Head Neck Cancer Symposium:

Original Article

Thymoma: First large Indian experience

Rathod S, Munshi A, Paul S, Ganesh B[1], Prabhash K[2], Agarwal JP

Departments of Radiation Oncology, [1]Biostatistics, [2]Medical Oncology, Tata Memorial Hospital, Mumbai, India

Correspondence to: Dr. Jai Prakash Agarwal, E-mail: agarwaljp@tmc.gov.in

Abstract

BACKGROUND: Thymoma is the most common tumor of the anterior mediastinum. Surgery is mainstay of treatment, with adjuvant radiation recommended for invasive thymoma. Because of rarity, prospective randomized trials may not be feasible even in multicentric settings hence the best possible evidence can be large series. Till date Thymoma has not been studied in Indian settings. **MATERIALS AND METHODS:** All patients presenting to Thoracic disease management group at our Centre during 2006-2011 were screened. Sixty two patients' with histo-pathological confirmation of thymoma medical records could be retrieved and are presented in this study. Mosaoka staging and WHO classification was used. The clinical, therapeutic factors and follow up parameters were recorded and survival was calculated. Effects of prognostic factors were compared. **RESULTS:** Sixty two patients were identified (36M, 26F; age 22-84, median 51.5 years) and majorities (57%) of thymoma were stage I-II. WHO pathological subtype B was most common 30 (49%). Mean tumor size was smaller in patients with myasthenia (5.3cm) than the entire group (7.6cm). Neoadjuvant therapy was offered to five unresectable stages III or IV a patient's with 40% resectability rates. Median overall survival was 60 months (Inter quartile-range 3-44 months) with overall survival rate (OS) at three year being 90%. Resectable tumors had better outcomes (94%) than non resectable (81%) at three years. Mosaoka Stage was the only significant ($P = 0.03$) prognostic factor on multivariate analysis. **CONCLUSION:** This is first thymoma series from India with large number of patients where staging is an important prognostic factor and surgery is the mainstay of therapy. In Indian context aggressive multimodality treatment should be offered to advanced stage patients and which yields good survival rates and comparable.

Key Words: Mediastinal mass, multidisciplinary management, thymoma

Introduction

Thymoma is the most common tumor of the anterior mediastinum with an incidence of 0.15 cases per 100,000. These biologically aggressive tumors are capable of local invasion but rarely metastasise.[1-4] Ninety percent of all Thymoma occur in the anterior mediastinum, with the remainder occurring in the neck or other mediastinal areas.[5] Surgery is the mainstay of treatment, with adjuvant radiation recommended for invasive thymoma.[5] These tumors are sensitive to both chemotherapy and radiation. Durable responses are achievable in incompletely resected and inoperable patients.[5] In various series, fiveyear survival rate of thymoma approximates 65%.[6] Because of its indolent natural history and rarity, prospective randomized trials may not be feasible hence the best possible evidence can be large series.

Till date there is no published literature regarding profile, management and outcomes of thymoma in Indian subcontinent patients. We present first series of thymoma patients managed at tertiary cancer centre in India.

Materials and Methods

All patients presenting to the Thoracic DMG (disease management group) at our Centre from January 2006 to December 2011 were screened. Sixty two patients' with histo-pathological confirmation of thymoma medical records could be retrieved and are presented in this study.

Pathological classification proposed by World Health Organization (WHO) in 2000 was used for these patients. This classification categorises tumors as type A, AB, B1, B2, B3 or C, based on the predominant cell type.[7] Stage was determined using the Mosaoka staging system.[8]

Access this article online

Quick Response Code:

Website: www.indianjcancer.com

DOI: 10.4103/0019-509X.138144

The clinical factors (age, sex, symptoms, and duration of symptoms, histological features, stage, and presence of myasthenia gravis), therapeutic factors (intent of treatment, treatment modality) and follow up parameters (overall survival) were recorded and evaluated appropriately with life table computational method. Comparisons made to analyze the prognostic effects of age, stage, histological findings, and presence of myasthenia gravis etc.

