



Characteristics of malignant mediastinal tumours presenting in tertiary care center in India and the problems the oncologists have faced over time

Rajit Rattan, Budhi Singh Yadav, Rakesh Kapoor, Pragyat Thakur

Department of Radiotherapy and Oncology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Correspondence to: Dr. Rakesh Kapoor, Professor, Department of Radiotherapy and Oncology, Post Graduate Institute of Medical Education and Research, Chandigarh, India. Email: drkapoor.r@gmail.com.

Abstract: Mediastinal neoplasms often present a diagnostic and therapeutic challenge for treating oncologists. Significant advances in the evaluation and diagnosis of these lesions have occurred in recent times. Multimodality treatment has contributed to improved survival for some malignant mediastinal tumor histology, however the overall prognosis remains dismal. This is a review of all the mediastinal tumors received and treated in our Regional Cancer Centre (RCC). The purpose of this analysis was to evaluate distribution of mediastinal tumours, the factors affecting the treatment intent, and understanding the reasons behind the generally known poor prognosis.

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Mediastinal neoplasms are uncommon tumors. They often present a diagnostic and therapeutic challenge for treating oncologists. Significant advances in the evaluation and diagnosis of these lesions have occurred in recent times, with the introduction of computerized tomography (CT), interventional radiology biopsies, tumor markers, and immune-histochemical techniques. Multimodality treatment has contributed to improved survival for some malignant mediastinal tumor histology, however the overall prognosis remains dismal. This is a review of all the mediastinal tumors received and treated in our Regional Cancer Centre (RCC). The purpose of this analysis was to evaluate distribution of mediastinal tumors, the factors affecting the treatment intent, and understanding the reasons behind the generally known poor prognosis.

Methods and materials

We performed a retrospective review of all patients with mediastinal masses registered, evaluated and treated at our RCC from January 2011 to December 2014. Records were

reviewed for patient demographics, clinical presentation, tumor characteristics, and patient management. Pediatric patients were defined as those less than 18 years of age. Lymphomas that were confined solely to the mediastinum only were included. Descriptive statistics were used to evaluate the distribution of tumors in-terms of patient characteristics, tumor characteristics and treatment characteristics. First reported predominant symptom was documented as presenting symptom, however some patients presented with constellation of symptoms including facial swelling, dyspnea and cough along with radiological features of superior vena cava obstruction (SVCO) and hence they were documented as such. Tumor location was designated as anterior, superior, middle, or posterior mediastinal (1) as per standard teaching, however in cases with a large tumor bulk transversing from one region to another a combined designation was given.

Review of patients' treatment based on the clinicians' intention of treatment was conducted. Two groups were made where distinction was made whether they were treated with a radical or a palliative approach. Correlation using cox

Table 1 Patient characteristics

Patient characteristics	Number of patients (%)
Age in yrs, median (range)	45 (2 to 76 yrs)
Sex	
Male	49 (69.0)
Female	22 (31.0)
Background	
Rural	58 (81.7)
Urban	13 (18.3)
KPS	
<70	54 (76.1)
>70	17 (23.9)
Smoking history	
Yes	28 (39.4)
No	43 (60.6)
Predominant symptomology	
SVCO	27 (38.0)
Chest pain	26 (36.6)
Dyspnea	8 (11.3)
Cough	6 (8.5)
Hemoptysis	1 (1.4)
Myasthenia	2 (2.8)
Asymptomatic	1 (1.4)

SVCO, superior vena cava obstruction.

regression analysis was done to evaluate the factors affecting the intention of therapy (radical *vs.* palliative) of overall treatment.

