

## Management of oral adverse effects related to cetuximab plus radiotherapy

Danilo da Silva Corrêa <sup>1</sup>  
Thaís Feitosa Leitão de  
Oliveira <sup>1</sup>  
Paulo Sérgio da Silva Santos <sup>1\*</sup>

### Abstract:

Squamous cell carcinomas of head and neck have an incidence of more than five hundred thousand cases a year worldwide. The standard treatment of this condition consists of platinum-based chemotherapy and radiotherapy. Nevertheless, in case of advanced age or reduced general condition the chemotherapy agent utilized is Cetuximab, a molecular targeted drug, used for metastatic colorectal cancer and head and neck cancer. Adverse effects associated with Cetuximab can be potentiated by the radiotherapy leading to oral mucositis and skin toxicities. We report a case of a 70-year-old caucasian woman who had removed a gingival squamous cell carcinoma at the left side of the mandible. During intensity modulated radiotherapy and Cetuximab chemotherapy she began to develop severe oral mucositis and perioral and neck skin toxicities. The pain associated with the oral mucositis prevented the patient from eating, causing a break in radio and chemotherapy. The treatment with systemic and topical medications and low-level lasertherapy was applied. The patient tolerated well the treatment and fifteen days after it began, radio and chemotherapy was reinitiated and concluded with no more adverse effects. It is important to the medical team to be aware of it, since the early identification and treatment of its signs and symptoms reduces the risks of breaks in the treatment and provides better quality of life to these patients.

**Keywords:** Antibodies, Monoclonal, Humanized; Cetuximab; Drug-Related Side Effects and Adverse Reactions; Mucositis.

<sup>1</sup> Universidade de São Paulo.

**Correspondence to:**  
Universidade de São Paulo.  
Al. Dr. Octavio Pinheiro Brisolla, 9-75, Vila  
Universitária, Bauru, São Paulo, Brazil.  
E-mail: paulosss@fob.usp.br

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## INTRODUCTION

Squamous cell carcinomas of head and neck have more than five hundred thousand cases a year worldwide<sup>1</sup> and an increasing number of these patients are 65 years old or more<sup>2</sup>. Cetuximab is a molecular targeted drug highly selective for the epidermal growth factor receptor (EGFR) used for the treatment of metastatic colorectal cancer and head and neck cancers in patients who cannot receive standard platinum-based chemoradiation due to advanced age or reduced general condition<sup>1,3</sup>.

The EGFR is a transmembrane receptor involved in cell proliferation, cycle regulation, angiogenesis, cell migration, invasion, and in metastases. Overexpression of this receptor is often present in squamous cell carcinomas of the head and neck and is associated with a poor prognosis.<sup>1</sup> When cetuximab is administered simultaneously with radiotherapy, an overlap of radiation and cetuximab induced skin reactions is seen in the radiation field which may lead to very severe skin toxicity<sup>1</sup>.

Adverse effects related to the combination of radiotherapy with cetuximab in the treatment of head and neck cancers, like skin toxicities and infusion reactions are well reported<sup>1,4-6</sup>. However, less attention has been paid to oral mucosa toxicities<sup>7</sup>. These toxicities reduce patients' quality of life due to pain and difficult to eat, and are also related to increased morbidity caused by a reduction of dose, break or even stop of radio and chemotherapy<sup>8</sup>.

## CASE REPORT

We report a case of a caucasian 70-year-old woman who underwent intensity-modulated radiation

therapy (IMRT - 30 cycles with a total dose of 6000 cGy) concurrent with cetuximab (first cycle of 400 mg, three cycles of 250 mg, and one last cycle of 187 mg) for the treatment of a resected gingival squamous cell carcinoma at the left side of the mandible.

The patient also received as supportive drugs ondasetron (16 mg/cycle), dexamethasone (12 mg/cycle), diphenhydramine (50 mg/cycle), and magnesium sulfate 20% (10 mg/cycle). After the fifth cycle of chemotherapy, the patient began to develop oral mucositis with several ulcers in tongue, buccal mucosa, and lips. She also presented severe trismus, dermatitis with intense erythema at the neck and perioral skin (Figure 1 A-B).

The pain associated with the lesions prevented the patient from eating and talking causing a break in the radio and chemotherapy cycles. Therefore, this condition was immediately treated with dexamethasone (4 mg every 12 hours, for 5 days), acetaminophen with codeine (30 mg every 12 hours, in case of pain), and topical mometasone fuorate for the skin lesions (every 12 hours, for 10 days).

Concurrently with drug therapy the patient underwent daily intraoral low-level laser therapy (AsGaAl, 660nm, 6j/cm<sup>2</sup>) for the oral mucositis<sup>9</sup>. Also, it were prescribed HPA lanolin to protect perioral skin and lips (6 times/day)<sup>10</sup> and topical benzydamine HCL (1,5 mg every 4 hours, in case of pain) to analgesia effects in oral pain.

The patient tolerated well the treatment and fifteen days after its begin, the signs and symptoms diminished, and radio and chemotherapy was reintiated and finished with no more adverse events.



**Figure 1 A and B.** Cheilitis, scabs and ulcers around the mouth, lips and neck. A clear limitation of mouth opening.

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## DISCUSSION

Cetuximab plus IMRT may display significant therapeutic efficacy in patients with unresectable locally advanced and recurrent or metastatic oral squamous cell carcinoma<sup>11</sup>. But the side effects may decrease de quality of life of the patients as showed by Bibault et al.<sup>12</sup> in their study found that adding cetuximab to IMRT had a significant dermal and oral toxicity since grade 3–4 oropharyngeal mucositis occurred in 87% of the patients, with 33% of the patients requiring short-term nasogastric feeding.

This severity was observed in the patient of this case report and proper oral care with lasertherapy, topical corticosteroid and benzydamine, and lanolin on the lips and perioral region improved the patient's general health condition and was well tolerated and effective.

Beyond affecting patients' quality of life, oral adverse effects related to the use of cetuximab concurrently to radiotherapy can be life threatening due to changes in the radio and chemotherapy regimen. This condition seems to be less known, so it is important to the medical team to be aware of it, since the early identification and treatment of its signs and symptoms reduces the risks of breaks in the treatment and provides better quality of life to these patients.

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