Adenoid Cystic Carcinoma of the Trachea-Dosimetric comparison of different techniques of Radiotherapy

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Abstract: Background Adenoid cystic carcinoma is a rare malignancy, usually originating in the salivary glands of the head and neck region, and frequently occurring in the proximal trachea with luminal narrowing and a multinodular goiter. She underwent total thyroidectomy with tracheal sleeve resection and primary anastomosis. Surgical resection is the treatment of choice. Radiotherapy is reserved for microscopically positive margins, neural invasion or unresectable disease. Materials and Method: A forty seven year old lady presented with a thyroid swelling for 4 years, dyspnoea on exertion for 3 months and noisy breathing for 3 weeks. CT neck showed an asymmetric circumferential thickening of proximal trachea with luminal narrowing and a multinodular goiter. She underwent total thyroidectomy with tracheal sleeve resection and primary anastomosis. Histopathology of the tracheal region was reported as adenoid cystic carcinoma with the inferior and superior margins involved by tumor, however, with negative nodes. She was planned for radiotherapy for the positive margins. It was decided to treat the patient with Intensity Modulated Radiation Therapy (IMRT). The Clinical Target Volume (CTV) was 1.5 cm and the Planning Target Volume (PTV) of 0.5 cm. The surrounding critical structures were contoured as Organs at Risk (OAR). Dosimetric study was done using various conformal plans and comparison was done with Intensity Modulated Radiation Therapy (IMRT) plan. The Dose Volume Histograms (DVH) generated were compared and the doses received by 95 dose to PTV (D95) Dose received by 98 of the PTV (D98) and dose received by 2 cc volume of PTV (D2cc) were compared. Maximum dose to spine and PRV spine were also compared. Results: Various plans - 3D CRT using various beam arrangements and IMRT were created, evaluated and compared. The IMRT plan was deemed the best dosimetrically. Conclusions: Adenoid cystic carcinoma of the trachea is a rare malignancy and there are no definite guidelines to treat these tumours. IMRT may be the preferred modality of radiotherapy for these tumours due to their location proximity to critical structures.

Keyword: Adenoid cystic carcinoma, trachea, conformal radiotherapy

INTRODUCTION

Adenoid Cystic Carcinoma (ACC) is a rare malignancy that usually originates in the salivary glands of the head and neck region and has been known to originate in the trachea and accounts for 0.2% of all malignancies of respiratory tract and 0.04% of all malignancies (1-3). There is no standard staging system for this disease or primary tracheal malignancies. ACC has a predilection for perineural invasion and a tendency for both local and distant recurrence. Surgical resection is the mainstay of treatment, but it also depends on other factors like tumor size, location and patient co-morbidities. Radiotherapy has mainly been described in patients with microscopically positive margins, invasion of a named nerve or unresectable disease (4). Adjuvant irradiation has been described in a setting where the margins have been histologically negative (10). Due to the rarity of the disease, there is a lack of robust prospective data and therefore the optimal local therapy for tracheal ACC remains undefined as of today. Better response rates with doses of 60Gy or higher for radical treatment and more than 50Gy in adjuvant setting have been reported in studies (5-8). Dose escalation in the form of endo-tracheal brachytherapy boost has been proposed considering certain worries concerning the radiotherapy dose delivery. These are under dosing of the tumor at the luminal surface, secondary to a lack of dose build up at the air-tissue interface with external radiotherapy. Acute side effects include esophagitis, tracheal oedema and dermatitis, while late side effects like tracheo-oesophageal fistula, tracheal stenosis, pharyngeal leak and esophageal stricture have been described. Due to the indolent nature of disease, these patients tend to survive for long periods and treatment side effects tend to become a matter of concern. Review of literature showed five year survival ranging from 66% to 99% for these tumors regardless of the treatment modality (9). For localized disease, the role of chemotherapy either alone or concurrent with radiation, is unknown. We report one patient treated in our department for adenoid cystic carcinoma of the trachea, problems encountered during radiotherapy planning and dosimetric study comparing various conformal radiation therapy techniques.

