JOURNAL OF medical updates
www.jmedupdates.org

Case Report / Olgu Sunumu

J Med Updates 2012;2(3):124-128
doi:10.2399/jmu.2012003008

Interesting 54 months survival after platinum based induction chemotherapy regimen alone in a patient with T2N0M0 supraglottic carcinoma

T2N0M0 supraglottik karsinomda, sadece platinum indüksiyon kemoterapisi sonrası 54 aylık ilginç sürvi

Melek Kezban Gürbüz[1], Hamdi Çaklı[1], Murat Dinçer[2], Durmuş Ediz[3], Emine Dündar[4], Erkan Özüdoğru[1]

[1]*Department of Otolaryngology, Faculty of Medicine, Eskişehir Osmangazi University, Eskişehir, Turkey*
[2]*Department of Medical Oncology, Acıbadem Hospital, Eskişehir, Turkey*
[3]*Department of Radiation Oncology, Faculty of Medicine, Eskişehir Osmangazi University, Eskişehir, Turkey*
[4]*Department of Pathology, Faculty of Medicine, Eskişehir Osmangazi University, Eskişehir, Turkey*

Abstract

The conventional treatment modalities are surgery and/or radiation therapy in patients with early stage squamous cell carcinoma of the supraglottic larynx. In the literature, there are different opinions about the success of chemotherapy regimens with curative or inductive intent in patients with early stage laryngeal carcinoma. In this case report, a patient with T2N0M0 squamous cell carcinoma of the supraglottic larynx who presented with local recurrence and regional metastasis after a 54 months of non-followed period which follows two courses of cisplatinum/5-FU induction chemotherapy alone was presented. The beneficial effects of the induction chemotherapy in patients with early stage laryngeal carcinoma are doubtful. However, this regimen may be useful to estimate the possible success of radiotherapy by counseling with the patients who initially refused the conservative partial laryngectomy and with their families.

Key words: Larynx, supraglottic carcinoma, cisplatin, 5-fluorouracil, induction chemotherapy.

Özet

Erken dönem skuamöz hücreli supraglottik larenks karsinomlu hastaların geleneksel tedavi şekli cerrahi ve/veya radyoterapidir. Literatürde larenksin erken dönem kanseri olan hastalarda indüksiyon veya küratif amaçla yapılan kemoterapinin başarısı ile ilgili farklı görüşler vardır. Bu çalışmada T2N0M0 supraglottik karsinom nedeniyle önerilen cerrahi tedaviyi kabul etmeyen ve radyoterapi öncesi iki kür sisplatin-5-FU indüksiyon kemoterapisi uygulanan; ancak önerilen radyoterapiyi görmeyerek 54 ay takip dışı kalan ve sonrasında lokal nüks ve bölgesel metastaz ile başvuran bir olgu sunulmuştur. Erken dönem larenks karsinomlu olgularda indüksiyon kemoterapisinin etkisi tartışmalıdır. Ancak parsiyel larenjektomiyi reddeden olgularda tedavi öncesi hasta ve ailesine verilen danışmanlık da radyoterapinin olası başarısını tahmin etmek açısından önemlidir.

Anahtar sözcükler: Larenks, supraglottik karsinom, sisplatin, 5 florourasil, indüksiyon kemoterapisi.

The conventional curative treatment modalities are surgery and/or radiation therapy in patients with early stage squamous cell carcinoma of the supraglottic larynx. According to our experiences, the main reason for refusing the conservative partial laryngectomy by the patients is possible preoperative decision for non-conservative surgical techniques i.e. near-total or total laryngectomy.[1] Advanced cross-sectional imaging studies (CT and MRI) have reduced this probability but it did not reach to zero. In patients who refused the surgical treatment, it is important to estimate the possible success of the radiation therapy for complete counseling of patients and their families prior to curative treatment.

