RESEARCH ARTICLE

Single Institution Experience of Thymic Tumor Treatment and Survival in Egypt

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Abstract

Thymic tumors are the most common tumors in the anterior mediastinum. Total resection is the main treatment and predictor of longer survival. Adjuvant radiotherapy alone or in combination with chemotherapy is recommended with incomplete excision or advanced disease. Thirty seven patients with thymic tumors were included in this retrospective study from January 2001 till December 2012. They were studied regarding age, sex, performance status, tumor size and invasion, stage, pathology, treatment given, overall and progression free survival. Myasthenia gravis was present in 18.1% of the patients. Masaoka stage III was diagnosed in 40.5% of the cases followed by stage II in 24.3% and the other stages with lower percentages. Pathology type B3 was the most frequent followed by B2 and B1 with percentages of 27, 24.3 and 21.7 respectively. Complete resection was conducted in 11 cases (29.75%). Partial resection or debulking was done in 15 (40.5%) and a biopsy was taken in 11 cases (29.8%) Adjuvant chemotherapy was given to 14 patients (37.8%) and neoadjuvant to 13 (35.2%). Adjuvant radiotherapy was given to 17 patients (46%) and neoadjuvant to 14 (37.8%). The 5-year overall survival by was 83% for stage I, 71% for stage II, 60% for stage III, and 44% for stage IV (p=0.0426). Five year progression free survival was 71% for stage I, 62% stage II, 42% stage III, and 37% for stage IV (p= 0.0532). In conclusion with the rare thymic tumors early stage and complete resection have the highest impact on overall and progression free survival.

Keywords: Thymic tumors - treatment - survival - Egypt

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Introduction

Thymic tumors are the most common tumors in the anterior mediastinum, though they are rare (Engels and Pfeiffer 2003). They occur in adults 40-70 years and are very rare in children or adolescents. Patients usually present with chest pain, cough and dyspnea and few cases are asymptomatic (Detterbeck and Parsons 2011). Fifteen to thirty percent of thymoma patients have myasthenia gravis. Thymomas can be locally invasive but seldom spread to lymph nodes or distant metastasis. Thymic carcinomas are more aggressive and frequently spread to lymph nodes and distant sites (Lopez et al, 2003; Kondo and Monden, 2003).

Thymic carcinoma and type B3 thymoma, have worse prognosis than types A, AB, B1, and B2. According to Masaoka staging, stage III and IV disease have worse prognosis and higher rate of recurrence in comparison to stage I and II. Five year survival rate for patients with thymoma stages I-III is 85% and 65% for stage IV. For thymic carcinomas 5 year survival ranges from 30-50% (Weksler et al, 2013).

Total resection is the main treatment and predictor of longer survival. Adjuvant radiotherapy is recommended in incomplete excision or advanced disease. Chemotherapy can be given as adjuvant treatment in incomplete resection of thymoma or thymic carcinoma. However, the role of adjuvant chemotherapy in the treatment of thymoma remains unclear (Detterbeck and Zeeshan, 2013; Usman et al, 2015).

Materials and Methods

Thirty seven patients with thymic tumors were included in this retrospective study from January 2001 till December 2012 in the center of radiation oncology Cairo University. Patients with incomplete records were not included. Patients were studied regarding age, sex, performance status, tumor size and invasion, stage, pathology, treatment given, overall and progression free survival.

Overall survival was determined as the interval between the date of diagnosis, and the date of death or last follow up. Progression-free survival was determined as the time interval between the last day of therapy, and the date of recurrence or last follow-up.

Patients were diagnosed by biopsy or following complete or partial resection. Two types of chemotherapy

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were given, cyclophosphamide, Adriamycin and cisplatin was given to most of the chemotherapy cases, while cisplatin/etoposide was given to 4 patients 2 with stage III and 2 with stage IVa. Chemotherapy was given as neoadjuvant for debulking prior to surgery or as adjuvant treatment post-operative. Radiation therapy either conformal or conventional was given as neoadjuvant treatment for debulking or as adjuvant treatment for residual tumor at a dose ranging from 45-54 Gy.

Statistical analysis

Data were statistically described in terms of range, mean ±standard deviation (±SD), frequencies and percentages. Kaplan-Meier survival for different parameters was done. A probability value (P value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2003 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

Results

Thirty seven thymic tumor patients were enrolled in this study from January 2001 till December 2012. Patient's age ranged from 34-61 with a mean of 45.3. Twenty two patients were males (59.5%) and fifteen were females (40.5%). Dyspnea was the main complaint in most of the cases (60%) followed by chest pain in 30% of the cases with ECOG performance status of 1 in 81% of the cases. Myasthenia gravis was present in 18.1% of the patients. Masaoka stage III was diagnosed in 40.5% of the cases followed by stage II in 24.3% then the other stages with lower percentage. Pathology type B3 was the most frequent one followed by B2 and B1 with percentages of 27, 24.3 and 21.7 respectively. Patients characteristics is shown in Table1.

