Immunotherapy monotherapy for patients with recurrent nonmetastatic larynx cancer who refuse salvage total laryngectomy

Courtney Shires, MD, FACS[1]; Merry Sebelik, MD, FACS, MAMSE[2,3]
[1]West Cancer Center, [2]Emory University, [3]Winship Cancer Institute

INTRODUCTION

Objectives/Hypothesis: Total laryngectomy has traditionally been recommended for patients with recurrent larynx cancer after radiation or chemoradiation. Some patients refuse salvage surgery. Historically, these patients have been placed on hospice or palliative chemotherapy. Immunotherapy has recently added another treatment modality to our armamentarium.

METHODS AND MATERIALS

8 patients with recurrent larynx cancer (after radiation with or without chemotherapy) and no metastasis were seen in our clinic. These patients were evaluated in a multidisciplinary clinic and were presented at our head and neck tumor board meeting. Our patients did not qualify for salvage partial laryngectomy due to size or location or tumor, preoperative swallowing dysfunction, or lung disease. We informed our patients that salvage total laryngectomy (TL) is the standard of care for treating recurrent larynx cancer after radiation +/-chemotherapy and was recommended for them. We discussed that even after TL, there continues to be a significant recurrence risk for their cancer. However, we discussed that TL also offers a potentially curative intent, while systemic therapy (chemotherapy or immunotherapy) is only considered palliative. Patients were told that if they declined surgery, that our goals would shift to disease control and symptom management rather than cure. All patients met with our Speech Therapist to discuss expected postoperative outcomes.

After consideration, all of our included patients declined salvage TL. Reasons for refusal included concerns about functional outcomes, postoperative quality of life, their ability to tolerate a surgery due to medical comorbidities, or the possibility of recurrence after this potentially curative surgery.

Staging was confirmed with PET scan. The patients were started on single agent immunotherapy (pembrolizumab). If progression was seen after 3-4 rounds of immunotherapy, chemotherapy (carboplatin and 5 fluorouracil) was added to immunotherapy. We recorded patients' demographics, initial cancer stage, initial cancer treatment, CPS values, need for tracheostomy, addition of chemotherapy to immunotherapy, median progression-free survival (PFS) for responders, common terminology criteria for adverse events (CTCAE), and response to therapy.

RESULTS

The average age of our patient was 72 years old (Table). Of our 8 patients, 62.5% (n=5) were African American, while 37.5% (n=3) were Caucasian. Most had early (stage 1 or 2 disease) at the time of initial diagnosis. 75% (n=6) had radiation alone as their initial treatment, while 25% (n=2) had chemoradiation. All of these patients had high CPS scores (>1). 37.5% (n=3) of our patients progressed on 3-4 rounds of immunotherapy and are deceased. Chemotherapy was added to the regimen of 50% of the patients after poor response (progression of disease) on immunotherapy alone. Glottis and supraglottis were the most common location of initial disease and recurrent disease.

75% (n=6) of the patients on immunotherapy with chemotherapy have been living 12-15 months after initiating salvage treatment. Median PFS for responders after combined chemotherapy and radiation was 10.3 months.

One patient (12.5%) has had a long-lasting positive response to immunotherapy alone with nearly no measurable tumor on imaging. She has been on immunotherapy for 20 months with no progression of disease.

75% (n=6) of our patients needed tracheostomy while on salvage treatment.

There were no Grade 3, 4, or 5 common terminology criteria for adverse events (CTCAE). 37.5% (n=3) of patients had grade 1 CTCAE, and one patient (12.5 %) had a grade 2 CTCAE. Half of the CTCAE were in patients that received only chemotherapy, and half of the patients that experienced CTCAE received chemotherapy and immunotherapy.

DISCUSSION

8 patients with recurrent larynx cancer (after radiation with or without chemotherapy) and no metastasis were seen in our clinic. These patients were evaluated in a multidisciplinary clinic and were presented at our head and neck tumor board meeting. Our patients did not qualify for salvage partial laryngectomy due to size or location or tumor, preoperative swallowing dysfunction, or lung disease. We informed our patients that salvage total laryngectomy (TL) is the standard of care for treating recurrent larynx cancer after radiation +/-chemotherapy and was recommended for them. We discussed that even after TL, there continues to be a significant recurrence risk for their cancer. However, we discussed that TL also offers a potentially curative intent, while systemic therapy (chemotherapy or immunotherapy) is only considered palliative. Patients were told that if they declined surgery, that our goals would shift to disease control and symptom management rather than cure. All patients met with our Speech Therapist to discuss expected postoperative outcomes.

After consideration, all of our included patients declined salvage TL. Reasons for refusal included concerns about functional outcomes, postoperative quality of life, their ability to tolerate a surgery due to medical comorbidities, or the possibility of recurrence after this potentially curative surgery.

Staging was confirmed with PET scan. The patients were started on single agent immunotherapy (pembrolizumab). If progression was seen after 3-4 rounds of immunotherapy, chemotherapy (carboplatin and 5 fluorouracil) was added to immunotherapy. We recorded patients' demographics, initial cancer stage, initial cancer treatment, CPS values, need for tracheostomy, addition of chemotherapy to immunotherapy, median progression-free survival (PFS) for responders, common terminology criteria for adverse events (CTCAE), and response to therapy.

