Original Article

18 Years Surgical Experience With Mediastinal Mature Teratoma

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Background/Purpose: Few studies have examined the surgical outcomes of mediastinal mature teratoma in Taiwan. In the present study, the clinicopathological characteristics of mature teratoma and their impact on surgical outcome were analyzed.

Methods: From 1988 to 2005, 57 cases of mediastinal mature teratoma were reviewed. We collected and analyzed data about patient age, sex, symptoms, blood sugar, pulmonary function, diagnosis, tumor size, histopathological features, operative methods, operative time, tumor adhesion, blood loss, ventilator requirement, intensive care unit stay, chest tube requirement, and postoperative hospital stay.

Results: There were 18 male and 39 female patients with a median age of 27 years. Forty-three patients received conventional open surgery, whereas 14 received video-assisted thoracoscopic surgery. The patients in the thoracoscopic group had a decreased operative time (106.4 ± 35.7 min *vs.* 205.4 ± 75.7 min, $p = 0.038$), fewer ventilator days (0.2 ± 0.4 *vs.* 0.5 ± 0.8, $p = 0.034$), and a shorter stay in the intensive care unit (0.6 ± 0.8 days *vs.* 1.5 ± 1.4 days, $p = 0.030$). Pancreatic tissue was identified in 21 of 57 tumors (36.8%). The patients with tumors that contained pancreatic tissue had more presenting symptoms and complicated surgery than those whose tumors were without pancreatic tissue (76.2% *vs.* 33.3%, $p = 0.002$, and 42.9% *vs.* 11.1%, $p = 0.008$). The patients with symptoms had a higher incidence of complicated surgery than those without (39.3% *vs.* 6.9%, $p = 0.004$).

Conclusion: Mediastinal mature teratoma commonly occurs in young women. Thoracoscopic surgery is a feasible technique for mediastinal mature teratoma resection if no dense adhesions are found during preoperative assessment. The presence of symptoms might be a relative contraindication for thoracoscopic teratoma resection because of its association with surgical complications.

Key Words: mediastinal neoplasms, minimally invasive surgical procedures, thoracoscopy

Mediastinal germ cell tumors (GCTs) are rare and have an incidence of 0.1–0.2 per 100,000 people.[1] Mediastinal GCTs appear similar in histopathology to their gonadal counterparts. Mature teratomas are the most common mediastinal GCTs,[2–5] and they are also benign, with resection being the primary treatment. Video-assisted thoracoscopic surgery (VATS) has gradually become a standard

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approach for a variety of intrathoracic diseases. However, few studies have been reported on resection of mediastinal mature teratoma using VATS. In this study, we reviewed our experiences of treating patients with mediastinal mature teratoma, and compared the results of conventional open surgery and VATS.

Materials and Methods

This study protocol was approved by the Research Ethics Committee of the National Taiwan University Hospital. From 1988 to 2005, 79 patients with mediastinal GCTs were treated at the Department of Surgery, National Taiwan University Hospital. The following were excluded from the study: two seminomas, 17 non-seminomatous malignant GCTs, one immature teratoma, and one teratoma with malignant transformation. Medical records from the 58 patients with mediastinal mature teratomas were reviewed retrospectively. We excluded one case because we were unable to locate the patient's chart. We analyzed the patients' age, sex, symptoms, blood sugar, pulmonary function, diagnosis, tumor size, histopathological features, operative methods, operative time, tumor adhesion, blood loss, ventilator requirement, intensive care unit (ICU) stay, chest tube requirement, and postoperative hospital stay. The tumor diagnosis was based on the final histopathological report from a surgical specimen or fine needle biopsy, and also included analysis of typical serum tumor markers such as α-fetoprotein and β-human chorionic gonadotropin. We divided the operative methods for mediastinal teratoma removal into two main groups: one was the conventional, open group, which included thoracotomy and median sternotomy procedures; and the other group received VATS. Patients who underwent surgery that involved intraoperative conversion from VATS to thoracotomy were included in the open group. The decision regarding whether a patient should undergo an open or VATS procedure was made on the basis of time period, tumor size and location, and potential adhesions as seen by

computed tomography (CT) during preoperative assessment.