In the literature, there are different opinions about the success of chemotherapy regimens with curative or induc-

Correspondence: Melek Kezban Gürbüz, MD. Osmangazi Üniversitesi Tıp Fakültesi, Kulak Burun Boğaz Hastalıkları Anabilim Dalı, 26480, Eskişehir, Turkey.
e-mail: mkezban@yahoo.com.tr
Received: September 20, 2012; **Accepted:** November 7, 2012; **Published online:** January 12, 2013

Online available at:
www.jmedupdates.org
doi:10.2399/jmu.2012003008
QR code:

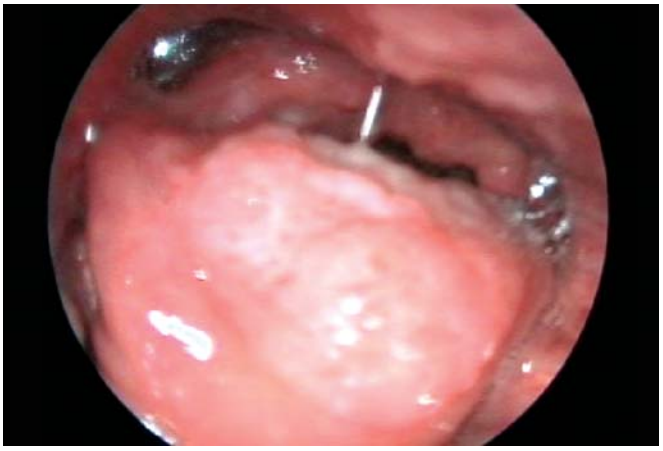

Fig. 1. Laryngoscopic view of the patient before chemotherapy in 2003.

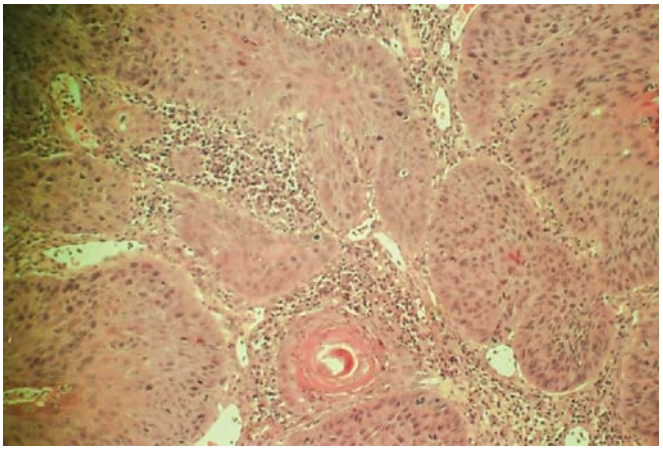

Fig. 2. Histopathologic view of the laryngeal biopsy specimen in 2003 (H-E x100).

tive intent in patients with early stage laryngeal carcinoma.[2-8] Wolf and Hong stated that there was no role of this regimen.[4] On the other hand, Laccourreye et al. stressed that induction chemotherapy might be effective to increase local control rate without detrimental effects on survival, especially in patients with early stage glottic carcinoma that invades anterior commissure.[7]

In this case report, a patient with T2N0M0 squamous cell carcinoma of the supraglottic larynx who presented with local recurrence and regional metastasis after a 54 months of non-followed period that follows two courses of cisplatinum/5-FU induction chemotherapy alone was presented.

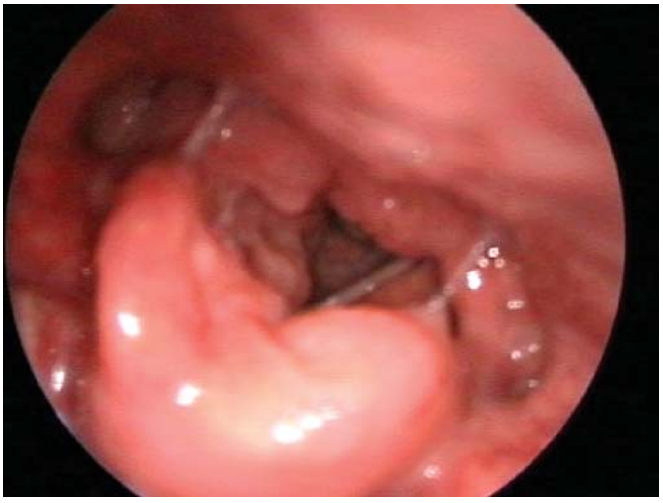

Fig. 3. Laryngoscopic view of the patient after the first course of chemotherapy in 2003.