CASE REPORT

A forty seven old lady presented with a swelling in the region of thyroid for 4 years, dyspnoea on exertion for 3 months and noisy breathing for 3 weeks duration restricting her day to day activities. Clinical examination showed a 6x5cm size, firm swelling in front of the neck more on the left side, which moved with deglutition. There was another 2x2cm, hard nodule in the upper pole of right lobe of thyroid. Trachea was deviated to the right, and there was no cervical lymphadenopathy. A Differential diagnosis of a primary thyroid malignancy with tracheal infiltration was considered. The Fine Needle Aspiration Cytology (FNAC) of the thyroid was reported as benign. CT scan of the neck showed asymmetric circumferential wall thickening of the proximal trachea with luminal narrowing from T1–T3 level, apart from...
multinodular goiter. Fat plane between trachea and thyroid was maintained and there was no regional lymphadenopathy. She was taken up for total thyroidectomy with tracheal resection and primary anastomosis based on imaging. Histopathology reported as nodular hyperplasia, total thyroidectomy specimen and adenoid cystic carcinoma, tracheal resection specimen. Inferior and superior margins were involved by tumor and tissue from pretracheal region showed tumor deposits, however, with negative nodes. Her post op CT scan showed minimal soft tissue thickening at the post op site. Synchronous metastases were ruled out. She was advised and treated with adjuvant conformal radiotherapy in view of positive margins, as local recurrence is the major factor deciding survival.

**MATERIAL AND METHODS**

A planning CT scan was done after immobilization in supine position with 3D head and neck ray cast and Vacloc. 3mm CT slices were obtained from vertex to T12. Clinical Target Volume (CTV) included post op bed and 1.5 cm margin for mucosal spread. A PTV of 0.5cm was given to account for organ motion and set up uncertainties. Given the low propensity of lymphatic spread, elective nodal irradiation was not considered. Normal tissue constraints are prioritized for treatment planning as follows:

Dosimetric study was done using various conformal plans and comparison was done with Intensity Modulated Radiation Therapy (IMRT) plan.

The conformal techniques planned were:

- 3D Conformal Radiation therapy with 3 beams
- 3D Conformal Radiation therapy with 4 beams (6 MV)
- 3D Conformal Radiation therapy with Oblique beam arrangement
- 3D Conformal Radiation therapy with combination of beams (6 MV and 15 MV combination)

Plans were done for 3D CRT using Plato software version sunrise 2.7.7 and IMRT plan was done on Eclipse software version 10.0. The Dose Volume Histograms (DVH) generated were compared and the dose. Geometric by 95% dose to PTV (D95%) Dose received by 98% of the PTV (D98%) and dose received by 2 cc volume of PTV (D2cc) were compared. Spinal cord is the organ which is considered as critical OAR and maximum dose to spine and PRV spine were also compared. Dose prescription to PTV was 60Gy to the 95% isodose in 30 fractions.

**RESULTS**

The main problems encountered during radiotherapy planning were proximity of tumor location to critical structures, concave shaped PTV around the spinal cord, difficulty in choosing beams due to neck-thorax contour difference and underdosing of tumor at the luminal surface secondary to a lack of dose build up at the air-tissue interface with external radiotherapy.

**Table: 1 Comparison of various doses for different conformal radiotherapy techniques and IMRT**

<table>
<thead>
<tr>
<th>Technique</th>
<th>D95</th>
<th>D98</th>
<th>D2cc</th>
<th>Max dose to spine</th>
<th>Max dose to PRV spine</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMRT</td>
<td>95.5%</td>
<td>93.6%</td>
<td>105%</td>
<td>39.20 Gy</td>
<td>47.52 Gy</td>
</tr>
<tr>
<td>3 fields 6MV</td>
<td>85.9%</td>
<td>89.9%</td>
<td>117%</td>
<td>39.56 Gy</td>
<td>61.11 Gy</td>
</tr>
</tbody>
</table>

Fig 1B-Cumulative DVH depicting doses to critical structures

Fig 1A and B shows that planning with IMRT resulted in homogenous dose to the tumor volume with sparing of critical structures. 95% of the PTV volume was covered by 96% of the dose prescribed. D2cc was 105% and dose to the Organ at Risk (OAR) were within acceptable limits. Maximum dose to the spinal cord with IMRT plan was 38.20Gy and none of the conformal radiotherapy plans could achieve this dose constraint for spinal cord.

