Review Article

Tracheal tumor: A diagnostic and therapeutic dilemma

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ABSTRACT

Tracheal tumors are quite rare, contributing only 0.1–0.4% of all tumors. We report a case of 42-year-old male who presented with right sided neck swelling along with pain and cough for last 1-month. He was diagnosed to be a case of tracheal squamous cell carcinoma. Surgical debulking followed by concurrent chemoradiation was planned. After 6 months follow-up, there was no residual disease and the patient is symptom-free. Along with the case, a brief review of the literature is also presented.

Key words: Radiotherapy, squamous cell carcinoma, tracheal tumor

INTRODUCTION

Tracheal tumor is quite rare,[1-3] contributing only 0.1–0.4% of all tumors.[4] This rarity makes research into the natural history and treatment very difficult.[5] Tracheal cancer presentation with secondary neck is extremely rare. Review of largely retrospective data has revealed several patterns: First, surgical resections mainstay of therapy; second, local recurrence is a major pattern of failure; third, adjuvant radiation seems to have some positive effect on the outcome.[6] The anatomy involved make surgery difficult. Incomplete or marginal resections are common and adjuvant treatment is paramount in all, but the rarest of cases. There also exists the possibility of definitive treatment with chemoradiation alone. Therefore, a multimodality treatment approach is needed. While epidemiology, histopathology, and survival statistics of these tumors are known, outcomes of radical nonsurgical approaches are sparse.[7] Both radiation and chemotherapy are used in the management of this disease.[8] While radiation has become more precise, newer chemotherapy agents have also been developed.[9]

Most primary tracheal tumors are malignant: Adenoid cystic carcinoma (ACC), squamous cell carcinoma (SCC), adenocarcinoma, mucoepidermoid carcinoma,[5] carcinoid tumor, oat cell carcinoma.[10] Benign tumors are xanthogranuloma and adenoma.[3] A carcinoma arising in the thyroid or esophagus can spread to the trachea; moreover, the trachea can be the site of metastases from recurrent carcinoid tumors in left main bronchus,[8] larynx, lung,[9] colon.[2]

Traditionally, ACC were considered the most common tracheal neoplasms, but recent reports suggest that the most prevalent histology worldwide is squamous cell (60–90%),[11] although ACC seems to be more common among nonsmokers. SCC is the most common pathology in smokers. The male to female ratio is 2/3:1 for SCC but is nearly equivalent for both the sex for ACC.[12]

CASE REPORT

A 42-year-old male heavy smoker and occasional alcoholic presented at our hospital for right-sided neck swelling with pain and cough for last 1-month. Patients also disclosed the three episodes of hemoptysis. He was a heavy smoker (30 pack years) with no other lung related

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medical history. The patient neither had a history of asthma or any allergic disorder in childhood nor in his family member. He denied of having other symptoms such as hoarseness, fatigue, difficulty in swallowing, and weight loss.

Physical examination revealed a 4 cm × 3 cm sized partially fixed firm nodal mass of the right level IV cervical node. All vitals were within normal limits. No added sound was auscultated. There was no organomegaly or any other lymphadenopathy noted.

The hematological and biochemical profiles were within normal limits. Fine-needle aspiration cytology was taken from the neck node which showed metastatic squamous carcinoma. The patient's chest X-ray was unremarkable except the intraluminal defect, not easily recognized in the lower part of the trachea. Barium swallow was unremarkable which ruled out esophageal involvement.

A contrast-enhanced computerized tomographic scan of the thorax showed an endotracheal mass of 1.8 cm in diameter originating from the right antero-lateral wall of the lower part of the trachea just 1 cm above from the carina [Figure 1]. The lumen of the trachea was occluded by about 50% due to the mass. The mass was smooth surfaced, well-marginated, uniformly dense arising from membranous wall of the trachea. There was right cervical level IV nodal enlargement 4 cm × 3 cm with central necrosis. There was no mediastinal or hilar node enlargement.