CONCLUSIONS

Our patients with nonmetastatic recurrent larynx cancer were found to have high CPS scores, which suggests favorable response to immunotherapy. Most patients with recurrent larynx cancer on immunotherapy required a tracheostomy. These patients had poor response on immunotherapy alone, but had prolonged survival with added chemotherapy. Salvage laryngectomy is the only curative option for these patients, but for those patients that refuse surgery, chemotherapy with immunotherapy has better results than immunotherapy alone. Our results reveal a possible clinical phenomenon, which needs to be confirmed by large sample studies.

Patient	race/ sex	age	previous XRT	trach	initial stage	chemo with immuno ?	CPS	status	time after immuno started that chemo was added	chemo agent	Progression-free survival for responders (after starting chemo)	CTCAE	Subsite of initial larynx cancer	Subsite of recurrent larynx cancer
A	AA M	81	yes	yes	T3N1M0	no	32	deceased after 9 months	NA	NA	NA	Grade 1	glottis and supraglottis	glottis (anterior commissure and thyroid cartilage)
B	WM	86	yes	yes	T1bN0M0	no	17	deceased after 11 months	NA	NA	NA	Grade 2	glottis	glottis and supraglottis
C	WM	66	yes	yes	T2N0M0	no	21	deceased after 12 months	NA	NA	NA	NA	supraglottis	supraglottis
D	AA M	54	yes	yes	T2N0M0	yes	9	living after 13 months	12 weeks	carboplatin, 5 fluorouracil	10 months	Grade 1	subglottis	sugblottis and glottis
E	AA M	72	yes	yes	T1N0M0	yes	14	deceased after 15 months	10 weeks	carboplatin, 5 fluorouracil	NA	NA	supraglottis	supraglottis
F	AA F	71	yes + chemo	yes	T2N1M0	yes	24	living after 15 months	11 weeks	carboplatin, 5 fluorouracil	12 months	Grade 1	supraglottis	supraglottis
G	WM	84	yes	no	T2N0M0	yes	16	living after 12 months	13 weeks	carboplatin, 5 fluorouracil	9 months	NA	glottis and supraglottis	glottis (anterior commissure and thyroid cartilage)
H	AA F	65	yes + chemo	no	T3N0M0	no	6	living after 20 months	NA	NA	17 months	NA	glottis and supraglottis	supraglottis and glottis

CONTACT

Merry Sebelik, MD, FACS, MAMSE
Emory University
Division of Endocrine Head & Neck Surgery
msebelik@emory.edu
404-778-3381

Courtney Shires, MD, FACS
West Cancer Center
Department of Head and Neck Surgery
coshires@westclinic.com

REFERENCES

1. Verro B, Saraniti G, Ottoveggio G, et al. Cancer and immune response: The role of PD-1/PD-L1 checkpoint in laryngeal carcinoma. Preliminary results. Eur Arch Otorhinolaryngol. 2024 Oct;281(10):5411-5417.
2. Okano S. Immunotherapy for head and neck cancer: Fundamentals and therapeutic development. Auris Nasus Larynx. 2024 Aug;51(4):684-695.
3. Fang Q, Li X, Xu P, et al. PD-1 inhibitor combined with paclitaxel and cisplatin in the treatment of recurrent and metastatic hypopharyngeal/laryngeal squamous cell carcinoma: efficacy and survival outcomes. Front Immunol. 2024 May 17;15:1353435.
4. Contrera KJ, Mahomva CR, Sharma BK, et al. Patterns of failure after salvage head and neck surgery. Oral Oncol. 2024 Oct;157:106957.
5. Ferris RL, Blumenschein Jr G, Fayette J, et al. Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. N Engl J Med 2016;375(19):1856–67.
6. Burtness B, Harrington KJ, Greil R, et al. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. Lancet 2019; 394(10212):1915–28.
7. Alsavaf MB, Issa M, Klamer BG, et al. Impact of Tobacco, Marijuana, and Alcohol Use on Overall Survival in Recurrent Metastatic Head and Neck Cancer Patients Treated With Immune Checkpoint Inhibitors. Asia Pac J Clin Oncol. 2024 Dec 20.
8. Chen S, Zhong Q, Zhang S, et al. Neoadjuvant immunochemotherapy in locally advanced laryngeal cancer and hypopharyngeal cancer: higher objective response rate and organ-preservation rate. Invest New Drugs. 2024 Dec;42(6):694-702.
9. Uppaluri R, Haddad RI, Tao Y, et al; KEYNOTE-689 Investigators. Neoadjuvant and Adjuvant Pembrolizumab in Locally Advanced Head and Neck Cancer. N Engl J Med. 2025 Jul 3;393(1):37-50.
10. Cohen EEW, Soulieres D, Le Tourneau C, et al.Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study. Lancet 2019;393(10167):156–67.
11. Zandberg DP, Algazi AP, Jimeno A, et al. Durvalumab for recurrent or metastatic head and neck squamous cell carcinoma: results from a single-arm, phase II study in patients with >/=25% tumour cell PD-L1 expression who have progressed on platinum-based chemotherapy. Eur J Cancer 2019;107:142–52.