

Management and Outcome of Thymoma: A Retrospective Analysis

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Abstract

Thymoma is a rare disease. The treatment of invasive thymoma remains controversial. To evaluate the outcome of thymoma we reviewed a seven years [1996-2002] experience with 26 patients at PGIMER Chandigarh. It constituted about 16% of all mediastinal tumours in our institutions. All the patients had surgical intervention and diagnosis was made on pathological study. Post-operative staging was made on modified Masaoka staging system. Out of 26 patients, six were with stage-1, 5 with stage-2, 7 with stage-3 and 8 with stage-4. The pathological classification included 6 lymphocytic predominant, 12 epitheloid and 8 mixed lymphoepitheloid histology. Myasthenia gravis was associated with 12 patients. Ten patients had complete surgical resection, 7 had incomplete surgery and 9 had only biopsy. All the patients received external beam radiation with doses ranging from 3000 Cgy to 5000 Cgy in 3 to 5 weeks with a fraction size of 180-200 Cgy. Three patients received systemic chemotherapy with multidrug platinum based regimens. The median follow up was 26.2 months. Patients who received adjuvant external radiation after complete surgery did better than who had incomplete surgery or only biopsy. Overall five years survival was 56.85. Post operative radiotherapy improved locoregional controls, however clinical stage and type of surgery were the two most important prognostic factors. Role of chemotherapy needs to be further assessed.

Key Words

Thymoma, Radiotherapy, Prognostic factors.

Introduction

Thymoma is a rare slow growing epithelial neoplasm arising from thymic epithelium (1). Thymoma is the most common tumor of the anterior mediastinum comprising about 20% of all mediastinal tumors in adults (2). Most thymoma are encapsulated but when microscopic or gross invasion of the capsule is present, it is termed as invasive thymoma (3). Most patients with thymoma are adults with median age of 52 years. There is an equal sex incidence. Thymoma is associated with a spectrum of diseases, most common is myasthenia gravis, others are pure red cell aplasia, hypogammaglobulinemia or polymyositis (4,5). There is no consensus regarding staging. The most commonly used staging system is "Modified Masaoka" staging system which defines the surgical and pathological extent of tumors (6). Surgery remains the cornerstone of primary treatment

irrespective whether the tumor is encapsulated or infiltrating (7). However in locally advanced stages complete resection is rarely attainable. Thymoma has been known to be relatively radiosensitive tumor. Radiotherapy is considered to be an excellent adjuvant therapy and is often mandatory for patients with invasive thymoma whether or not a complete resection is performed (8-10). Chemotherapy has been used for metastatic disease or for gross residual disease after surgery but its role is still to be defined (11).

Material and Methods

Twenty six patients were treated between 1996 to December 2002 with a diagnosis of thymoma at PGIMER Chandigarh. Out of these 57% (15) were male and 45% (11) were females with an age ranging from 19-75 yrs with a median age of 41.5 yrs (Table-1). These patients

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were followed up from 3-53 months with a median follow up of 26.2 months. At presentation myasthenia gravis was seen in 12 (46%) patients, 8(31%) patients presented with chest pain, cough and dyspnoea, where as 6 (23%) patients had other non specific symptoms (Table-2).

Staging and Pathology

All patients were staged according to “Modified Masoaka” staging (Table-3). Out of 26 patients, 6 were in stage-1, 5 in stage-2, 7 in stage3, and 8 were in stage-4 (Table-4). Patients were histologically classified as per Bernatz (12) classification. Six patients were with lymphocytic predominant histology, 12 with epithelial histology and 8 had mixed lymphoepithelial variants(Table-5).

Surgery

Ten patients had complete resection in this series and 7 had incomplete resection, whereas 9 patients had biopsy only. (Table-6)

Radiotherapy

All the patients received megavoltage external beam radiation after surgery. Most of these were treated with parallel opposed antero posterior mediastinal fields. These fields typically encompassed the tumour bed with 1 to 2 cms margin. The supraclavicular fossa were not treated. The radiation dose delivered ranged from 3000cGy-5000cGy in 3-5 weeks with a per fraction dose ranging from 180cGy – 200cGy and dose was calculated at mid plane depth.

