



Cetuximab Use in Laryngeal Squamous Cells Carcinoma: A 4-Years Follow-up Case Report

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Abstract

Cetuximab in laryngeal squamous cells carcinoma: We report the case of a 68-year-old male patient who was diagnosed in July 2014 with a stage II squamous cells carcinoma of larynx. After first recurrency Cetuximab-based therapy was administered achieving a partial response without disease relapse and no G3-G4 toxicity was reported. Currently the patient continues on therapy (September-2020) [PFS 71 months].

Keywords: Squamous cell carcinoma; Cetuximab; HNT; EGFR inhibitor therapy

Introduction

Squamous Cell Carcinoma (SCC) represents 95% of head and neck cancers [1,2].

EGFR expression is common in squamous cell carcinoma [3] and it is associated with negative severe prognosis and metastasis process with a median Overall Survival (OS) ranging between 6 and 9 months in most studies [4,5].

Current Standard of Care (SOC) for locally recurrent disease and/or metastatic disease in the first line setting is platinum-based doublet chemotherapy with cetuximab a monoclonal antibody acting on EGFR preventing interaction with ligand [6,7]. Effectiveness of EGFR inhibitor in cisplatin-combined therapy 10 has been proved in many studies among which the Phase 3 extreme study showing higher overall survival in the Cetuximab harm (10.1 months vs. 7.4 in chemotherapy alone harm) as well as mPFS (5.6 months versus 3.3 months) and Response Rate (36% vs. 20%) [8,9].

This case describes the effective use of cetuximab administered in cisplatin-combined schedule and later in monotherapy in a recurrent G2 HNSCC after six years administration.

Case Presentation

A 68 years old man, smoker (40 cigarettes/day for 40 years) without familiar history for cancer presented for dysphagia and pyrexia in April 2014. During the ear-nose-throat examination a laryngeal mass was detected and in July 2014 surgery was performed consisting in supraglottic laryngectomy with bilateral latero cervical lymph node debulking. Histology revealed a 7 cm keratinizing squamous cells carcinoma G2-G3 Stage II pTNM T2, N0 (0/79), M0, R0. Tumor board decided to adopt a wait-and-see attitude.

After four months from surgery (Nov, 2015) contrast CT scan showed nodal recurrence of the malignancy.

CT findings were: Colliquative adenopathies (the largest: 4 × 3.7 cm) in the left posterior cervical space in relationship with nearby muscle groups and no vascular involvement; bilateral adenopathies of I and II level; mediastinal adenopathies of the right hilum and a lesion of the base of tongue compressing contralateral oropharynx reaching hyoid bone which caused severe dysphagia.

Other findings were ground glass opacities of the URL (Upper Right Lobe) of the lung, dysventilation areas and centrilobular emphysema probably smoking-related (Figure 1A and 1C).

Based on acute symptoms and instrumental evaluation, tumor board decided to start CDDP plus 5-Fluorouracil chemotherapy plus Cetuximab. Patient gave his consent and followed the AL-SARRAF regimen for five cycles starting in December 2014.

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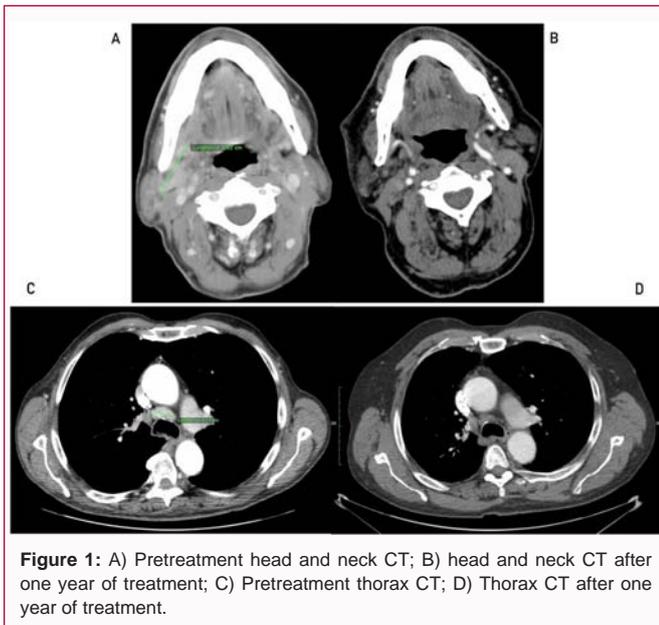


Figure 1: A) Pretreatment head and neck CT; B) head and neck CT after one year of treatment; C) Pretreatment thorax CT; D) Thorax CT after one year of treatment.

The schedule consisted in cisplatin 100 mg/m²; intravenous cetuximab 400 mg/m² for 2-h infusion (loading dose), then 250 mg/m² in 1-h intravenous infusion per week on day 1 and 5-FU 1000 mg/m² per day for 4 days, every three weeks.