Results

A total of seventy-one (n=71) patients were identified who received treatment at our institute. *Table 1* shows patient characteristics of mediastinal tumor. Data shows a median age of 45 years with a male preponderance (69%), majority of patients come from rural areas (81.7%). *Table 2* shows the demographic distribution, location, histology, bulk and the presenting stage of tumors in mediastinum. The miscellaneous tumors include, one each of paraganglioma, spindle cell carcinoma, poorly differentiated carcinoma and two patients who couldn't undergo biopsy or surgery for

Table 2 Disease characteristics

Disease characteristics	Number of patients (%)
Location	
Antero-superior	59 (83.1)
Middle	10 (14.1)
Posterior	2 (2.8)
Histology	
Thymoma	18 (25.4)
Thymic carcinoma	4 (5.6)
Non-small cell lung carcinoma	6 (8.5)
Small cell lung carcinoma	7 (9.9)
Neuroendocrine tumour	4 (5.6)
Non-Hodgkin lymphoma	11 (15.5)
Hodgkins lymphoma	2 (2.8)
Mesothelioma	3 (4.2)
Germ cell tumour	4 (5.6)
Malignant peripheral nerve sheath tumour	2 (2.8)
Carcinoma not otherwise specified; NOS	5 (7.0)
Misc.	5 (7.0)
Bulk of tumour	
<5 cm	4 (5.6)
>5–<10 cm	39 (54.9)
>10 cm	28 (39.4)
Stage	
I	3 (4.2)
II	9 (12.7)
III	17 (23.9)
IV	42 (59.2)

confirmation of diagnosis.

Symptoms associated were chest pain (36%), dyspnea (11.2%), cough (8.5%), with around 27% patients coming with evidence of clinical superior vena cava obstruction.

With respect to treatment of mediastinal tumors, surgical consult was the primary treatment approach whenever indicated. However, for tumors like lymphoma, germ cell tumors, small cell lung cancers and patients presenting with SVCO, primary treatment was non-surgical. Out of the 71 patients, 49 patients had a surgery consult out of which only

Table 3 Treatment received by patients

Treatment done	Number of patients (%)
Surgery done	
Yes	15 (21.1)
No	34 (47.8)
Not required	22 (31.2)
Resection margins	
R0	4
R1	5
R2	6
Radiation therapy	
Yes	58 (81.7)
No	13 (18.3)
Chemotherapy	
Yes	42 (59.2)
No	
Intent of treatment	29 (40.8)
Radical	38 (53.5)
Palliative	33 (46.5)

15 (19.7%) were found suitable for surgical intervention and underwent surgery. However only 4 (26.6%) of them had complete resection (R0 resection). Adjuvant or upfront radiation was received by 58 (81.7%) patients, 33 of which (56%) were amenable to radical doses. Forty-two (59.2%) patients were initiated on chemotherapy out of which 34 (80.9%) completed four or more cycles. *Table 3* shows the treatment received by the patients.

Immediate post treatment assessment of residual disease was done with the help of clinical examination, chest Xray or CT scan and rarely MRI. PET scan was done in select cases of lymphoma, lung carcinoma and germ cell tumors as a part of initial evaluation and post treatment follow up. *Table 4* shows the immediate post treatment outcomes in patients. Twelve patients didn't return of follow up post treatment and are not included in this table.

Radiation dose varied in palliative setting ranging from 8 Gy/# to 30 Gy/10# and the radical dose varied according to tumor histology as per our institutional protocol (data not shown). Chemotherapy used were different for different malignancies and hospital protocol based.

For treating a patient with either radical or palliative

Table 4 Response to treatment

Post treatment response	No of patients (%)
Complete response	16 (22.5)
Residual disease present	31 (43.7)
Progressive disease	12 (16.9)

Table 5 Patient related factors dictating treatment approach

Factors	Radical treatment	Palliative treatment	P value
Age in years (median)	38	33	0.1570
Sex			0.1000
Male	23	26	
Female	15	7	
K.P.S.			0.0220
More than 70	33	21	
Less than 70	5	12	
Smoking history			0.0006
Yes	7	21	
No	31	12	
Demography			0.5280
Urban	8	5	
Rural	38	28	

approach, various factors responsible were studied. *Table 5* and *Table 6* give the patient related and disease related factors that dictate the clinicians approach in managing mediastinal tumors.