Results

Median overall survival was 60 months (Inter quartile-range 3-44 months). Patient characteristics have been shown in Table 1. Patients had symptoms for median duration of 2.5 months. Sixty (97%) patients had good performance status with ECOG score 0-2. Histopathological confirmation was established with biopsy of mass in majority of cases.

Amongst surgical procedures excision of mass was the most common procedure. Complete excision was achieved in all the patients except in two. Radiotherapy and Chemotherapy details have been shown in Table 1. For radical intent treatment planned dose of radiation was 50-60Gy (2Gy/Fr). Palliative patient was offered radiation dose of 39Gy (3Gy/Fr).Radiation planning was most commonly done by 3D conformal radiotherapy.

Median overall survival rate (OS) at three year was 90% [Figure 1, Table 2]. Three year overall survival was 94% for stage I, 100% for stage II, 91% for stage III, and 69% for stage IV [Table 2].

Patients undergoing surgical treatment had a median three year OS of 94% whereas patients with inoperable disease had a median three year OS of 81%. Amongst patients underwent surgery, median three year OS was 92% among those who did not required adjuvant treatment vs. 100% for those who required post-operative adjuvant treatment. One patient recurred and was treated with radiation and a second patient developed sarcoma of the thigh.

Except Masoaka's staging other factors such as gender, presence of myasthenia gravis, other co-morbidities, ECOG status, and WHO pathological classification, dose of

radiation, chemotherapy agents were not found to affect the prognosis of thymoma [Table 2]. The prognostic value of positive resection margins could not be assessed as only a few patients had positive resection margins.

Table 1: Clinical and treatment characteristics *n*=50 (%)

Age years (median=51.5 years; range 22-84)	
>50	31 (50)
50 or less	31 (50)
Sex	
Male	36 (58)
Female	26 (42)
Presentation	
Symptomatic	54 (87)
Incidental	8 (13)
Myasthenia gravis	
Present	9 (15)
Absent	53 (85)
Imaging	
CECT chest	62 (100)
Size of lesion (median)	
Total group	7.6 cm
Myasthenia gravis	5.3 cm
Masaoka stage	
I	22 (36)
II	13 (21)
III	18 (29)
IV	9 (14)
WHO pathological type	
A	7 (10)
AB	14 (23)
B1	11 (18)
B2	11 (18)
B3	8 (13)
C	11 (18)
Treatment	
Radical	54 (87)
Palliative	8 (13)
Surgery	
Yes	44 (71)
No	18 (29)
Radiation	
Yes	17 (27)
No	45 (73)
Radiation intent (*n*=17)	
Adjuvant	13 (76)
Radical	3 (18)
Palliative	1 (6)
Chemotherapy	
Yes	15 (24)
No	47 (76)
Chemotherapy intent (*n*=15)	
Neo-adjuvant	5 (33)
Adjuvant	3 (20)
Concurrent	3 (20)
Palliative	4 (27)
Chemotherapy regimen (*n*=15)	
CODE	5 (33)
PE	3 (20)
CAP	3 (20)
Others	4 (27)

Discussion

This is first series studying profile of thymoma patients, management practices and outcomes in Indian settings. This study is a reference for Thymoma management in Indian settings.

Multimodality treatment is an approach to manage primarily unresectable tumors as frequently seen in Masaoka III, IVa, and IVb thymoma.[9,10] The median OS rates of our study correlate well with 95% in reported literature.[11,12] It was difficult to demonstrate the exact effect of chemotherapy on disease control, given the small number of patients in this subgroup. Larger prospective studies are needed to evaluate role of neoadjuvant chemotherapy in this disease.