In the VATS group, the patients were intubated with a double-lumen endotracheal tube while the semi-decubitus position. The camera ports were at the intersection of the eighth intercostal space and mid-axillary line. One working port, at the intersection of the sixth or seventh intercostal space and the vertical line 1 cm medial to the nipple, and one anterior minithoracotomy, without cutting the rib at the fourth intercostal space, were needed. If the tumor was cystic, intraoperative needle drainage of the intracystic fluid for tumor shrinkage was performed.

Statistical analyses were performed using SPSS version 13.0 (SPSS, Chicago, IL, USA). Comparison of the preoperative, intraoperative and postoperative data between the open and VATS groups was made with a χ^2 test for categorical variables and a Student t test for continuous data. Fisher's exact test was used for the small observed cell count. A p value of < 0.05 was considered to be statistically significant. Descriptive analyses are presented as median (range) or mean ± standard deviation.

Results

Clinical data
There were 39 female and 18 male patients (ratio = 2.2:1; female predominance) with a median age of 27 years (range, 6–69 years; mean, 28.8 ± 13.6 years). Of the 57 patients with mature teratomas, 28 (49.1%) were asymptomatic at the time of surgery, and the lesions were discovered incidentally on chest X-rays. The most common symptoms in the mature teratoma group included chest pain (31.6%), chest tightness or discomfort (14.0%), cough (7.0%), and fever (7.0%). One patient presented with concurrent mediastinal and ovarian mature teratomas.[6] We also analyzed the symptoms in the group of patients aged < 12 years old to ascertain if this group presented with different signs. There were four patients aged < 12 years, and three of these (75%) had fever. All of the

	Open (*n* = 43)	VATS (*n* = 14)	*p*
Table 1. Comparison between operative methods in patients with mediastinal mature teratomas*			
Age (yr)	27.7 ± 14.1	32.3 ± 11.7	0.278
Sex, male (%)	34.9	21.4	0.511
Tumor size (cm)	10.4 ± 4.7	8.5 ± 2.9	0.147
FVC (%)	90.7	101.6	0.119
FEV_1 (%)	86.1	98.3	0.066
Adhesions (%)			
Yes	79.1	78.6	0.968
No	20.9	21.4	
Blood loss (mL)	288.2 ± 406.6	68.2 ± 152.1	0.088
Operative time (min)	205.4 ± 75.7	106.4 ± 35.7	0.038
Ventilator days	0.5 ± 0.8	0.2 ± 0.4	0.034
ICU stay (d)	1.5 ± 1.4	0.6 ± 0.8	0.030
Chest tube stay (d)	5.0 ± 3.4	4.1 ± 2.1	0.350
Postoperative hospital stay (d)	8.1 ± 3.5	6.5 ± 2.7	0.118
Postoperative complication (%)	14.0	7.1	0.669

Data presented as % or mean ± standard deviation. VATS = Video-assisted thoracoscopic surgery; FVC = forced vital capacity; FEV_1 = forced expiratory volume in 1 second; ICU = intensive care unit.

lesions were in the anterior mediastinum. In total, 34 of the teratomas were located on the right side, 22 on the left, and one in the median area. The serum α-fetoprotein and β-human chorionic gonadotropin levels in all 57 patients were within normal limits. A total of 18 patients underwent preoperative fine needle aspiration, 16 underwent echo-guided aspiration, and two received CT-guided aspiration. No definite cytological or pathological diagnoses were made.

Surgical results

All 57 patients underwent surgical resection for the treatment of mediastinal mature teratomas. A total of 43 patients (75.4%) received surgery using an open approach, whereas 14 patients (24.6%) underwent VATS tumor excision. Prior to 1996, 24 patients underwent tumor resection, whereas only one received a VATS procedure. After 1997, 33 patients had surgical intervention. A total of 20 of these patients underwent an open procedure, and 13 received VATS. The mean age, male-to-female ratio, mean tumor size, pulmonary function, and level and condition of tumor

adhesion were similar between both groups. The operative time, duration of postoperative ventilator use, and length of ICU stay in the VATS group were significantly shorter than those in the open group (Table 1). The duration of chest tube placement and length of postoperative hospital stay were similar between both groups. The median postoperative follow-up period was 12 months (range, 1–167 months; mean, 24.7 ± 30.3 months). There was no mortality or tumor recurrence in either group.