Case Report

A 65-year-old man presented to the Otorhinolaryngology Head and Neck Surgery Department of Osmangazi University, Eskişehir, Turkey with a 3 months history of sore throat and pain effecting right ear in July 2003. Pharyngolaryngeal examination revealed a tumor mass invading whole epiglottis and right false cord (Fig. 1). The appearance and mobility of the true vocal cords and arytenoid cartilages and neck examination were normal. Histopathologic diagnosis was reported as moderately differentiated squamous cell carcinoma (Fig. 2). The tumor was classified as T2N0M0 according to AJCC 2002 classification. One course of induction chemotherapy was administered to the patient who refused the surgical treatment. This chemotherapy regimen was consisted of cisplatin 100 mg/m^2/day for first day and 5-fluorouracil 1 g/m^2/day for five days with antiemetics and adequate hydration. Twenty days later surgical treatment was suggested again to the patient who achieved nearly partial response to the first course (Fig. 3). However, he refused the surgical treatment again and second course was administered. At the end of the course the patient and family members were informed about the necessity of radiotherapy and referred to a radiation therapy center.

In January 2008 the patient presented again with a four months history of throat pain, difficulty in swallowing and hoarseness. A vegetative mass deforming epiglottis was found during fiberoptic laryngoscopy. Both vocal folds and arytenoid cartilages were mobile and in normal appearance (Fig. 4). Neck palpation revealed multiple lymphadenopathies in neck zones II and III at the right side.

Preepiglottic space infiltration was also detected in computerized tomography (Fig. 5). After laryngeal biopsy, histopathologic diagnosis was reported as moderately differentiated squamous cell carcinoma. The histopathologic appearance was similar with prior examination and there were some lower differentiated areas (Fig. 6). The patient informed that he did not receive radiotherapy after two chemotherapy courses in 2003. With these findings, the tumor was classified as T3N2M0 and surgical treatment was suggested to the patient. Nevertheless, he refused it again and two courses with 21 days interval cisplatin + 5-fluorouracil induction chemotherapy regimen were administered before radiation therapy. The doses were 80 mg/m^2/day for first cisplatin and 800 mg/m^2/day (5 days) for 5-FU. After this regimen, the patient received radiotherapy with a total dose of 70 Gy in 35 fractions each consisting 2 Gy/day followed by additional two courses of the same chemotherapy regimen. The video-laryngoscopic appearance after two months of the treatment was shown in Fig. 7.

In September 2008 (after three months of the treatment), PET CT evaluation revealed a 18 FDG accumulation which was found as meaningful for regional metastasis in the neck zone II at the right side. There was no positive finding for local recurrence or distant metastasis in this evaluation. The malignity was not reported after the third laryngeal biopsy and a comprehensive neck dissection was suggested to the patient, but he refused it again. Therefore, we planned additional chemotherapy courses that depend on the patient's tolerability and recently two courses were administered uneventfully.

Discussion

In the past three decades, some platin based induction chemotherapy regimens followed by radiation therapy were advocated to preserve larynx and increase local control and survival in patients with resectable locally advanced laryngeal carcinoma. Although the definite beneficial effect on survival of these regimens have not been demonstrated yet, high laryngeal preservation and local control rates were presented in many reports.[5,6] On the other hand, in a study with large series increasing free and overall survival rates were detected after induction chemotherapy regimen with cisplatin, fluorouracil and docetaxel in patients with unresectable head and neck cancer.[9]

In a retrospective study, Laccourreye et al. reported 27.3% (166 patients) complete clinical response rate to induction chemotherapy regimen in 607 patients with