Various histo-pathological studies carried out in the past but majority have produced conflicting results with regard to the ability of Histo-pathological analysis to predict biologic behavior.[13,14] However, the clinical stage of the tumor introduced by Masoaka has been a more reliable prognostic indicator, and is most commonly applied staging system.[8,14] This study also reports Masaoka clinical staging as significant prognostic factor on both univariate and multivariate analysis [Figure 2]. WHO histological classification is

Table 2: Survival and prognostic factors

	3 year survival %	Univariate P	Multivariate P
Age yrs			
>50	93	0.15	0.18
50 or less	88		
Sex			
Male	93	0.77	0.61
Female	87		
Myasthenia gravis			
Present	88	0.85	0.46
Absent	91		
Size			
8 cm or more	90	0.59	0.45
less than 8 cm	94		
Masaoka stage			
I	94	0.03	0.03
II	100		
III	91		
IV	69		
WHO pathological type			
A	82	0.67	0.82
AB	91		
B	90		
C	100		
Resectable			
Yes	94	0.05	0.18
No	81		
Treatment			
SX alone	95	0.06	0.45
Sx with adjuvant Rx	89		
NACT/CTRT	100		
Palliative	71		

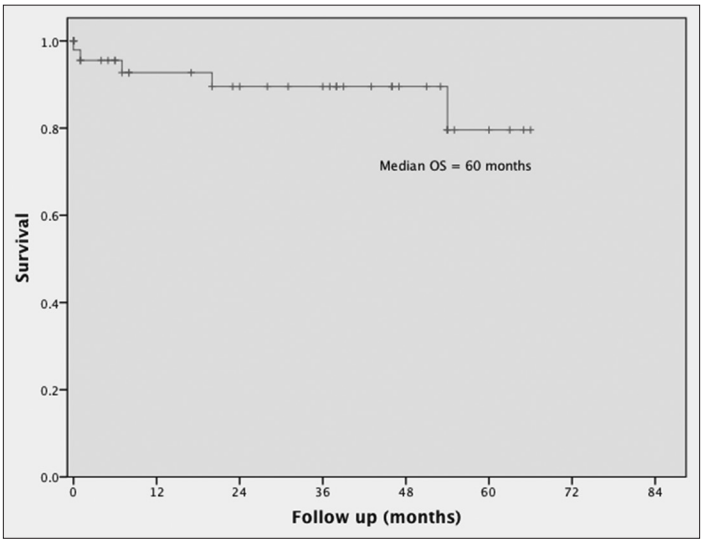

Figure 1: Overall survival

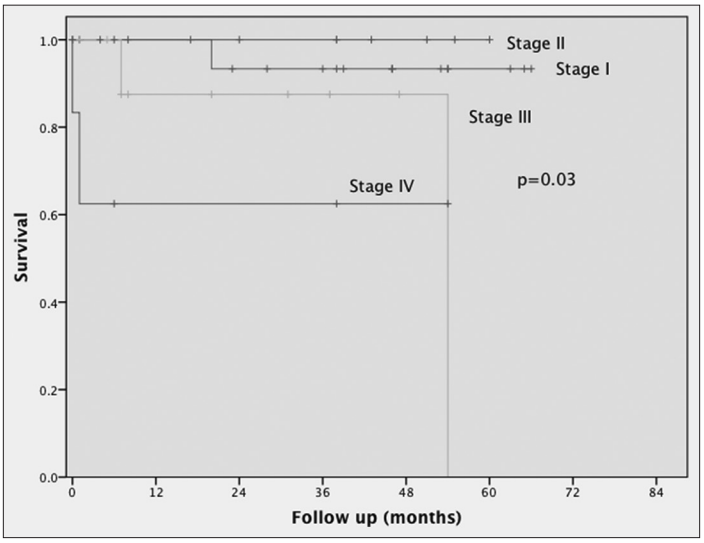

Figure 2: Overall survival stagewise

also reported as prognostic factor in various studies.[3,13,15] However this study could not elicit statistically significant correlation between histo-pathological subtypes and outcome probably owing to the small number of patients.

With thymoma various autoimmune diseases are associated[16] and up to 30% have been diagnosed with myasthenia gravis in reported series.[17] Our study found an associate of myasthenia gravis in 15% of patients with thymoma. Thymoma with associated gravis is usually B type.[18] This is corroborated with the findings of our study with 50% patients with myasthenia were type B histology.

Surgery remains the primary treatment in thymoma therapy and median sternotomy with complete thymectomy is the operative approach of choice.[19,20] In this study excision of mass was the most common procedure and surgically treated patient had better three year OS (94%) as opposed to 81% in inoperable patients. Whenever possible, completeness of resection has to be aimed for because it is an important prognostic factor for local control and survival.