**3 Beam (6MV) 3D Conformal Plan**

Fig 2A 3DCRT plan with 3 beams (6MV)

Fig 2 (A and B) shows that 3D CRT with 2 anterior oblique beams and direct posterior beam plan achieved a maximum dose of 117% with poor PTV coverage (95% of the dose prescribed is covering only 85.9% of the volume). The dose constraint was achieved for spinal cord but PRV spine received 61.11Gy, similar dose as the tumor.

**Fig 2B Cumulative DVH depicting doses to critical structures**

**4 Beam (6MV) 3D Conformal Plan**

Fig 3A 3DCRT plan with 4 beams (6MV)
3DCRT plan with 4 beams (2 lateral beams, anterior and posterior beam) resulted in better PTV coverage (96.95% of the volume receiving 95% of the dose). But the D2 dose of 115% was not acceptable and maximum dose to spine was 42.29Gy and PRV spine was 54.49Gy respectively which were higher than the tolerance limits.

**Fig.3B Cumulative DVH depicting doses to critical structures**

Obliques 3D Conformal Plan

**Fig.4A 3DCRT plan with oblique beams (6MV)**

Fig.4 (A and B) shows that 3DCRT plan with 2 anterior oblique beams and one anterior and a posterior field arrangement failed to achieve dose coverage to PTV (only 77.42% of PTV received 95% of the dose prescribed) and resulted in unacceptable dose to spinal cord (maximum dose to the spinal cord 59.99Gy and 60.44Gy to the PRV spine).

4 Beam combination (6MV/15MV) 3D Conformal Plan

**Fig:5A 3D CRT plan with combination of 6MV and 15MV beams**

3DCRT with 4 beams (combination of 6MV and 15MV) resulted in better PTV coverage, 94.06% of the volume receiving 95% of the dose, was more homogenous, D 2cc was 101.25%, but could not achieve the dose limit to spinal cord, the maximum of which was 49.75Gy and 52.64Gy to PRV spine.

**DISCUSSION**

The aim of radiotherapy planning is to achieve maximum therapeutic ratio which is increased dose to the tumor with decreased dose to the surrounding normal structures. Wedges or compensators were used in both conventional radiotherapy and 3DCRT to compensate for the missing tissue and attempts were made to achieve homogenous dose to the sloping or curved tumor volume. With the introduction of multileaf collimators (MLCs), it is possible to shape the beams conforming to the tumor shape. In 1982, Brahme proposed the concept of IMRT. He showed that intensity-modulated beams from multiple directions could be designed to produce dose homogeneity in the tumor volume with superior conformality, especially for concave or other complex shaped target volumes, thereby sparing nearby normal tissues (IMRTWG, 2001). IMRT attempts to achieve more optimal dose distributions by varying the beam intensity (fluence) with each incident beam, by subdividing the beam into a number of smaller segments and modulating each to achieve its selected fluence contribution. Modulation of the beam is greatly facilitated by the use of multileaf collimators or binary collimators combined with a moving couch. After the report on adjuvant radiotherapy (10), the same has been recommended to the region of anastomosis even if the stump was pathologically negative. Maziek (9) demonstrated the efficacy of radiation in unresectable ACC trachea patients, and reported a 5-year median survival of 97 months, and a 5-year actuarial survival of 54.1%. Literature review has shown that the preferred modality of treatment for radical treatment of ACC was IMRT because of the ability to modulate the fluence within the beam allowed for preferential dose delivery to the target while minimizing the dose to surrounding structures (11). In our study, ‘hot spots’ were higher in 3DCRT plan than IMRT. Better coverage was achieved with IMRT. Less dose to OARs was achieved with IMRT especially PRV spine where the PTV was in close proximity to the spinal cord as a concave structure. 3DCRT with combination of 6MV and 15 MV (AP and 2 laterals-45 degree wedges) was the best 3D CRT plan achieved. Field in field technique, and 3DCRT with 15MV (4 beams) dose distribution also failed to achieve the desired doses for PTV and OAR’s.

**CONCLUSION**

In the absence of randomized trials to dictate the optimal dose and fractionation radiotherapy for tracheal ACC, advanced modalities and techniques should be used to facilitate dose escalation and minimize long term toxicity. Sparring of lung, spinal cord, heart and esophagus was achieved with intensity modulated radiotherapy. IMRT may be the preferred modality of radiotherapy for these tumours due to their location and proximity to critical structures.

**BIBLIOGRAPHY**
