Original Article

DOI: 10.21276/APALM.2337

Mediastinal Germ Cell Tumors – A Clinicopathologic Study

Fatima Shamsuddin[1]*, Urmila N Khadilkar[2] and Debarshi Saha[2]

[1]Department of Pathology, Malabar Medical College& Research Centre, Kerala, India
[2]Department of Pathology, Kasturba Medical College, Mangalore, Karnataka, India

ABSTRACT

Background: Primary mediastinal extragonadal germ cell tumors (GCT) are relatively rare lesions and account for only 1 to 2 percent of all germ cell tumors. They are clinically distinct from testicular germ cell tumors despite their similar histologic features. Objective of this study is to classify and evaluate the histomorphology of mediastinal germ cell tumors and correlate the clinical findings with radiological and other serologic parameters.

Method: A 5 year study was done in Dept. of Pathology, of a private Medical College on mediastinal lesions. Total number of cases studied was 66, with GCTs making up 7 cases. Histopathology sections taken were stained with routine Hematoxylin and Eosin stains.

Results: The age range of patients with mediastinal GCTs were 6 months to 43 years with a mean of 23 years. Only one case was seen above 40 years. Both malignant GCTs were below 20 years. There was a male predominance with male:female ratio of 2.5:1.

Conclusion: Mediastinal GCTs are rare & interesting neoplasms, usually located in anterior compartment of mediastinum. A histomorphological analysis aided by radiology and serology permits an exact diagnosis in many cases.

Keywords: *Germ Cell Tumors, Matureteratoma,Mediastinum.*

Introduction

The origin of mediastinal germ cell tumors remains speculative. One of the most popular hypotheses asserts that mediastinal germ cell tumors and other midline extragonadal germ cell tumors originate from errant primordial germ cells during their midline migration from the yolk sac to the embryonic gonadal ridge. Freidman initially proposed that these tumors originate from 'germinal' cells somehow deposited in the thymus during embryogenesis.[1]

Primary mediastinal germ cell tumors have evoked an interest well out of proportion to their incidence. Some reports have questioned the existence of primary extragonadal germ cell tumors and attempted to show that they were, in fact, metastases from an occult or 'burned out' testicular primary tumor.[2]

However, in several autopsy series of patients with presumed extragonadal germ cell tumors, meticulous microscopic examination of the testes could not detect either occult tumors or focal scars.[3,4]

Primary malignant mediastinal GCT's are rare and represent only 1% to 4% of all mediastinal tumors.[5]

Materials and Methods

The present study was conducted in the Department of Pathology of Kasturba Medical College, Mangalore. The specimens were received from attached District Hospital, and other hospitals in and around Mangalore and North Kerala.

Duration of sample collection

Study involves samples of all mediastinal lesions received in the department for 5 years from January 2006 to June 2011.

Methodology

The patient's name, age, sex, detailed clinical history, laboratory investigations, Fine Needle Aspiration Cytology (FNAC) reports and radiological findings were recorded as per Data Proforma. The gross specimens obtained after surgery were examined in detail. Tissue was fixed in 10% buffered formalin, and processed by paraffin embedding. The blocks were serially cut, each of 3-5µ thickness and the sections counterstained with H & E. The histopathological findings were studied and correlated with serology.

Results

The number of cases and their distribution is given in Table 1 and Figure 1. The clinicopathologic data of patients are given in Table 2.

In the present study, there were 7 cases of germ cell tumors (GCT) of which 5 (71%) were benign and 2 (29%) were malignant. In all the benign cases, the patients were either asymptomatic or presented with compression symptoms. Whereas, in both the malignant GCT's the patients presented with acute symptoms like chest pain, cough and

fever. In all the benign GCT's, the serology were normal while in the malignant GCT's, β-HCG and LDH were increased. The malignant GCT's were also of higher stage at presentation compared to benign GCT's, all of which were Stage I at diagnosis.