Adjuvant therapy, specifically, postoperative radiation, is often recommended for invasive thymoma regardless of resection status. In patients with stage II and III disease, adjuvant radiotherapy after complete resection may be beneficial to reduce local recurrence without effect on survival.[19] With preoperative radiotherapy or chemotherapy, the rate of complete resection may be increased, the rate of local and pleural recurrence may be decreased and the survival improvement can be achieved.

Though not a treatment of choice in localized, surgically resectable thymoma, chemotherapy is being adopted in select patients with inoperable or gross residual disease.[14] This study reports use of chemotherapy in adjuvant, concurrent, neoadjuvant and palliative settings in this study. Rea and Berruti independently have reported neoadjuvant chemotherapy regimen in unresectable stage III or IVa, showing an improved resectability 46-65% and 0-20% respectively.[11,12] Our study reports 40% resectability rates after neoadjuvant chemotherapy.

Besides surgery, age is another factor that has been shown to have prognostic implication.[21] However this study could not support prognostic importance of gender, age, ECOG status, dose of radiation, chemotherapy agents. Naka-gawa and colleagues[22] have reported tumor size as a significant predictor of outcome.[15] Our study could not elicit prognostic importance of tumor size. Similarly myasthenia gravis has been cited as a negative prognostic factor in some studies. However, more recent large series have not found myasthenia gravis to negatively influence survival.[15,20] Our study too corroborates the latter view.

To summarise, Thymoma is curable disease with good clinical outcomes and needs multidisciplinary approach. Masaoka staging is an important prognostic factor and surgery remains the primary treatment. However in view of limited number of studies various aspects are yet to be explored. In view of rarity of thymoma, large prospective randomized studies with international collaboration are needed to enlighten current knowledge of thymoma.

Conclusion

This is first thymoma series from India with large number of patients and will serve a reference for future studies. Staging is an important prognostic factor. Treatment of thymoma depends on the resectability of the disease and surgery is the mainstay of therapy. Neoadjuvant treatment with chemotherapy or chemo-radiation may render the tumor resectable. Aggressive multimodality treatment should be offered to advanced stage patients and yields good survival rates.

References

1. Cohen AJ, Thompson L, Edwards FH, Bellamy RF. Primary cysts and tumors of the mediastinum. Ann Thorac Surg 1991;51:378-84;discussion 385-6.
2. Cowen D, Richaud P, Mornex F, Bachelot T, Jung GM, Mirabel X, *et al*. Thymoma: Results of a multicentric retrospective series of 149 non-metastatic irradiated patients and review of the literature. Radiother Oncol 1995;34:9-16.
3. Davis RD Jr, Oldham HN Jr, Sabiston DC Jr. Primary cysts and neoplasms of the mediastinum: Recent changes in clinical presentation, methods of diagnosis, management, and results. Ann Thorac Surg 1987;44:229-37.
4. Bergh NP, Gatzinsky P, Larsson S, Lundin P, Ridell B. Tumors of the thymus and thymic region: I. Clinicopathological studies on thymomas. Ann Thorac Surg 1978;25:91-8.