In the open surgical resection group, 10 patients received major organ resection, including four lung lobectomies, two lung wedge resections, four phrenic nerve resections, and one innominate vein resection with reconstruction. In the VATS group, four patients underwent lung wedge resection. During the postoperative course in the open group, six patients developed complications, including two diaphragmatic eventrations, one case of Horner syndrome, one brachiocephalic arterial tear, one case of lung atelectasis, one intubation for sputum impaction, and one instance of wound dehiscence. In the VATS group, only one

patient developed a complication secondary to excessive postoperative pleural drainage. Although there were no significant differences between the postoperative complication rates of the two groups (Table 1), the complications were less severe in the VATS than in the open group.

Three patients underwent intraoperative conversion from VATS to anterolateral minithoracotomy. The main reason for conversion was that the tumor adhered densely to the surrounding structure. It was noteworthy that one patient's tumor adhered to the phrenic nerve and another to the lung. Nevertheless, no major structure had to be resected in the three patients, and their postoperative course was uneventful.

Pathological characteristics

The most common components were skin or skin appendages and nerve tissue in the ectoderm; cartilage and fat in the mesoderm; and respiratory epithelium, pancreatic tissue, and gastrointestinal epithelium in the endoderm (Table 2). Pancreatic tissue was identified in 21 of 57 tumors (36.8%). There was no statistically significant difference in fasting plasma glucose level and tumor adhesion as to whether or not the tumors contained pancreatic tissue (Table 3). However, the patients with tumors that contained pancreatic tissue had more presenting symptoms than those whose tumors were without pancreatic tissue (76.2% $vs.$ 33.3%, $p=0.002$). A higher percentage of combined major organ resection was also noted in the patients with tumors that contained pancreatic tissue (42.9% $vs.$ 11.1%, $p=0.008$). Furthermore, there was a higher percentage of combined major organ resection in the patients

with symptoms than in those without (39.3% $vs.$ 6.9%, $p=0.004$).

Discussion

We reviewed retrospectively a series of 57 mediastinal mature teratomas from 1988 to 2005. This is currently the largest examined series of mediastinal mature teratoma cases in Taiwan. The median age and female predominance of the mature teratomas in our series are comparable to those

Table 2. Histopathology in mature teratoma

Histopathology	No. of cases
Ectoderm	
Skin or skin appendages	67
Nerve tissue	13
Salivary gland	4
Enamel	1
Sweat gland	1
Acini of breast tissue	1
Mesoderm	
Cartilage	27
Adipose tissue	18
Bone	8
Muscle	6
Endoderm	
Respiratory epithelium	38
Pancreatic tissue	21
Gastrointestinal epithelium	20
Hepatic tissue	2
Uroepithelium	2
Epithelium of Müllerian duct	1
Fallopian tube	1
Thyroid	1

Table 3. Relationship between pancreatic tissue in mediastinal teratoma and serum glucose level or adhesion*

	Pancreatic tissue		p
	Yes ($n=21$)	No ($n=36$)	
Serum glucose AC[†] (mg/dL)	90.8±11.4	89.1±13.1	0.668
Adhesions			
Yes	18 (85.7)	27 (75.0)	0.504
No	3 (14.3)	9 (25.0)	

*Data presented as n (%) or mean ± standard deviation; †fasting blood glucose.

from previous studies.[3,5] Mediastinal mature teratomas accounted for 73.4% (58/79) of mediastinal GCTs in our study, and this proportion is compatible with the 78.6% (11/14) reported in Kaohsiung, Taiwan,[2] and 73.6% (95/129) reported in Japan.[3] Although mature teratomas are the most common GCTs of the mediastinum, the incidence of these tumors in Western countries is lower than in Asia, with an incidence of 27.0% (87/322) in the United States[4] and 51.0% (50/98) in France.[5] It is not entirely correct to assume that the difference in incidence between countries in the Far East and the West is explained by the bias toward high-risk case selection in referral centers.[4,5] Further study of racial and genetic variation in mediastinal GCTs is needed before drawing further conclusions.