The age of patients with GCT ranged from 6 months to 43 years with a mean age of 23 years (Figure 2). There were 3 cases in 0-20 age group and 3 cases in 21-40 age groups. Only one case was seen above 40 years. Both malignant GCTs were below 20 years. There was a male predominance with a male:female ratio of 2.5:1.

The commonest presenting complaint was dyspnea, followed by chest pain and cough (Table 3). Two cases were discovered incidentally on routine chest X-ray.

Discussion

Mediastinal GCTs are derived from primitive germ cells that fail to migrate completely during early embryonic development.[6]

GCTs are found in young adults and represent 7% to 20% of mediastinal masses found in adults.[7,8,9,10,11] In the present study, GCTs constituted 10.6% of the total mediastinal masses.

Studies by Davis, Oldham, Sabiston[7] found GCTs mainly in the anterior mediastinum. In the present study also 71% of GCTs were found in the anterior mediastinum.

Malignant GCTs are more common (> 90%) in men. A mediastinal GCT should prompt a search for a primary

Table 1: Distribution of Mediastinal GCT.

Germ cell tumors	Number of cases	%
Benign	5	71
Malignant	2	29

Table 2: Clinicopathologic data of patients with Germ Cell Tumors.

Sl No	HP No	Age	Sex	Presenting symptoms	Serology	Stage	Microscopic diagnosis	Clinical course
1	1401/06	24	M	Asymptomatic	WNL	Stage I	Mature cystic teratoma	Alive and well after 2 yrs
2	6414/08	6 m	F	Respiratory distress	WNL	Stage I	Mature cystic teratoma	Alive and well after 1 yr
3	7018/08	20	M	Chest pain	LDH, βHCG, AFP – Increased	Stage II	Malignant GCT (Embryonal Carcinoma)	Received chemo. Alive after 2 yrs
4	3930/09	43	M	Respiratory distress	WNL	Stage I	Mature cystic teratoma	Alive and well after 1yr
5	1983/10	28	F	Respiratory distress	WNL	Stage I	Mature cystic teratoma	Alive and well after 6 months
6	5436/10	17	M	Persistent cough	LDH, βHCG – Increased	Stage III B	Malignant GCT	NA
7	8388/10	30	M	Asymptomatic	WNL	Stage I	Mature cystic teratoma	Alive and well after 4 months

WNL: within normal limits. NA: not available

Table 3: Clinical symptoms of patients with mediastinal germ cell tumors.

Symptom	No. of patients	%
Respiratory distress	3	43
Asymptomatic	2	29
Chest pain	1	14
Cough	1	14