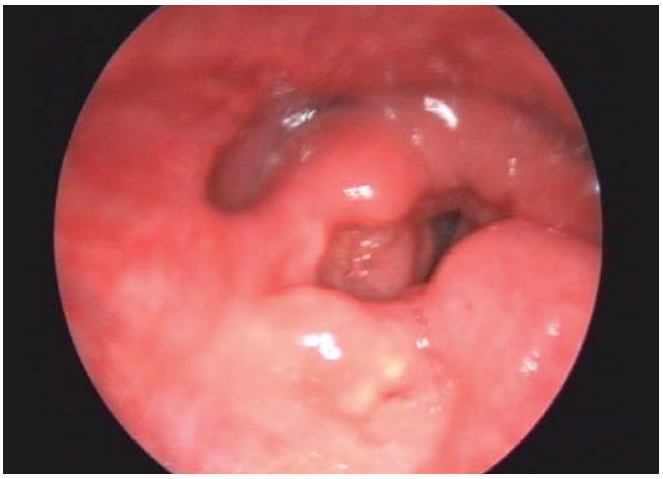

Fig. 4. Laryngoscopic view of the patient in 2008 (before treatment).

invasive squamous cell carcinoma of the pharyngolarynx classified as T1-T4N0M0.[7] In this series, 83.8% of the patients with glottic tumors and 46.4% of the patients with other pharyngolaryngeal tumors were classified as T1 and T2 and 40.3% of the complete clinical responders (67 of 166) were managed with 3-16 (mean 7) courses of chemotherapy regimen alone with curative intent. The authors reported five years actuarial survival, local control,

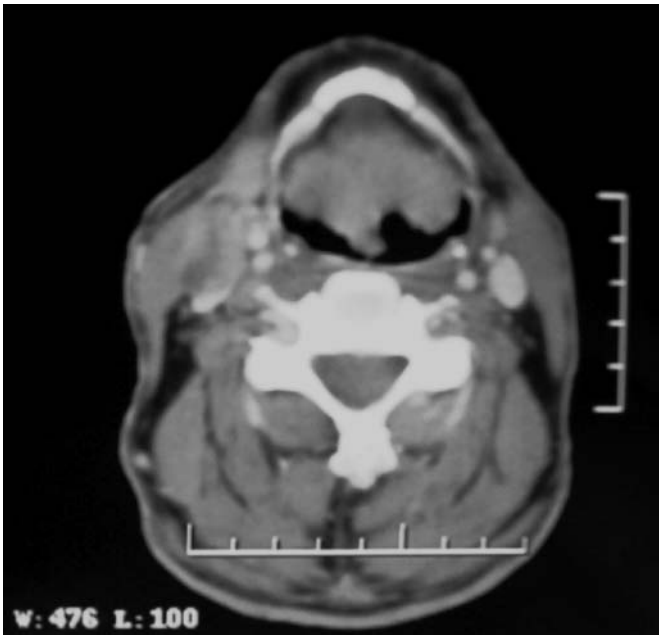

Fig. 5. Preepiglottic space infiltration and cervical lymphadenopathy in CT.

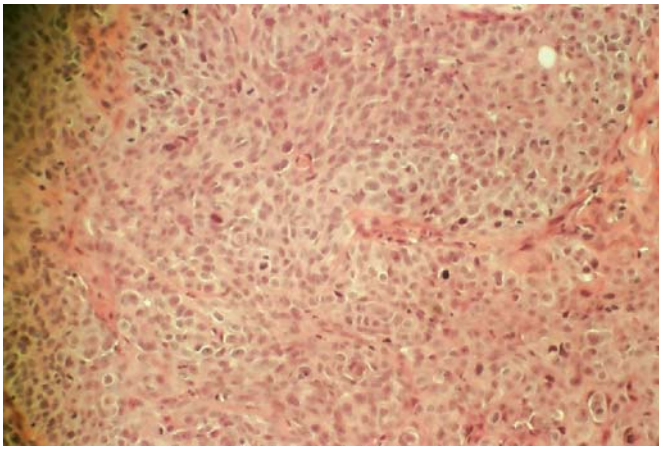

Fig. 6. The histopathologic view of the second laryngeal specimen in 2008 (H-E x100).

