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Oncology

THYMOMA : AN UNUSUAL PRESENTATION AND ITS MANAGEMENT BY ADJUVANT 3D CONFORMAL RADIOTHERAPY

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ABSTRACT Thymomas and thymic carcinomas are common tumors of anterior mediastinum and are very rare in incidence (1.5 case/million). The 5yr survival rate for thymoma is 78% and for thymic carcinoma is 40%. Most common classification system for thymic malignancies are the WHO and Masaoka system. Thymomas generally present in the age group of 40 to 60 yrs and are rare in children and adolescents. Primary modality of treatment for thymomas is surgery. Adjuvant treatment is not recommended for R0 resection. For R1 resection the recommended adjuvant treatment is post operative radiation therapy. In cases of advanced disease, chemotherapy with or without radiation is recommended and most common chemotherapy regimen used is cisplatin, doxorubicin and cyclophosphamide. . Here we present two cases of thymomas with unusual presentations and their management. The role of radiation in the management of thymomas and its relevance in the overall management of thymoma is discussed.

KEYWORDS : Thymoma Radiotherapy, Anterior mediastinal tumours Unusual tumors

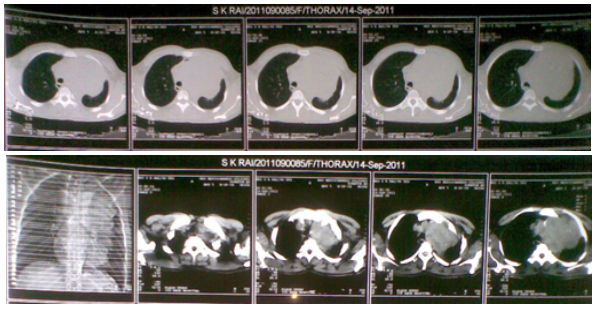
Introduction

Thymomas and thymic carcinomas are common tumors of anterior mediastinum and are very rare in incidence (1.5 case/million). The 5yr survival rate for thymoma is 78% and for thymic carcinoma is 40%. Most common classification system for thymic malignancies are the WHO and Masaoka system. Thymomas generally present in the age group of 40 to 60 yrs and are rare in children and adolescents. At presentation they are commonly asymptomatic or may present with chest pain, dyspnoea or cough. 30 to 50% patients of thymoma are generally associated with Myasthenia Gravis and hence should also be evaluated for the same. Most commonly they are locally invasive and rarely spread to lymph nodes. Primary modality of treatment for thymomas is surgery. Adjuvant treatment is not recommended for R0 resection. For R1 resection the recommended adjuvant treatment is post operative radiation therapy. Postoperative radiation is also recommended to reduce recurrence rates and improve local control of the disease, in capsular invasion and in stage III patients with macroscopic invasion of surrounding structures. Radiation therapy can be planned with advanced CT based planning technique with 3D CRT or IMRT to avoid dose to surrounding normal structures. Nodal irradiation is not recommended. Total dose recommended is 60 – 70 Gy for unresectable disease and for adjuvant treatment total dose of 45 – 50 Gy is recommended for clear margins and 54 Gy for microscopically positive margins. In cases of advanced disease, chemotherapy with or without radiation is recommended and most common chemotherapy regimen used is cisplatin, doxorubicin and cyclophosphamide. Here we present two cases of thymomas with unusual presentations and their management. The role of radiation in the management of thymomas and its relevance in the overall management of thymoma is discussed.