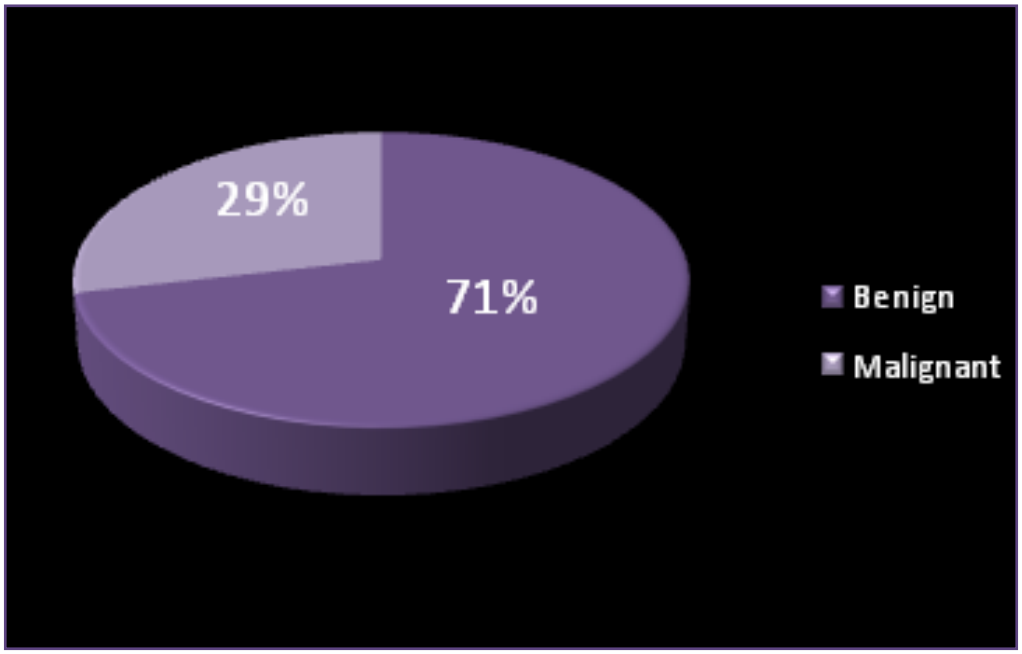

Fig. 1: Distribution of Germ cell tumors.

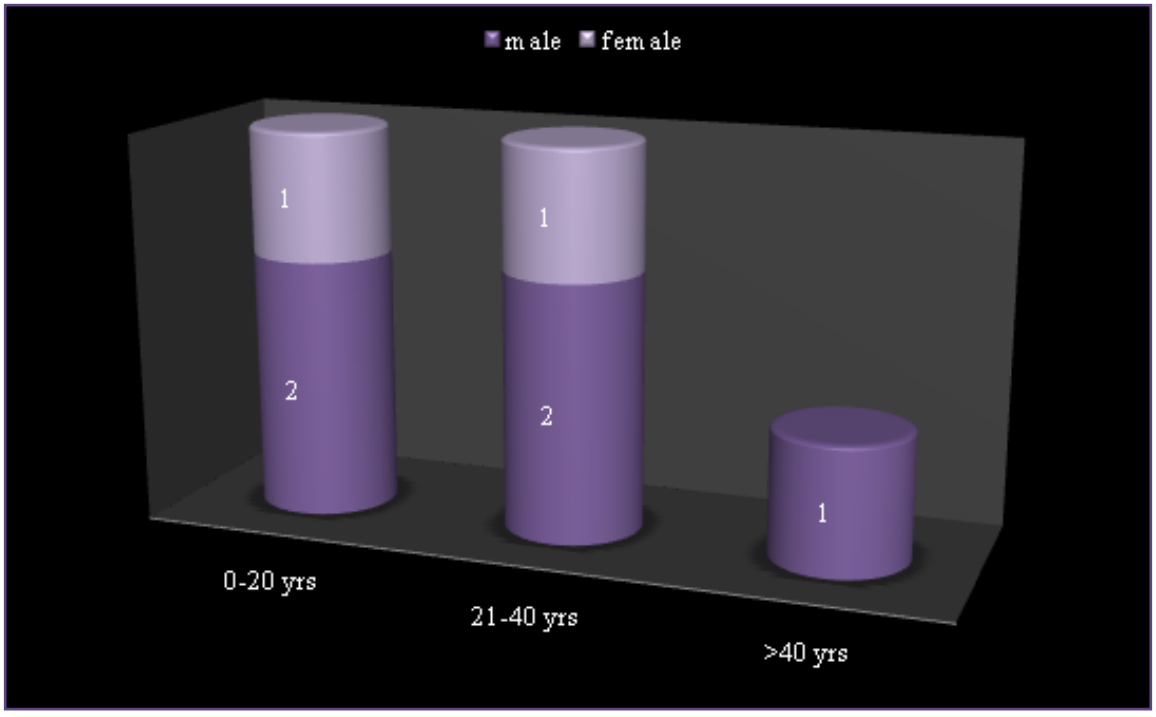

Fig. 2: Age and sex distribution of GCTs.