Mediastinal mature teratoma is a benign disease. However, resection can be surgically challenging because of potential adhesions to major organs, including the major vessels in the mediastinum as well as the heart, nerves and lungs.[7] VATS has gradually become the preferred approach for a variety of intrathoracic diseases. It is especially suitable for benign intrathoracic lesions such as pneumothorax and empyema. To the best of our knowledge, no study has described mediastinal mature teratoma resections using VATS, aside from a few case reports in English-language journals.[8–11] The present study is by far the largest series to have examined VATS in the treatment of mediastinal mature teratomas. In our series, the operative time, duration of postoperative ventilator use, and length of ICU stay in the VATS group were significantly shorter than that in the open group (Table 2). Although the VATS and conventional open surgery groups did not differ significantly in the length of postoperative hospital stay, this might have been attributed partly to similar durations of chest tube placement. In our institution, chest tubes are not removed until the volume of daily drainage is less than 100 mL and a satisfactory chest X-ray result is obtained. The limitation of our study is that it was a retrospective chart review, and the indications and criteria for VATS resection of mediastinal mature teratoma were judged by the surgeon. Smaller tumor size and less adhesion on CT scanning were indicative for VATS resection. In our practice, VATS was contraindicated if the tumor compressed the heart and compromised the hemodynamics, or adhered to the intrathoracic great vessels. Although we present a relatively large series of mediastinal mature teratomas, it might be too small of a dataset and inherently too biased with respect to the time period of surgery and postoperative care, and the lesser extent of resection required in the VATS group to be the focus of outcomes and conclusions.

In the current series, pancreatic tissue accounted for 36.8% of the mature teratoma tissue removed from the mediastinum. Pancreatic tissue is a characteristic finding in mature teratoma of the mediastinum, but it occurs only rarely in GCTs of other parts of the body.[12,13] Proteolytic enzymes secreted by pancreatic tissue often are associated with inflammation and dense adhesions surrounding the teratoma,[14] fistulas into tracheobronchial trees,[15] and expectoration of sebaceous material[16] or hair. Elevated amylase level in the cystic fluid of teratomas also has been reported.[14,17] These help to explain why patients with teratomas that contain pancreatic tissue had more presenting symptoms and complicated surgery than those without pancreatic tissue. In addition, we found that patients with symptoms had a higher incidence of undergoing complicated surgery than those without. Therefore, the presence of symptoms should be considered a relative contraindication of VATS for teratoma resection. Previous case reports have described that the endocrine function of pancreatic tissue in mediastinal mature teratomas can also cause hypoglycemia.[18,19] In our study, the pancreatic tissue in the mature teratomas was not associated significantly with tumor adhesion or serum glucose levels. A bias could have been present in this study because we did not calculate the percentage volume of pancreatic tissue or the exocrine or endocrine tissue present in the teratomas. Similarly, no patients with teratomas showed symptoms of hypoglycemia in the series

described by Suda et al.[12] Histopathologically, a central core of insulin-containing B cells, with additional differentiated functional endocrine cells in the peripheral region, is formed in the teratomatous pancreatic tissues, as in the normal pancreas.[20,21] This structure is thought to be important for the regulatory mechanisms of insulin functions by the pancreas.[20] This observation could explain the similar blood glucose levels in our patients, regardless of whether or not the teratomas contained pancreatic tissue.

In conclusion, in our 18-year experience with mediastinal mature teratomas, which most commonly occur in young adult women, we determined that VATS resection is a feasible choice, with shorter postoperative recovery time if there are no dense adhesions present in the preoperative CT scan. The presence of symptoms may be a relative contraindication of VATS for teratoma resection because of its association with surgical complications.

Acknowledgments

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