Treatment according to stage is shown in Table 2. For stage I all patients underwent complete resection and one patient received adjuvant conformal radiotherapy at a dose of 45Gy. In stage II patients, 66.7% underwent complete resection and 33.3% did partial resection. Four patients (44.4%) received adjuvant chemotherapy. Six patients (66.7%) received adjuvant radiation therapy 1 received conventional radiotherapy and 5 received conformal radiotherapy. Stage III patients 53.4% had partial resection, 33.3% had biopsy and 13.3% had complete resection. Neoadjuvant chemotherapy was given in 33.3% while adjuvant was given in 53.4%. Radiation therapy was given as neoadjuvant treatment in 46.7% and as adjuvant in 46.7% (7 patients each), 71.4% received conformal and 28.6% received conventional radiotherapy. In stage IVa debulking was done in 57.1% of the cases

Table 1. Characteristics of the Thirty Seven Patients

Characteristic	Number	Percent
Age		
<55	26	70.30%
≥55	11	29.70%
Sex		
Male	22	59.50%
Female	15	40.50%
PS (ECOG)		
0	2	5.40%
1	30	81.10%
2	5	13.50%
Myasthenia gravis		
No	30	81.10%
Yes	7	18.90%
Tumor size (cm)		
≤6	2	5.40%
>6	35	94.60%
Masaoka stage		
I	3	8.10%
II	9	24.30%
III	15	40.50%
Iva	7	19%
Ivb	3	8.10%
Pathology		
Type A	2	5.40%
Type AB	3	8.10%
Type B1	8	21.70%
Type B2	9	24.30%
Type B3	10	27%
Type C	5	13.50%

Table 2. Treatment According to Stage

Treatment	Stage I N (3) (%)	Stage II N (9) (%)	Stage III N (15) (%)	Stage IVa N (7) (%)	Stage Ivb N (3) (%)
Surgery					
CR	3 (100%)	6 (66.7%)	2 (13.3%)		
PR		3 (33.3%)	8 (53.4%)	4 (57.1%)	
Biopsy		0	5 (33.3%)	3 (42.9%)	3 (100%)
Chemotheapy					
No	3 (100%)	5 (55.6%)	2 (13.3%)	0	0
Neoadjuvant		0	5 (33.3%)	5 (71.4%)	3 (100%)
Adjuvant		4 (44.4%)	8 (53.4%)	2 (28.6)	0
Radiotherapy					
No	2 (66.7%)	3 (33.3%)	1 (6.6%)	0	0
Neoadjuvant	0	0	7 (46.7%)	4 (57.2%)	3 (100%)
Adjuvant	1 (33.3%)	6 (66.7%)	7 (46.7%)	3 (42.8%)	
Conventional RT		1 (16.7%)	4 (28.6%)	2 (28.6%)	3 (100%)
Conformal RT	1 (100%)	5 (83.3%)	10(71.4%)	5 (71.4%)	

Table 3. Histologic Subtype and the Relationship with Tumor Invasion

Histologic subtype	I	II	III	Iva	Ivb	Cases of invasion to neighboring organ n (%)
A	1	1				0%
AB		2	1			1 (33.3%)
B1	1	2	3	2		5 (62.5%)
B2	1	2	4	2		7 (77.8%)
B3		1	5	2	2	9 (90%)
C		1	2	1	1	5 (80%)