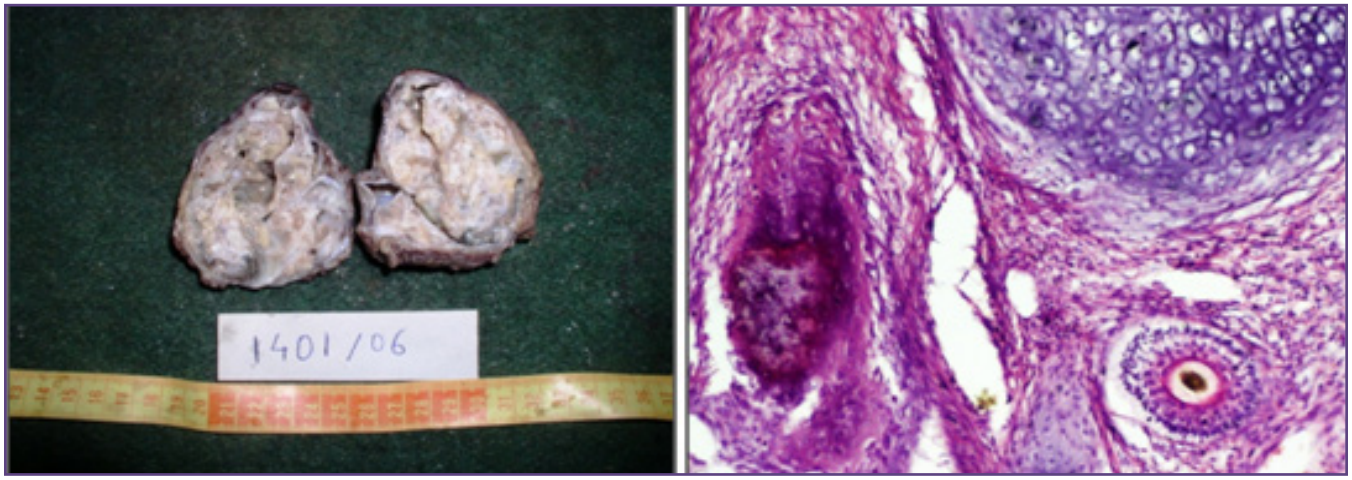

Fig. 3: Mature cystic teratoma (MCT): A. MCT showing solid and cystic areas. B. Areas of calcification, islands of cartilage and hair follicle in MCT [H&E x100].