After 3 cycles (Feb, 2015) CT scan showed reduction of pathologic tissue of the tongue; a hyperdense lesion appeared at the parapharyngeal space with 22 mm colliquative area; volume of first level lymph nodes appeared reduced to 15 mm in the Maximum Diameter (MD) as well as right paratracheal, subcarinal and hilar lymph nodes. Since the radiological and clinical partial response achieved and no symptoms with the exception of asthenia G1 at the beginning of the first cycle, the patient received two more cycles.

In May 2015, CT scan demonstrated a stable disease and a monotherapy treatment with weekly cetuximab 250 mg/m² (465 mg) was administered for maintenance. Checkups were conducted at every administration.

In September 2015 the follow-up CT scan showed a marked reduction of the parapharyngeal space pathological tissue but ovoid infra centimetric bilateral latero-cervical nodes were still described both in CT and in US and precarinal node remains stable (MD 15 mm). Considering the clinical benefit of the therapy, closing of the tracheostomy was performed.

In May 2016, the patient achieved his radiological best response Figure 1B and 1C in fact the CT scan demonstrated a complete response of the parapharyngeal space lesion which was no longer detectable and stable nodal disease. Since then radiological findings remain stationary for 28 months.

In September 2018 CT scan showed a slight volumetric gain of Barety Lodge (LB) and Aortopulmonary Window (APW) lymph nodes (MD 14 mm), not sufficient for declaring a disease progression.

From September 2018 until today the patient continues assuming weekly cetuximab in monotherapy with radiological and clinical stability and no signs of toxicity reaching 71 months of performance free survival.

Safety

Over the years the therapy has been well tolerated by the patient without any G3/G4 toxicity.

The only side effects reported were flu-like symptoms which led to an interruption of the weekly administration just three times in six years.

In March 2017 during a follow-up CT scan, a right jugular Deep Venous Thrombosis (DVT) was detected and treated with LMWH.

Patient experiences recurrent right epiphora with right conjunctivitis (May 2017, Nov 2017, Jan 2018, Mar 2018, July 2019, and Oct 2020) and temporary vision loss (Apr 2019). A relationship between ocular signs and symptoms and the DVT cannot be excluded. Epiphora shows a tendency towards spontaneous resolution in less than one week but since lasts two episodes resulted in bacterial sovra-infection, tobramycin plus antihistamines were prescribed with clinical benefit.

In February 2018, the patient reported wet cough, fatigue, and dyspnea. Clinical examination revealed harsh lung basis sounds and the follow-up CT scan showed a left pulmonary thickening for which a pulmonitis was suspected and Levofloxacin 500 mg 1 cp/die for 5 days was administered with clinical improvements. The next CT scan (September 2018) was negative for pulmonary thickening.

Discussion

The treatment of SCCHN is continually evolving, new agents and combination therapies utilizing drugs with different mechanisms of action become available.

In the past decade, targeted therapies have become the focus for drug research as well as the mechanism of action of biological molecules such as EGFR which plays a key role in the proliferation of solid tumors [7].

The EGFR (also known as HER1) is over expressed and/or up-regulated in most SCCHN tumors (80% to 100%); its aberrant activity plays an integral role in the growth and metastasis of solid tumors becoming a strong and independent unfavorable prognostic factor [10].

Adding cetuximab to the chemo/radiotherapy is considered effective, safe and it does not adversely affect the Quality of Life (QOL) of patients [11].

Several retrospective and observational studies have consistently confirmed the benefits of the extreme regimen in patients with first-line R/M HNSCC. There is also evidence that maintenance therapy until disease progression with cetuximab as a single agent following the extreme regimen is also well tolerated with a good compliance [12].

Some of the most common adverse reactions to the EGFR inhibitor are rash, acne, dry skin, interstitial lung disease, sepsis, hypokalemia, hypomagnesaemia, infusion reactions [13]. FDA and EMA respectively in 2016 and 2017 granted the first immunotherapeutic approval (the anti PD-1 immune checkpoint inhibitors nivolumab and pembrolizumab) for platinum-resistant tumors. Two years later FDA approved PD-1 inhibitors in the first line for unresectable, recurrent or metastatic HNSCC [14].

In our case-report cetuximab is exceptionally well tolerated, it is in fact impressive that in 71 months of treatment the patient did not

suffer from any of the above-mentioned reactions.

Immunotherapy appears to be the new frontier but EGFR-inhibitor therapy remains a cornerstone for head and neck tumors. To date, cetuximab is indeed the only target agent approved for treatment in the first line for recurrent and metastatic SCCHN by EMA.

Conclusion

In this case report, response with cetuximab was assessed as long as six years reaching a PFS >71 months (total number of administrations: 211; last administration on October 20th, 2020).

No G3-G4 toxicities were reported by our patient during EGFR-inhibitor therapy.

The only undesirable effects referred were flu-like symptoms and epiphora with conjunctivitis, the latter was probably not directly caused by the tumor; these toxicities were classified maximum as G2.

Our patient kept receiving dense dose therapy with no temporary reduction or suspension during the six year of cetuximab therapy.

In our report, cetuximab has proved to be extremely effective in disease control with very light side effects consistent with current scientific evidence for which this monoclonal antibody in association with chemotherapy represents the standard of care.

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