Fiberoptic laryngoscopy showed no remarkable findings in the oral cavity, oropharynx and hypopharynx. Fiberoptic bronchoscopy revealed an intraluminal tumor of the right antero-lateral wall of the lower trachea [Figure 2]. The tumor which was bleeding on touch obstructed about 50% of the lumen and scope passes easily through narrowed part. The tumor was located just 1 cm above from carina. Histopathology was suggestive of SCC [Figure 3]. On immunohistochemistry analysis, positive staining for cytokeratin 3/5 and involucrin was observed confirming the diagnosis of SCC. According to Bhattacharya staging system, tumor was staged as stage-IV (T1N1M0) while Macchiarini staging system suggested stage-IV (T1aN0M1).

Surgical debulking followed by concurrent chemoradiation was planned. The patient was simulated in the supine position using a computed tomography (CT) scanner with hands placed at the patient's sides. The datasets were imported into our planning systems, namely Eclipse™ for three-dimensional conformal radiotherapy (RT). Radiation therapy volumes were defined as follows: Gross tumor volume (GTV) included all gross visible disease on imaging and endoscopy. The GTV was expanded 2 cm craniocaudally, and 1 cm circumferentially to generate a

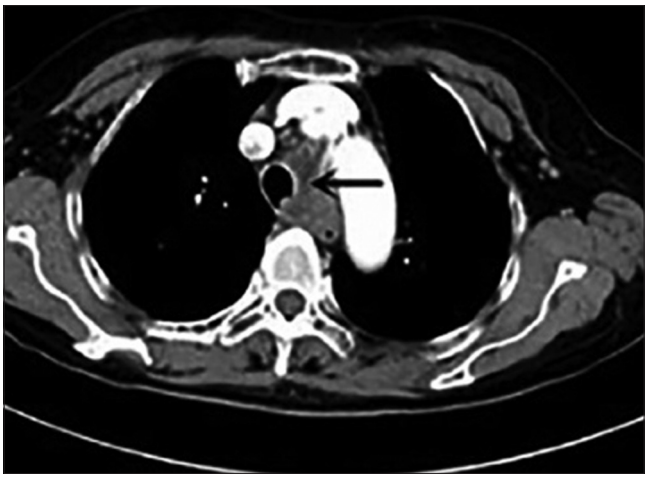

Figure 1: Contrast-enhanced computed tomography scan of the thorax showing growth in trachea at the level of arch of the aorta

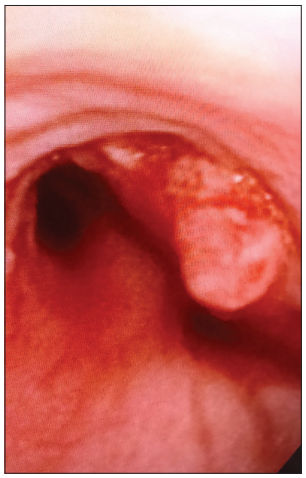

Figure 2: Fiberoptic bronchoscopy revealing an intraluminal tumor of the right antero-lateral wall of the lower trachea

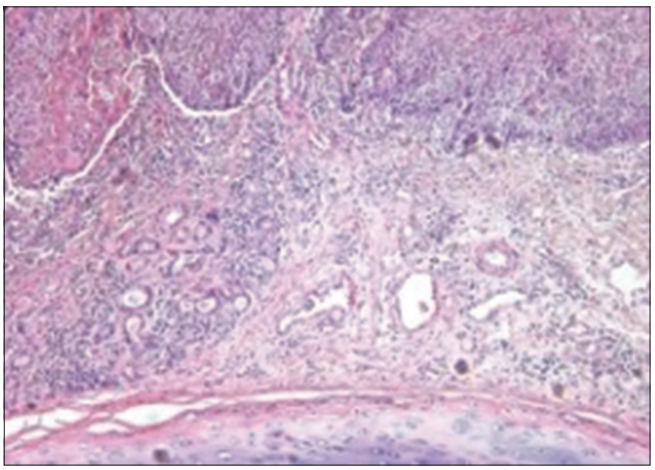

Figure 3: Photomicrograph showing tumor cells arranged in nests located below the ciliated columnar epithelium (H and E, ×40)

clinical target volume (CTV). The planning target volume was created by adding a uniform 7 mm expansion to the CTV as no image guidance was used. Weekly chemotherapy in the form of paclitaxel 50 mg/m^2 and carboplatin (area under the curve 2) was given with radiation of 60 Gy in 30 fractions. No adverse events occurred during or after chemoradiation except esophagitis grade 2 and pneumonitis grade 1 (radiation therapy oncology group). After 6 months follow-up, there was no residual disease and patient was symptom-free.

