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Management of thymoma: A retrospective review of 50 cases from a tertiary cancer centre

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Abstract

Introduction: Thymoma is the most common neoplasm of the anterior mediastinum which originates from the epithelial cells of the thymus. Thymomas are typically slow-growing tumors that spread by local extension. Metastases are usually confined to the pleura, pericardium, or diaphragm, whereas extra thoracic metastases are uncommon. Surgery is the treatment of choice followed by adjuvant treatment in from of radiation and chemotherapy and role of debulking is still controversial. Paraneoplastic syndromes are associated with approximately 70 percent of cases.

Aims and objective: In this study tried to find out the role of different treatment options of thymoma, its outcome, prognostic factors in current scenario.

Material and methods: It is a retrospective analysis of 55 patients of histologically proven cases of thymoma out of which five cases were excluded due to Unresectability determined pre-operatively. Data collected from hospital data base from 1998 to year 2008. Tumor was staged according to Masaoka staging system and histopathological typing was done according to WHO classification. After clinical evaluation, staging work-up includes contrast enhanced computed tomography examination. Thymectomy was performed wherever feasible, if not then debulking was done.

Results: Average age of presentation was 51 years with male to female ratio of 1.2:1. 30% patients have associated myasthenia gravis syndrome. Cough was the most common symptom followed by dyspnoea and chest pain. Out of 50 patients 44% were Masaoka's stage I.35/50 underwent curative resection. Myasthenia crisis was reported in four patients whereas post-operative mortality was 7%. Reported five year survival was 60%.

Conclusion: Surgery remains the mainstay of treatment regardless of stage for all thymic neoplasms. extended Thymectomy should be done in advance cases. Ongoing studies showed benefit of neoadjuvant chemotherapy and radiation in locally advanced tumors. Resection margin is the most important predictor of recurrence, final outcome and determining factor for adjuvant treatment. Multidisciplinary team discussion is required before treatment planning.

Keywords: Thymoma, Thymectomy, Mediastinal tumor, Masaoka staging

1. Introduction

Thymomas are the rare malignancies with annual incidence of 0.15/100,000 population. They arise from the thymic epithelium and constitute 30 % and 15 % of anterior mediastinal masses in adult and children respectively [1]. Majority of thymoma are asymptomatic and detected incidentally on routine check-up whereas symptoms, if present are due to compression, invasion of adjacent structures or paraneoplastic syndromes. Common paraneoplastic syndromes are myasthenia gravis, pure red cell aplasia and hypogammaglobulinemia which constitutes 40 %, 5%, and 5-10% respectively [2].

Currently the term invasive and non-invasive thymoma are commonly used rather than benign and malignant variant. Distant metastasis and infiltration to surrounding structures are features suggestive of malignancy but histopathological examination is the most definitive way to differentiate between two. Liver and bone is the common site of metastasis. Local recurrence is also very common even after Ro resection [3].

Histopathological classification given by WHO in 1999 is still the most commonly used system which categories thymoma in category A, AB, B (B1, B2, B3) and C and also holds the prognostic significance. Category B3 and C are also known as thymic carcinoma [2]. Masaoka staging system is a four tier system used for thymoma based on final

histopathology and has prognostic significance. Established ten year survival based on this system is 67%, 60%, 58% and 0 % for stage I, II, III, and IV respectively.

Surgery, chemotherapy and radiotherapy are treatment options available. Surgery is the mainstay of treatment. Due to rarity of the disease majority of the recommendations are based on the review of retrospective studies. In this study tried to find out the role of different treatment options of thymoma.

2. Material and methods

We retrospectively reviewed 55 cases thymic epithelial tumors diagnosed during the period of 1998 to 2008 at Kidwai Memorial Institute of Oncology Bangalore. 55 patients were diagnosed as thymoma during this period. Out of which 50 patients were included in our study. Five patients were found to have either World Health Organization type C disease or Masaoka stage IV-B disease and were excluded from analysis. We reviewed all the pathological specimens using the current World Health Organization classification. Patient characteristics, surgical procedures, and postoperative courses were studied. Staging was performed according to the modified Masaoka system based on surgical and pathological findings. Preoperative workup included a complete history and physical examination, laboratory tests, chest roentgenograms, contrast enhanced computed tomography scan. Our strategy for clinically suspected thymoma patients without any clinical evidence of dissemination was surgery i.e., surgical exploration for histologic diagnosis and potential resection. The surgical procedure consisted of a total Thymectomy, together with excision of invaded tissue whenever possible, through a median sternotomy or a Thoracotomy based on the tumor location. Patients were operated on with every effort to remove the tumor. If complete resection was not feasible, then a partial resection (debulking) was carried out. When even a debulking was difficult, the procedure turned into mere biopsy. Surgical specimens were further examined by our pathologists to determine the histology as well as the margins of resection. The most common surgical approach was sternotomy, which was utilized in 32(64%) patients in our series. In addition to total Thymectomy, 4 of our patients additionally had partial pleurectomy, wedge resections of lung & lobectomy.