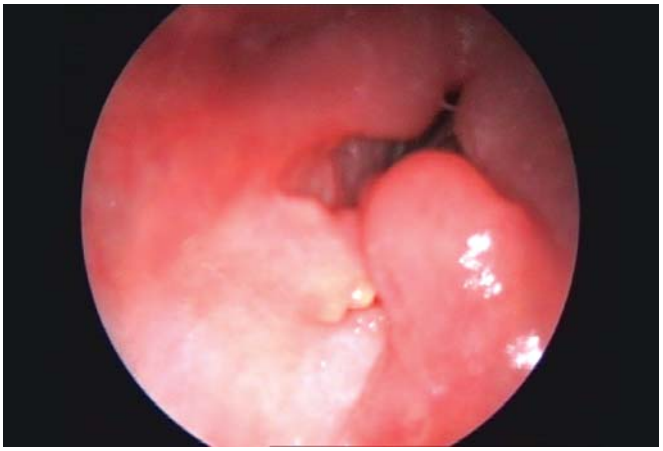

Fig. 7. Laryngoscopic view of the patient after 2 months of the treatment.

lymph node control and distant metastasis estimates as 71.1%, 52.6%, 82.4% and 4.5%, respectively. After the salvage treatments with radiation therapy or surgery (partial or total laryngectomy) of the patients who experienced local failure to chemotherapy, local control and laryngeal preservation rates were reported as 91% and 89%, respectively. The main causes of death were metachronous second primary tumor and intercurrent disease. At the end of the study authors concluded that chemotherapy alone with curative intent might be innovative treatment option, especially in patients with early stage glottic carcinoma who achieved complete clinical response.[7]

One of the most important causes that decreases survival in patients with laryngeal and hypopharyngeal tumors is regional metastasis. Tumors of the supraglottic larynx are more capable of involving lymph nodes than tumors originating from glottis. Just as in the study mentioned above, the authors reported 5-year actuarial lymph node control rate as statistically more in patients with glottic tumors than in patients with tumors originating from the other sites of pharyngolarynx.[7] Initially the tumor of our patient was classified as T2N0M0 supraglottic carcinoma. Fifty-four months survival without distant metastasis with only two courses of chemotherapy regimen alone may due to initial N0 stage.

Chemotherapy related toxicity may compromise survival and restricts the using of induction chemotherapy, especially in patients with early stage laryngeal carcinoma who are treatable with conservative partial laryngectomy or radiation therapy alone. In a meta-analysis, of 24 trials mortality rate due to toxic effects of the chemotherapeutic agents was reported as 6.5% for head and neck carcinomas.[10] On the other hand, in three reports from the same institution Laccourreye et al.[5,7,8] noted that toxicity of cisplatin/5-fluorouracil chemotherapy regimen never resulted in death. During two courses in 2003, we also did not observe any serious toxic symptoms and/or findings in our patient.

The degree of clinical response to induction chemotherapy may be very important in respect to local control. Laccourreye et al.[5] defined the complete clinical response as the disappearance of the tumor with normal motion of the true vocal cords and the partial response as at least a 50% decrease in the size of the lesion in an analysis of previously untreated 100 patients with T2 glottic carcinoma who treated with induction chemotherapy and partial laryngectomy. In this study, complete clinical and histological response rates were reported as 24% and 31% respectively and a significant statistical relation was noted between these rates. Our patient did not achieve complete clinical response after the first course of chemotherapy and we could not evaluate the clinical response to second course since he stayed out of follow up examinations. Although nearly partial response was achieved after the first course, 54 months survival without distant metastasis was an interesting finding for us.

The response to induction chemotherapy can also be used for determining the radioresistant cases. It could be more difficult to control the disease with irradiation in patient who experienced incomplete response to induction chemotherapy. This difficulty may due to chemotherapy related alteration of the cell kinetics of the drug resistant

cells.[11,12] Conservation surgery can be a solution in such cases.[6] Therefore, the patients and their families must be counseled again for surgical treatment.