Discussion

Mediastinum is a unique location for cancer symptomatology and therapeutics. The clinical symptoms range from subtle heaviness of chest to marked dyspnea leading to what is known as superior vena-cava syndrome. This retrospective review doesn't show much similarity to demographic, clinical presentation, and tumor histology data to that previously published from other institutions (2-11). Our proportion of lung tumors, lymphomas, are generally lower than reported in other series. This may reflect our tertiary cancer hospital referral pattern and the fact that-our policy of only including primary mediastinal lymphomas is

Table 6 Disease related factors dictating treatment approach

Factors	Radical treatment	Palliative treatment	P value
Location in mediastinum			0.3230
Anterior	29	18	
Middle	2	8	
Posterior	1	1	
Superior	6	6	
Histology	–	–	0.1540
Bulk			0.6410
Less than 5 cm ²	–	2	
5 to less than 10 cm ²	20	9	
10 cm ² or more	16	12	
Stage			0.0770
I	–	–	
II	–	–	
III	–	–	
IV	–	–	
SVCO	10	17	0.0006
Resection margin			0.0010
R0	–	–	
R1	–	–	
R2	–	–	

SVCO, superior vena cava obstruction.

probably responsible for this. The presenting stage and bulk of tumors also seems higher than what can be anticipated from other series.

The diagnosis was established with CT or bronchoscopy guided FNAC or biopsy, post-surgical specimens, VATS (video assisted thoracoscopy). However, due to the retrospective nature of the study, accurate frequency of these procedures cannot be commented upon.

As far as the patient related characters are concerned, median age of patients is around 45 years with male preponderance (69%). Despite the urban location of our institute, the predominant population comes from rural background (81.7%). This, however, does corresponds to the demographic distribution of Indian population where 72.2% population comes from rural background (12).

We observed a high proportion of patients i.e., 39.4% with bulky disease (defined by volume of disease more

than 10 cm³) and 59.2% were with stage IV tumors. The frequency of these large sized, locally infiltrative lesions is far greater than the average number seen throughout the world. Performance scale of the patients coming to our tertiary care center also seems to be the major cause for concern as proportion of patients with K.P.S. score of less than 70 was about 24%, a higher percentage than standard population. Low KPS scores can be explained by delay in the diagnosis of disease. The factors associated could be, initial nonspecific symptoms leading to delay in consultation, delay at primary health centers due to lack of awareness among health workers for such rare presentations and complex methods of diagnosis (13,14); leading to delay in diagnosis and eventual long duration of illness. Smoking habits also contribute to the low KPS scores. Eighty-three point one percent patients had locally advanced disease and the compounding factor was their poor performance status as 76.1% of them had a KPS of <70.

An important predictor of survival from the treatment point of view is the intent of treatment. If the treating physician feels that the patient will benefit from and is suitable for a radical treatment, then it can be expected that a few of such patients can have long term survival. The analysis reveals that only around 53.4% of the patients were treated with a radical intention and the rest were treated with a palliative approach. With this review of the data, the attempt was aimed at identifying the factors that are responsible for determining the intention of treatment.

Among all the factors studied in multivariate analysis, low KPS, smoking index >400, presence or absence of SVCO, stage of the tumor (stage I and II versus III and IV) and resection margin (positive versus negative) came out to be the significant contributors toward determining the intention of treatment. Age, sex, duration of illness (more than or less than 3 months), demographic background (rural or urban), bulk of tumor were the notable factors that didn't show any statistical significance in decision making during the analysis.

The presence of SVCO in 38% of our patients with mediastinal tumors, though seems increased, is confounded by the referral system of our institute where SVCO is primarily managed by radiation therapy. Presence of SVCO makes the management decisions more complex and inadvertently more in favour of a palliative approach. Reasons for this can be the lack of surgery as primary treatment, initial focus on providing symptomatic relief leading to change from the standard protocol for the

disease, higher stage of the disease, associated with low performance status of the patient; leading to reluctance in the use aggressive multimodality approach (15,16).