DISCUSSION

Tracheal carcinoma can present with a variety of symptoms including cough, dyspnea, dysphagia, and hemoptysis. Yuan *et al*.[13] reported cough to be the most common symptoms (presents in 72% of patients), followed by dyspnea (66%), stridor (39%), hemoptysis (39%), dysphonia (31%). Hemoptysis is the more likely the presenting symptoms of SCC,[13] and dysphasia is considered an ominous sign. In one study of nonadenoidcystic/nonsquamous cell tracheal tumors, benign tumors presented with dyspnea, whereas malignant tumors associated with hemoptysis.[14] In 40–50% of cases, ACC diagnosed with synchronous metastases,[15] but survival is relatively long despite metastasis.

Tracheobronchoscopy and CT, in coronal projection, are basic examinations for these problems.[16] Bronchoscopy is necessary for tracheal malignancies and preoperative surgical planning. Esophagoscopy is suggested for all tumors to rule-out esophagus invasion. The main advantage of imaging is the demonstration of tracheal wall thickening and extra-luminal changes.[16] The radiological appearance of the tumors can be classified as: Intraluminal, wall thickening, exophytic form. Endoscopic evaluation reveals that the majority of the tumors are bulky and obstructive in nature.

Postoperative complications are mediastinitis, bilateral pneumonia, and wound-healing disorders. Persistent or progressive local disease can cause complications: Fatal hemorrhage, esophago-tracheal fistula, tracheal necrosis, tracheal stenosis.[17,18] Management of tracheal tumors includes interventional endoscopy, surgery, RT, endoluminal brachytherapy.[3] The sleeve trachea resection is one of the optimal surgical modalities, the other options are: Partial tracheal wall resection, immediate tracheal reconstruction, total laryngectomy + partial resection of trachea and thyroid lobectomy, resection and primary reconstruction, laryngotracheal resection, cervico-mediastinal exenteration, carinal resection, and reconstruction.[13,17,19] Debulking surgery, followed by RT, may provide effective and permanent control in ACC and can be effective in obviating local recurrence.[20,21] This approach has offered <15% survival for more than a year. RT alone is a possible treatment option in inoperable cases. Mornex *et al*.[4] concluded radiation alone to be a good alternative to surgery. Their study identified performance status and radiation dose (> 60 Gy) as significant prognostic factors. With a mean follow-up of 141 months, their series showed overall 1-, 2-, and 5-year survival rates of 46%, 21%, and 8%, respectively.

Makarewicz and Mross[5] arrived at similar conclusions in their study of 23 patients, where a dose escalation combination using external beam radiation and brachytherapy was utilized. Almost a third achieved local control, and this was more frequent in patients receiving >60 Gy. Their mean survival was 26 and 7.2 months for the curative and palliative group, respectively.

Jeremic *et al*.[7] explored correlation between dose and outcome in a retrospective study of 22 patients. Their median survival was 24 months, and 5-year survival was 27%. Mediastinal lymph node involvement was a bad prognostic factor. Survival was not significantly different at a dose of 70 Gy versus 60 Gy, whereas tracheal toxicity was. The largest series reporting on outcomes using radiation therapy alone utilized portals which included the gross tumor along with the adjacent superior mediastinum and supraclavicular lymph nodes.[5]

Brachytherapy has also been used in the management of tracheal tumors. This approach had an overall response rate of 89%. The pattern of failure was predominantly local (73%). Our approach has been to include the gross tumor only and exclude elective irradiation of the adjacent nodal areas. This approach combined with conformal three-dimensional radiation planning perhaps helps to achieve dose escalation while limiting toxicity. The pattern of relapse was predominantly locoregional. Elective nodal irradiation might have a role for this subset of patients. Xie *et al*.[22] have recently demonstrated a survival benefit for radiation in tracheal tumors. Radiation was particularly associated with better survival for the squamous cell histology and patients who did not undergo resection.