The possibility of the patient's reluctance to receive curative treatment modalities (irradiation or surgery) after achieving complete or partial response to induction chemotherapy is an important disadvantage. Our patient informed us that he had no complaint after the first course of chemotherapy although he experienced nearly partial clinical response on physical examination. According to us this excessive optimistic opinion caused the patient to leave the treatment.

Conclusion

In conclusion, the beneficial effects of the induction chemotherapy in patients with early stage laryngeal carcinoma are doubtful. However, this regimen may be used to estimate the possible success of radiotherapy by complete counseling of the patients who initially refused the conservative partial laryngectomy.

Conflict of Interest: No conflicts declared.

References

1. Ozüdoğru E, Cingi E, Cakli H, Keçik MC, Cingi C, Gürbüz MK. Patient selection for near-total laryngectomy and oncologic results. [Article in Turkish] Kulak Burun Bogaz Ihtis Derg 2002;9:121-5.
2. Laccourreye O, Weinstein G, Brasnu D, et al. A clinical trial of continuous cisplatin-fluorouracil induction chemotherapy and supracricoid partial laryngectomy classified as T2. Cancer 1994; 74:2781-90.
3. Laccourreye O, Brasnu D, Bassot V, Ménard M, Khayat D, Laccourreye H. Cisplatin-fluorouracil exclusive chemotherapy for T1-T3N0 glottic squamous cell carcinoma complete clinical responders: five-year results. J Clin Oncol 1996;14:2331-36.
4. Wolf GT, Hong WK. Induction chemotherapy for organ preservation in advanced laryngeal cancer: is there a role? Head Neck 1995;17:279-83.
5. Laccourreye O, Diaz EM Jr, Bassot V, Muscatello L, Garcia D, Brasnu D. A multimodal strategy for the treatment of patients with T2 invasive squamous cell carcinoma of the glottis. Cancer 1999;85:40-6.
6. Laccourreye O, Bassot V, Brasnu D, Laccourreye H. Chemotherapy combined with conservation surgery in the treatment of early larynx cancer. Current Opinion in Oncology 1999; 11:200-3.
7. Laccourreye O, Veivers D, Hans S, Ménard M, Brasnu D, Laccourreye H. Chemotherapy alone with curative intent in patients with invasive squamous cell carcinoma of the pharyngolarynx classified as T1-T4N0M0 complete clinical responders. Cancer 2001;92:1504-11.
8. Laccourreye O, Veivers D, Bassot V, Ménard M, Brasnu D, Laccourreye H. Analysis of local recurrence in patients with selected T1-3N0M0 squamous cell carcinoma of the true vocal cord managed with a platinum-based chemotherapy-alone regimen for cure. Ann Otol Rhinol Laryngol 2002;111:315-21.
9. Vermorken JB, Remenar E, van Herpen C, et al.; EORTC 24971/TAX 323 Study Group. Cisplatin, fluorouracil, and docetaxel in unresectable head and neck cancer. N Engl J Med 2007;357:1695-704.
10. Stell PM, Rawson NSB. Adjuvant chemotherapy in head and neck cancer. Br J Cancer 1990;61:779-87.
11. Poulsen M, Aldren C, Tripcony L, Walker Q. Is surgery necessary in stage III and stage IV cancer of the head and neck that responds to induction chemotherapy. Arch Otolaryngol Head Neck Surg 1996;122:467-71.
12. Clark JR, Busse PM, Norris CM Jr, et al. Induction chemotherapy with cisplatin, 5-FU and high dose leucovorin for squamous cell carcinoma of the head and neck:long term results. J Clin Oncol 1997;15:3100-10.

Please cite this article as: Gurbuz MK, Cakli H, Dincer M, Ediz D, Dundar E, Ozudogru E. Interesting 54 months survival after platinum based induction chemotherapy regimen alone in a patient with T2N0M0 supraglottic carcinoma. J Med Updates 2012;2(3):124-128.