Stage is also an important prognostic factor in most malignancies. Stage of tumor not only dictates the symptomology and performance score (17), it also is an indicator of tolerance of the patient towards a treatment, its response to therapy and eventual outcome.

Surgical approach whenever leading to a R0 surgery has also shown to impact the decision making, in this analysis. These patients may be the ones that are now symptom free and of a good KPS score, so a selection bias may be one reason. Besides this, after bulk tumor removal the treating oncologists' confidence in getting long term control are increased and a further use of adjuvant therapy is also often minimized.

Drawbacks

No long-term survival analysis was done because of poor follow up and heterogeneous population. Being a retrospective study, a selection and a recall bias can't be fully excluded.

Conclusions

Mediastinal tumors are a group of heterogeneous tumors and require diverse approaches with multimodality therapy. Often there is a delay at diagnosis due to innumerable causes and whenever patient comes to the tertiary care center to seek treatment, more often than not, the stage, resectability and the general condition of such patients makes cure improbable. Palliative approach with the use of palliative dose of radiation, chemotherapy and various symptom oriented management strategies in these patient remains the mainstay of treatment in most of these patients. Thus, there is a need to address the disease entity as a site-specific problem rather than individual diagnostic and treatment problem.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/ace.2019.08.03>).

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Informed consent was waived due to the retrospective nature of the study.

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References

1. Luketich JD, Ginsberg RJ. The current management of patients with mediastinal tumors. *Adv Surg* 1996;30:311-32.
2. Benjamin SP, McCormack LJ, Effler DB, et al. Primary tumors of the mediastinum. *Chest* 1972;62:297-303.
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. 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.
5. Cohen AJ, Thompson L, Edwards FH, et al. Primary cysts and tumors of the mediastinum. *Ann Thorac Surg* 1991;51:378-84; discussion 385-6.
6. Wychulis AR, Payne WS, Clagett OT, et al. Surgical treatment of mediastinal tumors: a 40 year experience. *J Thorac Cardiovasc Surg* 1971;62:379-92.
7. Ovrum E, Birkeland S. Mediastinal tumours and cysts. A review of 91 cases. *Scand J Thorac Cardiovasc Surg* 1979;13:161-8.
8. Nandi P, Wong KC, Mok CK, et al. Primary mediastinal tumours: review of 74 cases. *J R Coll Surg Edinb*

- 1980;25:460-6.
9. Azarow KS, Pearl RH, Zurcher R, et al. Primary mediastinal masses. A comparison of adult and pediatric populations. *J Thorac Cardiovasc Surg* 1993;106:67-72.
 10. Adkins RB Jr, Maples MD, Hainsworth JD. Primary malignant mediastinal tumors. *Ann Thorac Surg* 1984;38:648-59.
 11. Mullen B, Richardson JD. Primary anterior mediastinal tumors in children and adults. *Ann Thorac Surg* 1986;42:338-45.
 12. Anon, (2019). Available online: <https://enacademic.com/dic.nsf/enwiki/8738> [Accessed 14 Sep. 2019].
 13. Park SJ, Heo MJ. Severe hypoxemia and hypotension during general anesthesia of a patient with an anterior mediastinal mass: A case report. *Korean J Anesthesiol* 2009;57:754-7.
 14. Adler OB, Rosenberger A, Peleg H. Fine-needle aspiration biopsy of mediastinal masses: evaluation of 136 experiences. *AJR Am J Roentgenol* 1983;140:893-6.
 15. Chan RH, Dar AR, Yu E, et al. Superior vena cava obstruction in small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 1997;38:513-20.
 16. Chen YM, Yang S, Perng RP, et al. Superior vena cava syndrome revisited. *Jpn J Clin Oncol* 1995;25:32-6.
 17. Chow E, Harth T, Hruby G, et al. How accurate are physicians' clinical predictions of survival and the available prognostic tools in estimating survival times in terminally ill cancer patients? A systematic review. *Clin Oncol (R Coll Radiol)* 2001;13:209-18.

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