Chemotherapy

Only three patients in our series were given chemotherapy with cisplatinum (50mg/m2), adriamycin (50mg/m2) and cyclophosphamide (600mg/m2). Each cycle was repeated every three weeks from day one of first cycle. Chemotherapy was used for patients with metastatic disease and who had only biopsy.

Results

Out of 26 patients, initial complete responses were seen in 14 (53.84%) patients. Six out of 6 patients in stage-1, 4 out of 5 in stage-2, 4 out of 7 in stage-3 and none out of 8 in stage-4 had initial complete responses.(Table-7). When the response was evaluated as per the type of surgery, ten out of 10 patients with complete excision of tumour responded, whereas the response was 3 out of 4 and 1 out of 8 in incomplete surgery and in patients with biopsy respectively (Table-8). 47% of patients were disease

free at last follow up, 38% had residual / recurrence of disease and 15% of the patients were lost to follow up (Table-9). While evaluating the pattern of failures (Table-10), ten out of 26 patients (38%) had failure to treatment, three (30%) patients failed locally whereas seven (70%) had metastatic disease also. The five year actuarial disease free survival was seen in 56.8% of patients in this series (Table-11). The use of chemotherapy did not effect local relapse. Also there was a significant relationship between the extent of surgery and the percentage of relapse, the local failure rate was seen mostly in patients who had incomplete surgery or biopsy. None of the patients who had complete surgery, failed locally.

Table 1. Age & Sex distribution

Age Range - 19 to 75 years
Median Age - 41.5 years

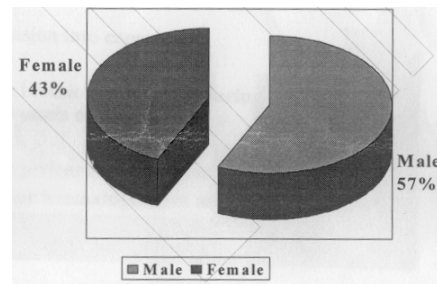


Table 2. Clinical Presentation

Symptoms	N	%age
Myasthenia Gravis	12	15.38
Chest pain, Cough, Dysnoea	8	23.08
Other Symptoms	6	30.77

Table 3. Masoaka Staging

Stage I	Macroscopically completely encapsulated and no microscopic capsula invasion.
Stage II	(i) Macroscopic invasion into surrounding fatty tissue or mediastinal pleura. (ii) Microscopic invasion into capsule.
Stage III	Microscopic invasion into neighbouring organs (pericardium, great vessels or lungs).
Stage IV	(i) Pleural or pericardial dessimination of thymoma. (ii) Lymphomatous or haematogeneous metastatis.

Table 4. Clinical staging (Masoaka Staging)

Stage	N	%age
I	4	15.38
II	6	23.08
II	8	30.77
IV	8	30.77

Table 5. Histology

Type	N	%age
Splindle Cell	2	7.69
Lymphocytic predominant	6	23.08
Mixed/ Lymphoepithelial	8	30.77
Epithelial	10	38.46

Table 6. Surgery

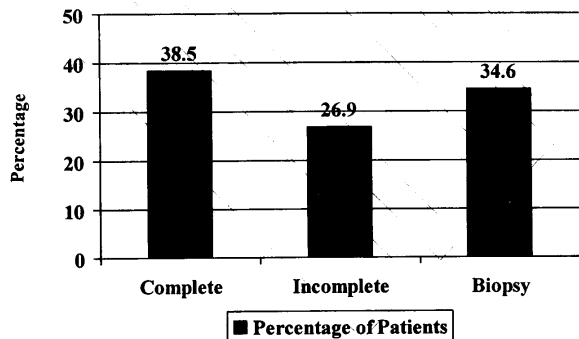


Table 7. Stage wise response

Initial complete response seen in 14/26 (53.84%) patients

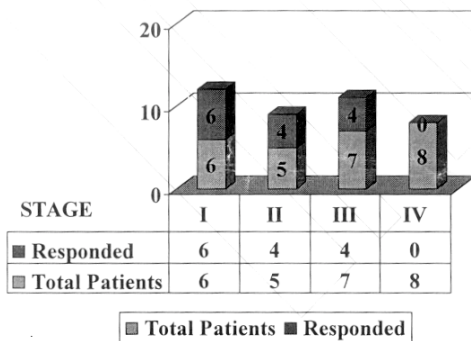
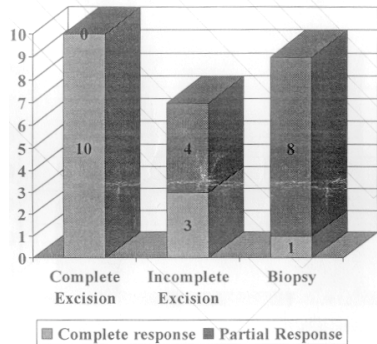