3. Result

Average age of presentation was 51 years with male to female ratio of 1.2:1. 30% patients have associated myasthenia gravis syndrome. Cough was the most common symptom (34%) followed by dyspnoea (24%) and chest pain (16%), whereas 20 % of patients were asymptomatic. Features of SVC obstruction were found in three patients. 15/50 patients had features of myasthenia gravis. 35 patient underwent complete resection whereas partial resection was done in 11 patients. 4 patients underwent biopsy only. Pre-operative biopsy was not performed in any cases as per institute protocol. After final histopathology staging was done according to Masaoka staging system which constitute 44 % stage I, 32 % stage II, 14% stage III and 10 % were stage IV. [Table 1] The complete resection rate of stages I and II tumors was significantly higher than stages III and IV tumors (88.57% vs. 11.43%;). There were significantly more stage I and stage II cases in histologic types A, AB, and B1 tumors than in B2, B3 tumors (76% vs.

24%.), and their complete resection rate was significantly higher than the latter group (90.91% vs. 9.09%). [Table 2]. In post-operative period four patients developed myasthenia crisis out of which one died while two had respiratory failure managed conservatively. Two patient had pneumonia treated with antibiotics. One more patient died in post-operative period due to cardiac arrest. Patients with stage II or more underwent adjuvant radiotherapy 50.4 Gy, whereas chemo-radiotherapy offered to patients with margin positive resection. Paclitaxel and Carboplatin doublet was given in adjuvant chemotherapy group. Mean follow-up period was 60 months. 66 % patients were alive whereas nine lost to follow up.

Table 1: Staging of thymoma

Masaoka stage	Number of patients
Stage 1	22(44%)
Stage 2	16(32%)
Stage 3	07(14%)
Stage 4-A	05(10%)

Table 2: Surgery performed according to stage of the disease

	Completely resected(35)	Partially resected(11)	Biopsy only(4)
Stage 1	20	02	00
Stage 2	11	05	00
Stage 3	03	04	00
Stage 4	01	00	4

4. Discussion

Thymoma is potentially curative malignancy with good five year survival. WHO classification and Masaoka staging system is widely used for thymomas and holds prognostic significance as well. Surgery is the mainstay of treatment and adjuvant chemotherapy and radiotherapy is decided by the stage and margin of resection [4]. Multidisciplinary team discussion is important regarding the management of thymomas for proper patient selection. Surgery performed with aim of complete excision and if required extended Thymectomy should be done in locally advance tumor which includes resection of pleura, pericardium, diaphragm and ipsilateral phrenic nerve. Extended thymectomy is associated with prolong disease free and overall survival even in stage III and IV patients (69% - stage III and 50 % stage IV) [5]. Median sternotomy and clam-shell procedures are the traditional methods of surgery for mediastinal tumor. With advancement in technology now minimal invasive techniques are standard of care with equal oncological outcome better side effect profile which includes video assisted Thoracoscopic surgery and robotic assisted surgery. [6] Though various studies have shown benefit of neoadjuvant chemotherapy and radiation NCCN guideline recommends its use in stage IV A and primary surgery should be tried in stage I- III with aim of R0 resection. adjuvant therapy in from radiation to decided on resection margin and final stage. Despite of curative resection local recurrence is a major problem encountered in thymoma management. Review of literature showed Tumor histology, Masaoka stage, completeness of resection, and the tumor size as an independent predictor of recurrence with reported incidence of 16 – 26% for stage II and III [7]. In present study 26 patients received adjuvant treatment and we found 5(14%) recurrences in completely resected group during a follow-up period of 60 months. out of these patient

3 have recurrence in pleura and two were in diaphragm underwent re-excision. 3 patient who underwent partial excision developed distant metastasis as well as local recurrence which were not salvageable and provided with best supportive care.

Myasthenia gravis associated with thymoma reported in approximately 40 % of cases. Prior complete neurological examination required and specific treatment should be offered before surgery [8]. In our study 15 patients with myasthenia gravis were found and 13 responded well after thymectomy. Myasthenia crisis occurred in four patient and one died.

No separate guideline for thymic carcinomas are available due to rarity of the disease still retrospective studies showed clear benefit of complete resection with improved survival in early stage cancer [9]. Even for advance carcinoma surgery should be offered with intention to cure the disease like thymomas. Adjuvant treatment is required to further decrease the local recurrence [10].

5. Conclusion

There is no alternative to surgical excision and the goals of surgery were achieved safely with very few serious complications and no surgical deaths. surgical approach should be chosen wisely depending on the expertise and availability. For small thymoma VATS or robotic assisted surgery has equal outcomes. Completeness of resection is the most commonly cited statistically significant prognostic factor in thymoma. Our experience also proves that both the WHO criteria and the modified Masaoka staging are prognostic factors of thymomas. Long-term disease-specific survival can be expected not only after surgery for early stage thymoma but also after surgery for advanced disease. Adjuvant treatment should be offered to patients be margin positive resection or higher stage.

6. Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

7. Abbreviations

VATS- Video Assisted Thoracoscopic Surgery, WHO – World Health Organisation, NCCN- National Comprehensive Cancer Network

8. Competing interests

The authors declare that they have no competing interests

9. Authors' contributions

The department of surgical oncology was involved in the diagnosis, management and post-operative recovery of the patients. The Pathology department was responsible pathological report of the cases. All authors have contributed with the literature review and with the preparation of this manuscript. All authors read and approved the final manuscript.

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