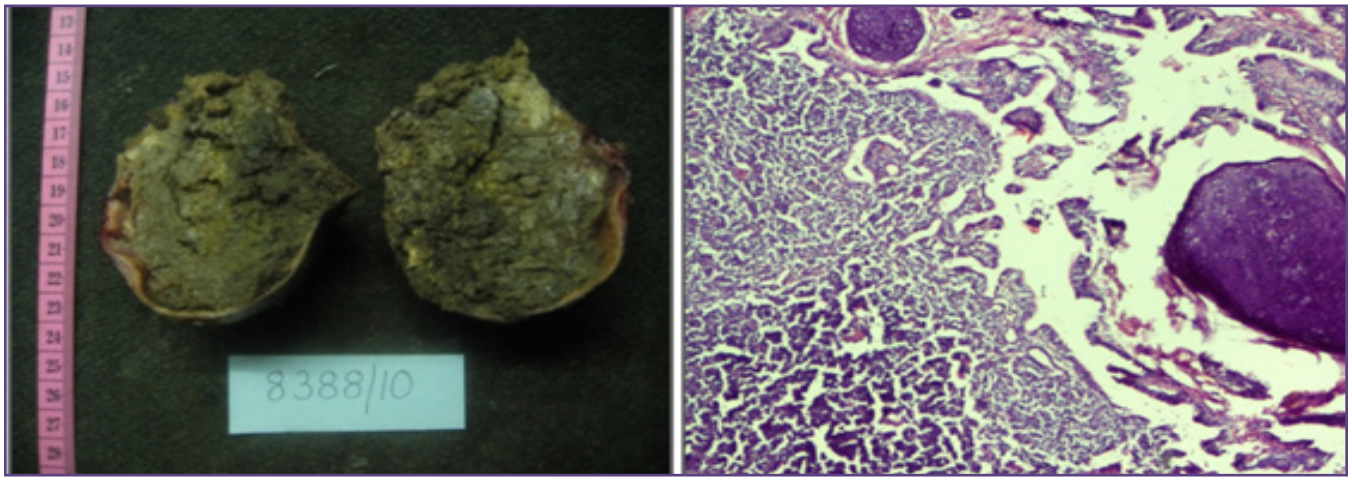

Fig. 4: Mature cystic teratoma (MCT): A: Cut surface showing pultaceous material. B. MCT showing thymic tissue in close apposition with the teratomatous elements [H&E x40].

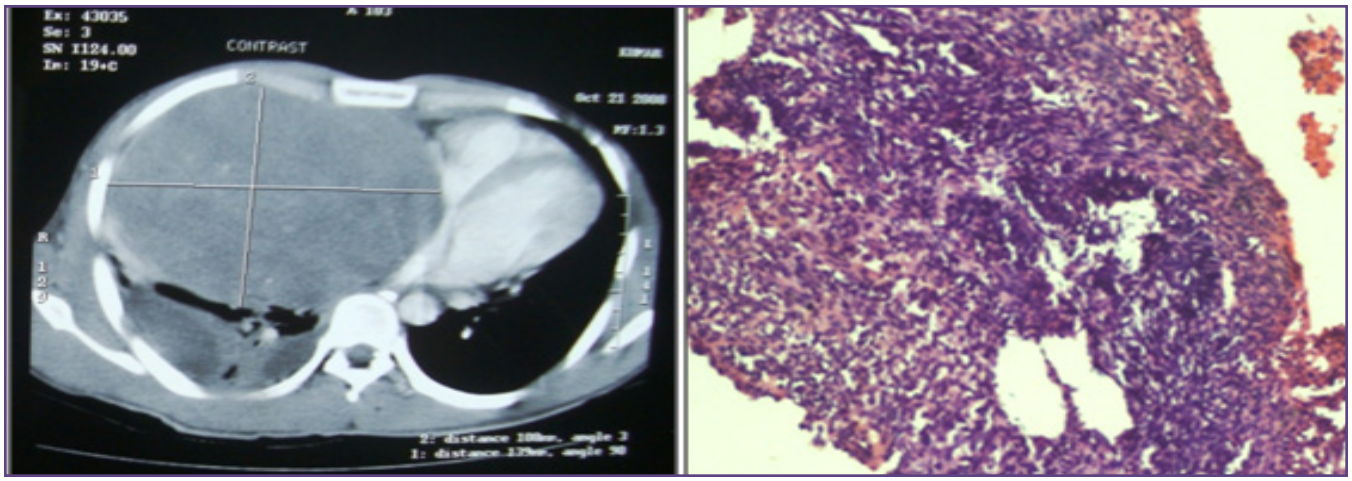

Fig. 5: Non-seminomatous germ cell tumor (NSGCT): A. CT chest showing large lobulated mass in anterior mediastinum encasing aorta and extending from thoracic inlet to the diaphragm. B. NSGCT showing sheets of undifferentiated cells and neuroepithelial structures [H&E x100].

gonadal malignancy.[12] In the present study there was a male predominance with a male:female ratio of 2.5:1. There was no evidence of extragonadal GCT in any of the cases.

In one of the largest studies done to date, 322 cases of primary mediastinal GCT's were studied histologically and immunohistochemically by Moran, Suster[13] in 1997. Teratomatous lesions represented the most frequent type (44%) of primary GCTs in the mediastinum followed by pure seminomas (37%); yolk sac tumors, embryonal carcinomas, and choriocarcinomas (16%); and combined nonteratomatous GCTs (3%). The patient population was overwhelmingly composed of men (320 men vs. 2 women). The tumors were observed in every age group, however most of the cases occurred in younger individuals. None of the patients had a prior history of gonadal or retroperitoneal tumor. Clinical staging showed that all mature teratomas were in Stage I while non-seminomatous GCT's (NSGCT) were mainly in stage III (WHO staging).