5. Riedel RF, Burfeind WR Jr. Thymoma: Benign appearance, malignant potential.Oncologist 2006;11:887-94.
6. Arriagada R, Bretel JJ, Caillaud JM, Garreta L, Guerin RA, Laugier A, *et al*. Invasive carcinoma of the thymus: A multicenter retrospective review of 56 cases. Eur J Cancer Clin Oncol 1984;20:69-74.
7. Graeber GM, Tamim W. Current status of the diagnosis and treatment of thymoma. Semin Thorac Cardiovasc Surg 2000;12:268-77.
8. Masaoka A. Staging system of thymoma. J Thorac Oncol 2010;5 (10 Suppl 4):S304-12.
9. Bretti S, Berruti A, Loddo C, Sperone P, Casadio C, Tessa M, *et al*. Multimodal management of stages III-IVa malignant thymoma. Lung Cancer 2004;44:69-77.
10. Shin DM, Walsh GL, Komaki R, Putnam JB, Nesbitt J, Ro JY, *et al*. A multidisciplinary approach to therapy for unresectable malignant thymoma. Ann Intern Med 1998;129:100-4.
11. Rea F, Marulli G, Girardi R, Bortolotti L, Favaretto A, Galligioni A, *et al*. Long-term survival and prognostic factors in thymic epithelial tumors. Eur J Cardiothorac Surg 2004;26:412-8.
12. Berruti A, Borasio P, Gerbino A, Gorzegno G, Moschini T, Tampellini M, *et al*. Primary chemotherapy with adriamycin, cisplatin, vincristine and cyclophosphamide in locally advanced thymomas: A single institution experience. Br J Cancer 1999;81:841-5.
13. Lardinois D, Rechsteiner R, Läng RH, Gugger M, Betticher D, von Briel C, *et al*. Prognostic relevance of Masaoka and Müller-Hermelink classification in patients with thymictumors. Ann Thorac Surg 2000;69:1550-5.
14. Tomaszek S, Wigle DA, Keshavjee S, Fischer S. Thymomas: Review of current clinical practice. Ann Thorac Surg 2009;87:1973-80.
15. Wright CD, Wain JC, Wong DR, Donahue DM, Gaissert HA, Grillo HC, *et al*. Predictors of recurrence in thymictumors: Importance of invasion, World Health Organization histology, and size. J Thorac Cardiovasc Surg 2005;130:1413-21.
16. Souadjian JV, Enriquez P, Silverstein MN, Pépin JM. The spectrum of diseases associated with thymoma. Coincidence or syndrome? Arch Intern Med 1974;134:374-9.
17. Wright CD. Management of thymomas. Crit Rev Oncol Hematol 2008;65:109-20.
18. Cheney RT. The biologic spectrum of thymic epithelial neoplasms: Current status and future prospects. J Natl Compr Canc Netw 2010;8:1322-8.
19. Haniuda M, Kondo R, Numanami H, Makiuchi A, Machida E, Amano J. Recurrence of thymoma: Clinico pathological features, re-operation, and outcome. J Surg Oncol 2001;78:183-8.
20. Regnard JF, Magdeleinat P, Dromer C, Dulmet E, de Montpreville V, Levi JF, *et al*. Prognostic factors and long-term results after thymoma resection: A series of 307 patients. J Thorac Cardiovasc Surg 1996;112:376-84.
21. Zhu G, He S, Fu X, Jiang G, Liu T. Radiotherapy and prognostic factors for thymoma: A retrospective study of 175 patients. Int J Radiat Oncol Biol Phys 2004;60:1113-9.
22. Nakagawa K, Asamura H, Matsuno Y, Suzuki K, Kondo H, Maeshima A, *et al*. Thymoma: A clinic pathologic study based on the new World Health Organization classification. J Thorac Cardiovasc Surg 2003;126:1134-40.

How to site this article: Rathod S, Munshi A, Paul S, Ganesh B, Prabhash K, Agarwal JP. Thymoma: First large Indian experience. Indian J Cancer 2014;51:109-12.
Source of Support: Nil, **Conflict of Interest:** None declared.

News

9th SFO (SAARC Federation of Oncologists), conference 2014
Organizing Chairman : Dr. Ashok Vaid
Web: www.sfo2014.com
Mail: saarconcology14@gmail.com

News

31st ICON Conference.
Organizing Secretary : Dr. T. P. Sahoo,
12th - 14th September, 2014
Web: www.iconconferences.com
Mail: 31sticon@gmail.com

News

Next APLCC meeting will be held in Kuala Lumpur from 6-8 November 2014.
The deadline for abstract submission is 1 July 2014.
Conference Secretariat of 2014 IASLC Asia Pacific Lung Cancer Conference (APLCC2014):
19-5, Dutaria, Jalan Dutamas Raya, 51200 Kuala Lumpur, MALAYSIA
Tel: +60 3 6241 3850 Mobile: +60 17 2215 123
Email: jessica.tan@myconference.com.my
Website: www.aplcc2014.com