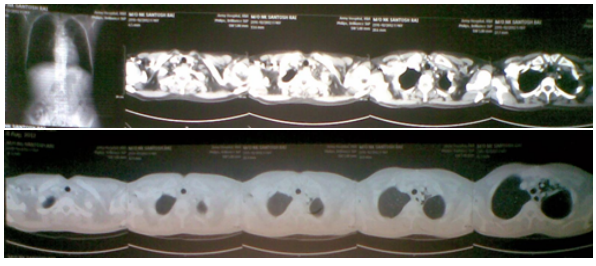
Case 1

46 Yrs old lady presented with history of cough, dyspnoea, fever and sweating. She was evaluated with CECT chest revealing 10 x 10 cm sized lobulated enhancing lesion in sup mediastinum pushing trachea, aortic arch and Rt brachiocephalic trunk to the right, encasing Lt Common carotid artery and Lt subclavian artery posteriorly. Lt sided minimal pleural effusion was present. There was no endobronchial lesion on FOB evaluation. PFT revealed mild restriction. Open biopsy and frozen section from the lesion was suggestive of thymic malignancy. She was inoperable in view of large thymic lesion which was adherent to pleura, pericardium and was engulfing trachea and innominate vein with invasion of pericardium and dense adherence to pulm artery and Lt hilum. Histopathology from this mass was suggestive of Mixed thymoma type AB. IHC panel was positive for CD 10 , CK , LCA , CD 3 , and CD 5. CD 68 was positive in histiocytes. PET CT scan revealed infiltrating lesion 17 x 12 cm with SUV of 4. Extent was from thoracic inlet to diaphragmatic pleura, along with multiple pleural deposits over diaphragmatic pleura on Lt Side. Tumour board consensus for Radiotherapy followed by adjuvant chemotherapy was taken. She was treated by 3 D CRT technique on linear accelerator by three fields with 15 MV photons up to a dose of 26 Gy over 21 days with 200 cGy daily fractionation. The patient chest X ray revealed significant reduction in the size of the primary. She also had significant reduction of her dyspnoea. However, further radiation was not given in view of cardiac tolerance and multiple pleural deposits. Thereafter, she was treated with Inj CDDP, Inj Doxorubicin and Inj cyclophosphamide based chemotherapy for 08 cycles. She was evaluated with PET CT scan post treatment which revealed significant resolution of size and metabolic activity of the lesion with disappearance of pleural deposits. At present patient is on close follow up and is asymptomatic.

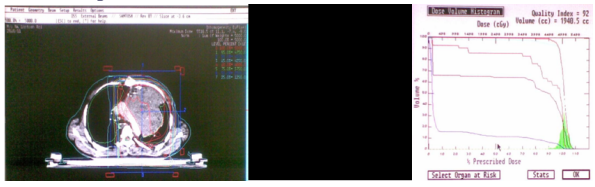
Photo – Pre treatment:



Post treatment:



Radiation plan on TPS:



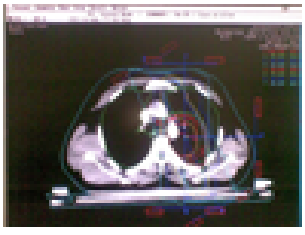
Case 2

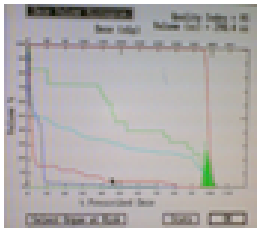
42 yrs old male, completely asymptomatic was found to have a mediastinal lesion which on CECT Chest which was suggestive of well defined smoothly marginated enhancing mass lesion in posterior aspect of superior mediastinum extending to Lt hemithorax with a size of 9 x 9 cm with nodular calcification within. The lesion was abutting the Lt Subclavian vessels and Lt brachiocephalic vessels and 2nd to 5th rib. Medially the lesion was abutting oesophagus and trachea and

inferiorly the lesion was abutting arch of aorta. He underwent surgery with left thoracotomy and piecemeal excision of tumour. Histopathology was suggestive of Thymoma WHO type B1. The treating surgeon was of the opinion that the surgery to be considered as R1 resection in view of piecemeal excision. In view of the above the patient was treated with adjuvant radiation to mediastinum with 3D CRT on linear accelerator with five fields with 15 MV photon energy at 2 Gy per fraction to a total dose of 54 Gy. Patient tolerated the treatment well and is presently convalescing without any signs or symptoms.

Photo – pre treatment:

Radiation plan on TPS:





Discussion

Surgery is the mainstay of treatment of thymomas with perioperative mortality being less than 1% . The completeness of surgery is the most important prognostic factor. However it is achieved in only 60 – 75 % cases. The approach for surgery is generally median sternotomy or a cervical or a VATS approach. The role of adjuvant treatment only arises if the disease is inoperable or incompletely resected or stage II/III disease. Adjuvant treatment is given by radiotherapy or chemotherapy. Neoadjuvant radiation or chemotherapy or concurrent chemo radiation has been used to improve resectability or as a definitive modality of management for inoperable disease. Multiple retrospective reviews suggest that radiotherapy reduces recurrence rates and improves outcome for incompletely resected stage II–IV thymoma. The role of post-op radiation for completely resected stage II–III thymoma is controversial. Forquer et al. reviewed 901 patients with surgically resected thymoma or thymic carcinoma in SEER database. Post-op radiotherapy improved 5-year OS for patients with Stage II–III disease (66- 76%), but not CSS (91 vs. 86%). No benefit of postop radiotherapy was seen in Stage I patients. In multivariate analysis age and stage were the most important prognostic factors. Kondo and Monden in review of 1,320 patients with thymic epithelial tumours concluded that stage I disease is treated with surgery alone however stage II–III thymoma and thymic carcinoid are treated with surgery and radiotherapy. Stage IV disease is treated with radiotherapy and concurrent chemotherapy. Masaoka clinical stage is an excellent predictor of prognosis for thymoma and thymic carcinoma, but not thymic carcinoid. Complete resection is the most important prognostic factor. Post-op radiotherapy did not significantly reduce recurrence rate for patients with completely resected stage II–III thymoma. Study done by Zhu et al. concluded that post op radiation improves local control in stage II by 96%, in stage III by 56%, in stage IVA by 43% and in stage IVB by 22%. Curran et al. in a retrospective study suggested that there were no recurrences amongst stage I patients after total resection without radiation. Fifty-three percent with stage II/III thymoma had mediastinal recurrence without post operative radiation vs. 0% after total resection with radiation, and 21% after subtotal resection or biopsy with radiation. In a study done by Monden et al. radiotherapy reduced recurrence from 30 to 15%. Combined modality management with surgery followed by radiotherapy and chemotherapy by Mornex et al, Kim et al and Wright et al concluded that adjuvant treatment in stage III and IV improved local control and survival rates. Although six different combination regimens are provided in NCCN algorithm, cispaltin/Doxorubicin based regimens yield the best outcome.

Radiation is given by simulating the patient in supine position with arms overhead and adequate immobilization. Conformal, image-based planning techniques are preferred (IMRT, 3D-CRT, tomotherapy) to minimize dose to surrounding normal structures. Surgical clips denoting the extent of surgical resection and/or regions of residual disease are important for design of post-op fields. PTV is equal to GTV/tumour bed and clips +1.5–2.0 cm margin. There is no need for SCF field unless involved. The dose generally prescribed for pre-op radiotherapy is 45 Gy. For stage II post operatively the doses is 45–50 Gy and in stage III post operatively 50–54 Gy. In cases of gross residual disease the dose is in the range of 54–60 Gy. Tolerance dose limits for organs at risk should be respected. For spinal cord less than or equal to 45 Gy, for Lung, limit the volume receiving 20 Gy, V20 to <30 – 35% and for heart limit V 45 <60%. For oesophagus limit mean dose to less than 34 Gy. Post treatment complications can be either acute or chronic in the form of skin reactions, fatigue, dysphagia, odynophagia, cough, dyspnea, L'hermitte's syndrome, acute pneumonitis, pericarditis, restrictive cardimyopathy, myocardial infarction, CHF and pulmonary fibrosis. Follow up should include annual chest CT scan. Late recurrences are not uncommon and hence long-term follow-up for at least 10 yrs is indicated.

References

1. Curran WJ Jr., Kornstein MJ, Brooks JJ, et al. Invasive thymoma: the role of mediastinal irradiation following complete or incomplete surgical resection. J Clin Oncol. 1988;6:1722-1727.
2. Forquer JA, Rong N, Fakiris AJ, et al. Postoperative radiotherapy after surgical resection of thymoma:differing roles in localized and regional disease. Int J Radiat Oncol Biol Phys.2010;76(2):440-445.
3. Kim E, Putnam J, Komaki R, et al. Phase II study of a multidisciplinary approach with induction chemotherapy, followed by surgical resection, radiation therapy, and consolidation chemotherapy for unresectable malignant thymomas: final report. Lung Cancer 2004;44:369-379.
4. Kondo K, Monden Y. Therapy for thymic epithelial tumors: a clinical study of 1,320 patients from Japan. Ann Thorac Surg. 2003;76(3):878-884.
5. Monden Y, Nakahara K, Iioka S, et al. Recurrence of thymoma: clinicopathological features,therapy, and prognosis. Ann Thorac Surg. 1985;39:165-169.
6. Mornex F. Radiotherapy and chemotherapy for invasive thymomas: a multicentric retrospective review of 90 cases. Int J Radiation Oncology Biol Phys. 1995;2:651-659.
7. Wright CD, Choi NC, Wain JC, et al Induction chemoradiotherapy followed by resection for locally advanced Masaoka stage III and IVA thymic tumors. Ann Thoracic Surg.2008;85(2):385-389.
8. Zhu G, He S, Fu X, et al. Radiotherapy and prognostic factors for thymoma: a retrospective study of 175 patients. Int J Radiat Oncol Biol Phys. 2004;60(4):1113-1119.