Ectodermal tissues, which usually predominate, include skin, hair, sweat glands, and tooth-like structures. Mesodermal tissues, such as fat, cartilage, bone, and smooth muscle are less common, as are endodermal structures like respiratory and intestinal epithelium. If a teratoma contains fetal tissue or neuroendocrine tissue, it is defined as immature and malignant. In children, the prognosis is favorable, but it can often recur or metastasize.[14]

Consisting of tissue from at least two of the three primitive germ layers, benign teratomas are the most common mediastinal GCT. The majority of mediastinal teratomas are mature teratomas that are histologically well-defined and benign.[15]

Among 29 cases of primary mediastinal GCTs, Albuquerque & colleagues[16] showed that all the benign teratomas occurred in younger age group. The patients were generally asymptomatic with normal serology, and complete resection resulted in cure.

The present study also showed a predominance of mature cystic teratomas (71%) while there were only 2 cases of malignant GCTs. All the patients were less than 30 years except one patient who was 43 years. There was a slight male predominance (male:female = 1.5:1). All the patients with mature cystic teratoma were asymptomatic with normal serology. All patients were in Stage I at diagnosis and surgical resection resulted in complete cure and all are alive and well, at follow-up.

Mediastinal nonseminomatous GCTs are often symptomatic and malignant, and predominantly affect young men. These tumors often produce serologic markers such as α-feto protein (AFP) and human chorionic gonadotropin (HCG), which can be useful in the diagnostic evaluation.[12]

Moran, Suster, Koss[17] studied 64 cases of yolk sac tumor (YST), embryonal carcinoma (EC), choriocarcinoma (CC), and combined germ cell tumors (CGCTs) without teratomatous components. The patients were all between 14 and 63 years with a mean age of 38.5 years. Their clinical symptoms included chest pain, shortness of breath, chills, fever and SVC syndrome. None of the patients had history of testicular neoplasm or tumor elsewhere. Histologically, the tumors displayed morphological features similar to their gonadal counterparts.

The study by Albuquerque & colleagues[16] showed that NSGCT presented in a more advanced stage. Most of the patients were symptomatic with cough, dyspnea, chest pain, SVC syndrome, hoarseness or weight loss. All were males with an average age of 25 yrs. AFP and β-HCG were normal in seminomas while it was increased in majority with NSGCT. They were also found to have a bad prognosis compared to benign MGCT.

Similar to the above studies, the 2 cases of NSGCTs in the present study were both males younger than 20 years. They presented with acute symptoms like chest pain, cough and fever. They also showed increase in serum β-HCG and LDH and were of higher stage at diagnosis (stage II and IIIB) compared to the remaining mature cystic teratomas, all of which presented in stage I at diagnosis.

In various studies, seminoma was found to be the most common malignant GCT of the mediastinum and has been reported to occur in 21% to 50% of the patients with malignant GCTs. In the present study there were only 2 cases of malignant GCT and both were NSGCTs.[7, 18, 19]

Conclusion

Malignant GCTs comprised the third common primary mediastinal neoplasm. There were only 2 cases of malignant GCTs (3.8%), both occurred in young males with elevated β-HCG and LDH. Sarcoma (2), carcinoma (2), mesothelioma (1), adenocarcinoma (1), MPNST (1) and LCH (1) comprised the remaining primary malignant mediastinal lesions. Mature cystic teratoma was the commonest benign primary mediastinal lesion (9.4%) followed by schwannoma (7.5%) and solitary fibrous tumor (1.9%).

CT and MRI have greatly aided in the evaluation and anatomical definition of mediastinal lesions. However, histomorphologic diagnosis of mediastinal lesions are a strong determinant for the treatment options ranging from medication and surgery to irradiation and chemotherapy.