Positive lymph nodes or invasive disease at resection margins appear to have an adverse effect on the management of SCC; such an effect is not demonstrable with ACC.

Another approach toward therapy intensification is the addition of concurrent chemotherapy with radiation. Concurrent chemotherapy may be of special significance as SCC is the predominant histology. Concurrent chemotherapy is well-established in the radical treatment

of locally advanced head and neck cancer and lung cancer. This approach may well be of value in the treatment of tracheal carcinomas. Available literature is in the form of case reports. Concurrent chemoradiation with paclitaxel and carboplatin has been used for definitive management.[16,17] Palliative chemotherapy for tracheal malignancies is an unexplored area. Although radiation therapy is well-established for palliation, chemotherapy responses have received scarce attention. Paclitaxel and carboplatin seem to have activity in the metastatic setting as evidenced by our case. Various agents have shown activity in ACC of salivary gland origin.[22] The combination of paclitaxel and carboplatin has also shown activity in SCC.[20]

However, laser therapy is very useful in improving the obstructive symptoms; RT is the only curative method resulting in a long-term control of the disease. Endo-bronchial high-dose-rate brachytherapy has been used for tracheal carcinomas as a boost to external beam irradiation. Total dose and dose per fraction have not been well-recognized, up to the present moment. Reports on the combination of external and endoluminal RT are rare.

Endo-bronchial high-dose-rate brachytherapy may be used for tracheal tumors, even as a boost for external beam irradiation or in recurrences. Long-term survival may also be expected, particularly for tumors with adenoid cystic histology. Palliation has improved with the introduction of laser resection, brachytherapy, and stents. SCC may have a better prognosis, in the trachea, than in the lung. Carvalho *et al*.[9] presented their experience with high-dose-rate endo-bronchial brachytherapy; they reported a good local control, at the time of the first bronchoscopic control. They treated 4 patients with nonresectable tracheal tumor: Two patients with SCC died at the 6th and 33rd month, respectively, after treatment, only the second presented local recurrence. The other two patients were alive after 64 and 110 months of follow-up. Table 1 provides a summary of results of resection with adjuvant radiation for primary tracheal carcinoma.

CONCLUSIONS

The aim of our case discussion is that the SCC variant of tracheal cancer can occur in early age, may present with metastatic neck node and concurrent chemoradiation after surgery may be the best modality of choice. Although tracheal cancer can present with a variety of symptoms, including cough, dyspnea, dysphasia, and hemoptysis, the presentation as metastatic neck node without any ominous sign like dysphasia, dyspnea, or stridor makes it a very unusual presentation of tracheal neoplasms. In this presenting case, only cough and three episodes of hemoptysis suggested for bronchoscopy to rule out endobronchial neoplasm. The SCC variants typically present at sixth decade of life, whereas ACC seems to present at younger ages. Presenting case shows that SCC can present in early age also.

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Table 1: Summary of results of resection with adjuvant radiation for primary tracheal carcinoma

Study	Histology	Treatment given	Median Survival (time or rates)
Grillo and Mathisen[19]	Squamous (*n*=70)	Surgery±RT	34 mo
		RT	10 mo
	Adenoid cystic (*n*=80)	Surgery±RT	118 mo
		RT alone	28 mo
Licht *et al*.[23]	-	Surgery alone (*n*=6)	48% (5yr actuarial)
		RT alone (*n*=35)	7%
		Laser/cautery+RT (*n*=24)	28%
		RT+chemo (*n*=2)	0%
Chow *et al*.[24]	-	Surgery alone (*n*=5)	16 mo
		RT alone (*n*=12)	26 mo
		Surgery+RT (*n*=5)	61 mo
Regnard *et al*.[25]	-	R0+RT (*n*=31)	74%(5-yr actuarial)
		R0 (*n*=27)	53%(p=ns)
		R1,2+RT (*n*=15)	47%
		R1,2 (*n*=6)	0%(p<0.5)
Maziak *et al*.[26]	Adenoid cystic (*n*=35)	R0+RT (*n*=14)	9.8 yr
		R1,2+RT (*n*=15)	7.5 yr
		RT alone	6.2 yr

RT: Radiation therapy; Chemo: Chemotherapy; R0: Complete resection; R1,2: Incomplete resection

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