Case Series

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Skin metastasis within radiation field in treated squamous cell carcinoma of larynx

Vinodh Kumar Selvaraj, Deleep Kumar Gudipudi*

Department of Radiation Oncology, Basavatarakam Indo-America Cancer Hospital and Research Institute, Hyderabad, Telangana, India.

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*Correspondence:

Dr. Deleep Kumar Gudipudi,

E-mail: deleep.gudipudi@gmail.com

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ABSTRACT

Background: Cutaneous metastasis from squamous cell carcinoma (SCC) of larynx is very uncommon. Skin mestatsis in a treated of case of SCC larynx is considered to be a sign of impending distant metastasis and dismal prognosis. There are very few case reports in literature describing such presentations, and very minimal information on treatment options available for these patients. Here, we describe two cases of locally advanced SCC larynx treated with chemoradiation upfront, who later presented with cutaneous metastasis in neck within the previous radiation field. Evaluation for distant metastasis was done and started on palliative chemotherapy. The first patient had complete resolution of cutaneous nodules post 8 cycles of weekly palliative chemotherapy. However, post 18 cycles of chemotherapy, he developed a metachronous primary in upper thoracic oesophagus and disease progressed locoregionally too. The second patient's general condition deteriorated after 1st cycle of palliative chemotherapy, hence was offered best supportive care. Cutaneous nodules in a treated SCC of larynx must raise the suspicion of metastasis, warranting histological examination, and whole-body imaging work-up to rule out distant metastasis. Palliative chemotherapy must be advocated in all eligible patients to delay disease progression. Best supportive care can be offered in patients not eligible for chemotherapy.

Keywords: Cutaneous nodules, Palliative chemotherapy, Rare presentation, Squamous cell carcinoma larynx, Skin metastasis

INTRODUCTION

Skin metastases (SM) from non-cutaneous primary malignancies are rare and are reported in only 0.7 to 9% of patients with internal malignancies.¹ They are commonly seen in lung, large intestine and oral cavity cancers in males, and breast cancers in females.² Skin metastasis in squamous cell carcinoma (SCC) of head and neck is very uncommon and reported in only 1-2% of cases.³ That too, metastasis to skin in a treated case of SCC of the larynx is extremely rare.⁴⁻¹² It generally denotes impending distant metastatic spread or locoregional recurrence, and poor prognosis. On review of literature, there were only few reports of cutaneous metastasis in treated SCC of larynx and limited

information on potential treatment options. Here, we described two cases of SCC of larynx treated in our hospital, who developed cutaneous metastasis post-treatment. We have also discussed the treatment modalities adopted and outcomes in these patients.

CASE SERIES

Case 1

A 63-year-old male, with known history of smoking, was diagnosed to have a growth in supraglottic region and underwent excision six years ago. Post-operative histopathological report was initially reported as poorly differentiated malignancy, however blocks review at

higher cancer center was not suggestive of any malignancy, hence no adjuvant treatment was offered. After 6 years, he presented to our institute with complaints of hoarseness of voice, dysphagia and swelling in right side of neck. On evaluation, laryngoscopy showed a proliferative lesion involving right pharyngeal wall, right pyriform sinus, and right aryepiglottic fold. Bilateral vocal cords were normal. Positron emission tomography computed tomography (PET CT) scan showed increased metabolic uptake in the same areas as in laryngoscopy along with extension to posterior pharyngeal wall and right side of epiglottis with multiple cervical lymph nodes on level II, III and IV on left side. Based on imaging and biopsy report, a diagnosis of supraglottic squamous cell carcinoma cT2N2bM0 was made. He was treated with concurrent chemoradiation. A radiation dose of 70/59.45/54.45Gy was delivered in 33 fractions by simultaneous integrated boost-intensity modulated radiotherapy (SIB-IMRT) using Rapid Arc technique along with 2 cycles of weekly cisplatin and 4 cycles of weekly carboplatin. Cisplatin was changed to carboplatin after second cycle of chemotherapy due to raised serum creatinine. Post-treatment he was apparently asymptomatic and was on regular follow-up.

Two years post-treatment, patient presented with skin nodules in the neck. There was a large nodule on skin to the right side of midline in anterior neck along with few other tiny nodules dispersed in neck (Figure 1). Fine needle aspiration cytology (FNAC) from the skin lesion was suggestive of metastatic carcinoma. To rule out distant metastasis, PET CT scan was done. It showed hypermetabolic nodular soft tissue density lesions in skin and subcutaneous aspect of lower anterior neck. There was also increased metabolic uptake in bilateral cervical lymph nodes, soft tissue nodule in post cricoid region on left side, ground glass opacity in left lung lower lobe and few small mediastinal lymph nodes. He was started on weekly palliative chemotherapy. Post 8-cycles of weekly paclitaxel and carboplatin, PET CT showed complete resolution of skin deposits, bilateral cervical lymph nodes and left lung ground glass opacity. He was continued on paclitaxel and carboplatin for another 6 weeks (14 cycles). From 15th to 18th cycle chemotherapy, carboplatin was replaced with cisplatin due to grade III adverse events. Re-evaluation PET CT revealed metabolically active asymmetrical thickening in upper thoracic oesophagus, suggestive of metachronous primary due to field cancerization (Figure 2). There was also progression noted in mediastinal lymph nodes and appearance of multiple cervical lymph nodes, skin, and soft tissue nodules. In view of progressive disease, he was switched to oral metronomic chemotherapy (methotrexate), epidermal growth factor receptor inhibitor (erlotinib) and non-steroidal anti-inflammatory drugs (NSAIDs - Celecoxib). Following which he lost to follow-up due to COVID-19 situation.



Figure 1: Cutaneous mass in right side of neck with multiple small nodules seen all over the neck.