Acknowledgement

This project would not have been possible without the kind support and help of many individuals. I would like

to extend my sincere thanks to the Head of Department, Dr P D Bhandari and all my colleagues for giving me such attention and time.

References

1. Friedman NB. The comparative morphogenesis of extragenital and gonadal teratoid tumors. Cancer 1951;4(2):265-76.
2. Meares EM Jr, Briggs EM. Occult seminoma of the testis masquerading as primary extragonadal germinal neoplasms. Cancer 1972;30(1):300-6.
3. Oberman HA, Libcke JH. Malignant germinal neoplasms of the mediastinum. Cancer 1964;17:498-507.
4. Cox JD. Primary malignant germinal tumors of the mediastinum. A study of 24 cases. Cancer 1975;36(3):1162-8.
5. Takeda S, Miyoshi S, Ohta M, Minami M, Masaoka A, Matsuda H: Primary germ cell tumors in the mediastinum: a 50-year experience at a single Japanese institution. Cancer 2003, 97:367–376.
6. Parker D, Holford CP, Begent RH, et al. Effective treatment for malignant mediastinal teratoma. Thorax 1983; 38(12):897-902.
7. Davis RD, 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 ThoracSurg1987;44(3):229–37.
8. Cohen AJ, Thompson L, Edwards FH, Bellamy RF. Primary cysts and tumors of the mediastinum. Ann ThoracSurg 1991;51(3):378-84.
9. Mullen B, Richardson JD. Primary anterior mediastinal tumors in children and adults. Ann ThoracSurg1986;42(3):338-45.
10. O'Gara RW, Horn RC Jr, Enterline HT. Tumors of the anterior mediastinum. Cancer 1958;11(3):562-90.
11. Nelson TG, Shefts LM, Bowers WF. Mediastinal tumors: An analysis of 141 cases. Dis Chest 1957;32(2):123-53.
12. Strollo DC, Rosado-de-Christenson ML, Jett JR. Primary mediastinal tumors. Part 1: Tumors of the anterior mediastinum. Chest 1997; 112(2):511-22.
13. Moran CA, Suster S.Primary germ cell tumors of the mediastinum: I. Analysis of 322 cases with special emphasis on teratomatous lesions and a proposal for histopathologic classification and clinical staging. Cancer 1997;80(4):681-90.
14. Carter C, Bibro MC, Touloukian RJ. Benign clinical behavior of immature mediastinal teratoma in infancy and childhood: report of two cases and review of literature. Cancer 1982; 49(2):398-402.
15. Nichols CR. Mediastinal germ cell tumors: clinical features and biologic correlates. Chest 1991; 99(2):472-9.
16. Albuquerque KV, Mistry RC, Deshpande RK, Desai PB. Primary germ cell tumors of the mediastinum. Indian J Cancer 1994;31(4):250-6.
17. Moran CA, Suster S, Koss MN.Primary germ cell tumors of the mediastinum: III. Yolk sac tumor, embryonal carcinoma, choriocarcinoma, and combined nonteratomatous germ cell tumors of the mediastinum—a clinicopathologic and immunohistochemical study of 64 cases.Cancer1997;80(4):699–707.
18. Azarow KS, Pearl RH, Zurcher R, Edwards FH, Cohen AJ. Primary mediastinal masses: A comparison of adult and pediatric populations. J ThoracCardiovascSurg1993;106(1):67-72.
19. Temes R, Chavez T, Mapel D, et al. Primary mediastinal malignancies: Findings in 219 patients. West J Med 1999;170(3):161-6.

***Corresponding author:**
Dr Fatima Shamsuddin, Postal Address: Malabar Medical College & Research Centre, Modakkallur, Atholi, Kozhikode, Kerala. India. PIN: 673315
Phone: +91 9526206868
Email: fatimahaneeshkhanie@gmail.com

Financial or other Competing Interests: None.