued at that time.

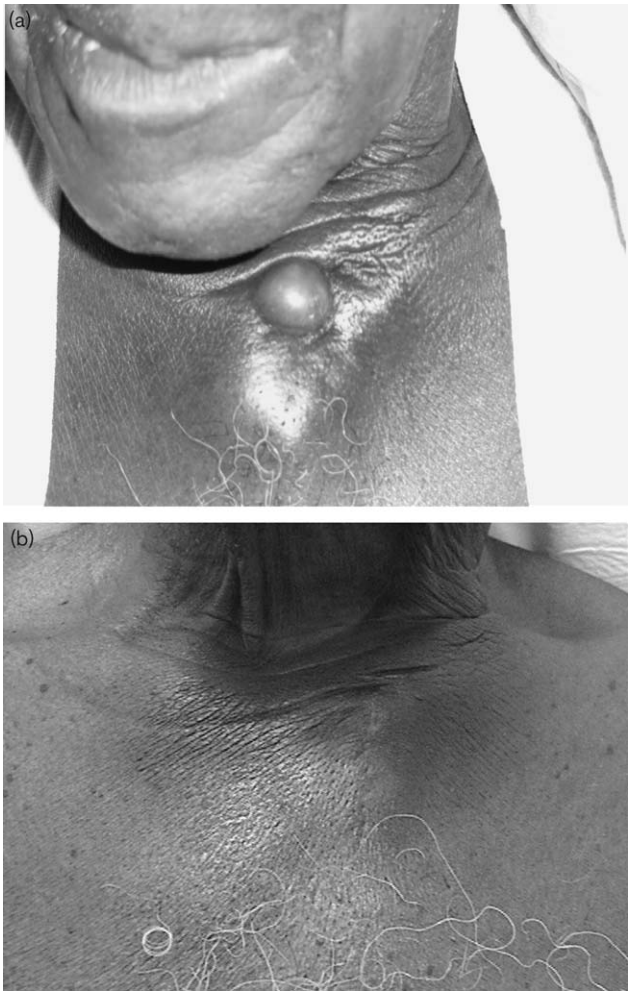
One month after discontinuation of cetuximab, cancer recurred at the midline of the sternum and invaded the clavicle. An enlarging area of induration and inflammation surrounded the tumor (Fig. 2a). Cetuximab was promptly reinitiated at the same weekly dose without a loading dose. After seven infusions, he again achieved a complete

Fig. 1



(a) Pathologic finding from the resected cutaneous mass showing poorly differentiated squamous cell carcinoma hematoxylin and eosin. (b) Epidermal growth factor receptor staining demonstrating 3+ membrane staining.

Fig. 2



(a) Rapid and aggressive recurrence of the tumor after cessation of the first seven doses of cetuximab single-agent therapy. (b) Recurrent lesion shows clinical response to another 7 weeks of cetuximab therapy.

clinical response (Fig. 2b). He continued to respond to weekly treatments, but after 2 months he became refractory to cetuximab. He then received single-agent IV fluorouracil (600 mg/m^2/day) for 5 days every 2 weeks. The dose in the second and final cycle was reduced to 450 mg/m^2/day owing to grade 2 oral mucositis and fatigue. Disease progression was noted on re-evaluation and a decision for comfort care was made. He died 4 weeks later.

Discussion

To our knowledge, this is the first clinical report to demonstrate anticancer activity of single-agent cetuximab in recurrent SCC of the skin. Although most primary cutaneous SCCs present with localized disease and have a high clinical cure rate, a small subset have a poor prognosis causing 2000 deaths per year in the US [3,4]. Systemic chemotherapy is reserved for when local therapies fail; however, no regimen is considered the standard in this setting. Cetuximab has demonstrated anticancer activity in EGFR-expressing squamous tumors of the head and neck and lung cancers [5–7]. Cetuximab was chosen for our patient based on this information, and in view of his advanced age and numerous comorbidities.

In summary, this case illustrates anticancer activity of cetuximab in squamous cell cancer of the skin with strong EGFR expression. This therapy should be considered as an alternative to traditional cytotoxic therapy.

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