Table 8. Response according to surgery



Discussion

Although surgery remains the first choice of treatment for stage-I to III thymomas, still there is controversy

Table 9. Status at last followup

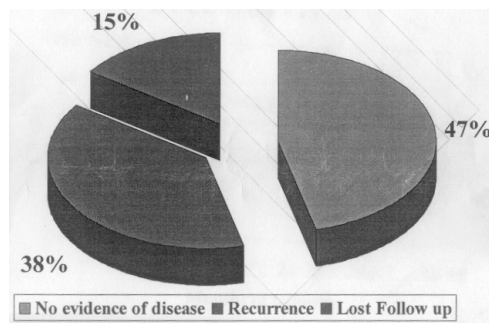


Table 10. Site of Recurrence

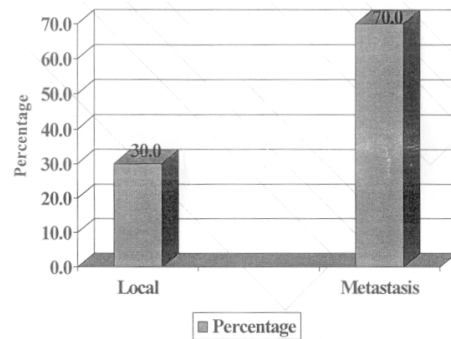
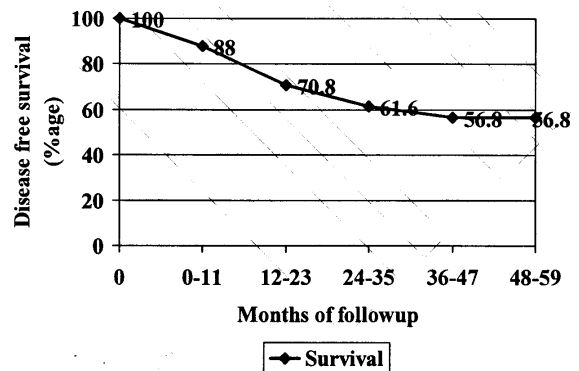


Table 11. 5 year actuarial disease free survival



regarding the optimum adjuvant treatment of thymoma after complete resection. Most of the studies report no or very few relapses after surgery without any adjuvant therapies (13-14). In our series no recurrence of stage-I thymoma after surgery with mediastinal irradiation was observed. These results suggest that probably routine post operative radiation is not indicated in stage-I thymoma. Because of less number of patients in stage-I in our series we used adjuvant radiation in all the patients. In stage-II

patients and in patients who had pleural dissemination chances of local recurrence are high. Post-operative mediastinal irradiation seems to be most effective adjuvant therapy in reducing the risk of the local recurrence and prolonging survival in these group of patients (15,16). In our series the local recurrence is seen in 38% of patients. Monden describes a 27% relapse rate in stage-III and Stage-IVA patients (15). Relapse rate and type of surgery are significantly related in Monden's series which is 53% in incomplete resection and 73% in patients with biopsy only ($p < 0.001$). In our series also 3 patients in incomplete surgery group and only one patient in biopsy group showed response rate thus contributing to a local failure rate of 66.6%. These findings support a policy of complete resection whenever possible.

In our series only three patients received chemotherapy with CAP regime. All the patients completed six cycles of chemotherapy but they did not have any evaluable impact on survival or response. The potential role of chemotherapy needs to be evaluated as an adjuvant treatment and for metastasis disease or relapse. However, in our study there was some amount of subjective symptom relief in these patients which may be correlated to lymphocytic component present in their histology and thus showing some response to alkylating agents, but it needs to be assessed in larger group of patients.

To conclude, surgery remains the mainstay in the treatment of thymoma, with post operative radiotherapy contributing to improve locoregional control of disease. Clinical stage and extent of surgery are the two most important prognostic factors. Role of chemotherapy needs to be further studied.

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