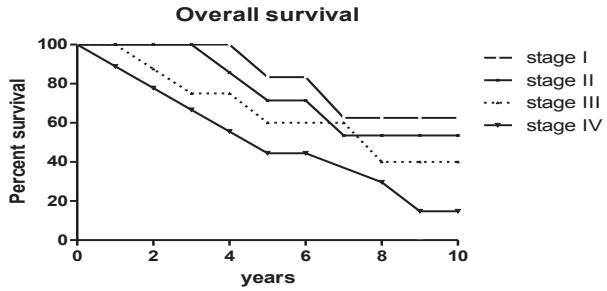

Figure 1. Comparison of Overall Survival for Different Masaoka Stages

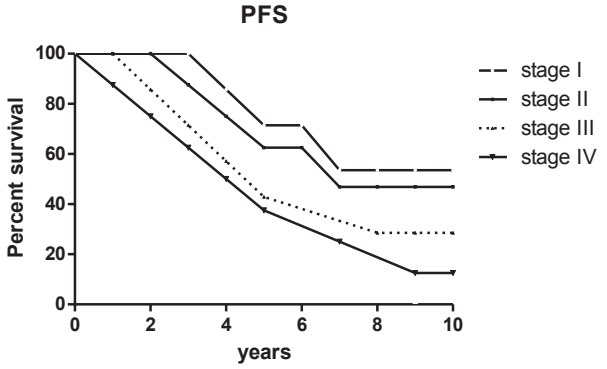

Figure 2. Comparison of Progression free Survival for Different Masaoka Stages

and biopsy was done in 42.9%. Five patients (71.4%) received neoadjuvant chemotherapy, while 2 patients (28.6%) received adjuvant chemotherapy. Neoadjuvant and adjuvant radiotherapy were given in 57.2% and 42.8% of the patients respectively, where 28.6% received conventional and 71.4% received conformal radiotherapy. For stage IVb the 3 patients did biopsy, received neoadjuvant chemotherapy and neoadjuvant conventional radiotherapy.

Histologic subtype and relationship to tumor invasion showed; type C had 80% invasion, B3 had 90% invasion to the neighboring organs, type B2 had 77.8% invasion, type B1 had 62.5% invasion, type AB had 33.3% invasion, and type A had no invasion the results were not statistically significant table.3.

Five year overall survival for different stages was statistically significant (p=0.0426). The 5-year OS by was 83% for stage I, 71% for stage II, 60% for stage III, and 44% for stage IV figure.1. Five year progression free survival was 71% for stage I, 62% stage II, 42% stage III, and 37% for stage IV (p= 0.0532) figure. 2.

Discussion

Thymic tumors are the most common tumors in the anterior mediastinum, they occur in adults aged 40-70 years. Patients usually present with chest pain, cough and dyspnea, and myasthenia gravis is present in 15-30% of the patients (Detterbeck and Parsons 2011; Lopez et al, 2003).

In this study patient's age ranged from 34-61 with a mean of 45.3, 59.5% were males and 40.5% were females. Dyspnea was present in 60% of the patients and chest pain in 30%. Myasthenia gravis was present in 18.1% of the patients.

In our study 8.1% patients had Masaoka stage I, 24.3% had stage II, 40.5% had stage III, and 27.1% had stage IV, thus stage III had the higher percentage. This was in accordance to the study done by Usman et al, where 5% of the patients had Masaoka stage I, 17% had stage II, 45% had stage III, and 33% had stage IV disease (Usman et al, 2015).

Complete resection was done in 11 cases (29.75%) with stage I, II and 2 with stage III. Partial resection or debulking was done in 15 cases (40.5%) and biopsy was done in 11 cases (29.75%) stages III and IV. Adjuvant chemotherapy was given in 14 patients (37.8%) and neoadjuvant was given in 13 patients (35.2%) stages III and IV. Adjuvant radiotherapy was given in 17 patients (46%) and neoadjuvant was given in 14 patients stages III and IV (37.8%).

The 5-year OS by was 83% for stage I, 71% for stage II, 60% for stage III, and 44% for stage IV (p=0.0426). Five year progression free survival was 71% for stage I, 62% stage II, 42% stage III, and 37% for stage IV (p=0.0532). Thus longer overall and progression free survival was associated with early stages who underwent complete resection with or without adjuvant radiotherapy or chemotherapy.

This was consistent with the previous studies where complete resection has improved survival (Venutaet al, 2010; Chung 2000). In Weksler et al, the median survival for patients who underwent complete excision was 105 months with 5-year survival of 58%; median survival for patients who did partial excision or biopsy was 29 months with 5-year survival of 26% (Weksler et al., 2013). Also, the survival of 154 patients with thymic carcinoma done by Kondo and Monden revealed 5-year survivals of 67% after total resection, 30% after subtotal resection, and 24% with biopsy (Kondo and Monden, 2003).

Our results were also comparable to Usman et al results where the 5-year OS by stage was 80% for stage I/II, 63% for stage III, 42% for stage IVa, and 30%for stage IVb. The 10-year OS was 60%for stage I/II, 42% for stage III, 28% for stage IVa, and 13% for stage IVb (Usman et al, 2015).

In conclusion, thymic tumors are rare tumors usually present late however detection in early stages and complete resection has the highest impact on overall and progression free survival. For advanced stages multimodality treatment is mandatory to improve results.

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