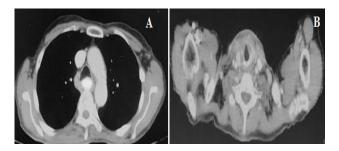


Figure 2: PET CT axial images showing increased metabolic uptake (A) In thoracic oesophagus (B) In subcutaneous plane in neck.

Case 2

A 60-year-old male, with known smoking history, presented with complaints of hoarseness of voice. On evaluation, endoscopy revealed a growth involving left vocal cord and aryepiglottic fold. Contrast enhanced CT of neck showed a heterogeneously enhancing ill-defined lesion in right epiglottis, right pharyngo-epiglottic fold, right aryepiglottic fold, right para glottic space, obliterating pyriform sinus, right true and false vocal cords, infiltrating the anterior commissure to involve left true and false vocal cords (Figure 3). Enlarged lymph node (1x1cm) was seen in right level II lymph nodal region. Biopsy from the lesion was suggestive of well differentiated keratinizing squamous cell carcinoma. Hence, he was staged as SCC larynx cT3N1M0 and planned for concurrent chemoradiation. He received radiation to head and neck region, a total dose of 70Gy was delivered in 35 fractions by conventional technique along with 5 cycles of weekly cisplatin. He was on regular follow-up. After 8 months post-treatment, he presented with skin nodules in the neck. FNAC from the skin lesion was positive for malignancy. Therefore, he was started on palliative chemotherapy with cisplatin and 5-fluorouracil. But his general condition deteriorated after 1st cycle chemotherapy, therefore further chemotherapy was withheld, and best supportive care offered.



Figure 3: CT Neck images showing heterogeneously enhancing ill-defined lesion in right side of larynx (A) In axial plane (B) In coronal plane.

DISCUSSION

Squamous cell carcinoma is the most common histology of tumours originating in larynx.¹³ They usually arise from glottis (59%), supraglottis (40%), or infraglottis (1%).14 The disease usually spreads to regional lymph nodes or distant organs. Almost three-fourth of metastases from SCC of head and neck was involving lung (70-75%), followed by liver (17-38%), and bones (23-44%).¹⁵⁻¹⁷ Cutaneous metastases from SCC of head and neck malignancies is rare accounting for less than 10% of all distant metastasis. 18 Skin metastasis can present as multiple or solitary nodule, plaque, inflammatory or granulation tissue.19 The exact mechanism of development of dermal metastasis in SCC of head and neck is not completely understood. It is postulated that dermal metastasis could be a result of direct extension by contiguous spread, or through dermal lymphatic spread, or through haematogenous spread.²⁰

Table 1: Skin metastase in previously treated squamous cell carcinoma larynx- review of literature.

Author/year	Age of patient (years)	Time since treatment of primary (months)	Location of skin nodules	Treatment	Outcome
Veraldi et al	-	24	Forehead and left arm	Nil	5 months, lung metastasis
Debois et al	-	Few	Skin metastasis	-	-
Bottoni et al	64	2	Right supraclavicular and infraclavicular region	-	-
Shamsadini et al	58	9	Left shoulder	Planned for RT	NR
Aydin et al	61	20	Left palm (MCP joint of left fifth finger)	Planned for excision	5 months, died of lung and disseminated skin metastasis
Ramin et al	75	2	Left buttock	Nil	3 months died of lung metastasis
Kumar et al	55	24	Tips of fingers and nail bed of left hand	Nil	2 months died of lung and liver metastasis
Das et al	60	3	Chin, neck, trunk, thigh and left little finger	Oral chemo therapy Metho trexate 15mg (once a week)	NR
Trehan et al	55	18	Right forearm	Palliative RT (6Gy in single fraction)	NR
Present case 1	62	24	Neck - right of midline	Palliative chemotherapy (weekly Paclitaxel + Carboplatin)	At 6 months progression, started on second line chemotherapy

Continued.

Author/year	Age of patient (years)	Time since treatment of primary (months)	Location of skin nodules	Treatment	Outcome
Present case 2	60	8	Neck	Palliative chemotherapy (cisplatin + 5- fluorouracil)	Discontinued treatment after 1 st cycle

MCP=Metacarpophalangeal, NR=Not applicable, RT=Radiotherapy

They have been reported to occur at different sites all throughout the body such as head, neck, thorax, upper extremities, abdomen, buttock, and lower extremities. Laborates on sites of metastasis, treatments offered and outcomes in patients with skin metastasis in treated cases of SCC larynx. Treatment options such as radiotherapy, chemotherapy, and excision of skin lesions were considered. Treatment intent was mainly palliation and was often aimed at providing symptomatic relief. The prognosis after development of cutaneous metastasis is poor. The mean survival after diagnosis of skin metastasis is about three to six months.

In our report, despite a disease-free interval of 2 years, the first patient presented with cutaneous metastases which heralded rapid progression of the disease. Initially, weekly chemotherapy with paclitaxel and carboplatin resulted in complete resolution of all lesions. However, after 6 months of receiving chemotherapy, the disease progressed, and patient developed a metachronous primary in oesophagus too. Hence, he was started on oral metronomic chemotherapy and targeted therapy as second line agents. The second patient, on the other hand, could not tolerate chemotherapy and was offered best supportive care.

CONCLUSION

In treated cases of SCC larynx, during follow-up, in addition to loco-regional examination, thorough inspection for presence of cutaneous lesions must be carried out. Any suspicious skin lesion must be biopsied to rule out metastasis. In the event of diagnosis of metastatic lesion, metastatic workup is mandatory to evaluate distant spread. Despite the prognosis being poor, palliative chemotherapy can be attempted to delay progression in all eligible patients without distant failure. Patients with widespread disease or poor general condition are offered best supportive care.

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