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ORIGINAL ARTICLE

Verification of the diagnostic strategy for anterior mediastinal tumors

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Abstract

Background For thymic epithelial tumors (TETs), the National Comprehensive Cancer Network guideline has suggested that complete excision of the tumor should be performed without a preoperative biopsy when resectable. However, little evidence has been provided to support this strategy. The purpose of this study was to review our diagnostic process and to evaluate the validity of radical resection of anterior mediastinal masses (AMMs) without pathological confirmation.

Methods A total of 254 patients underwent surgical resection for AMMs between 2004 and 2015. This study included 181 patients with likely TETs according to clinical features, serum levels of tumor markers and autoimmune-antibodies, and radiological findings. In addition, AMMs likely TETs were classified into resectable or unresectable tumors. We retrospectively reviewed the diagnostic process of those patients and validated surgical resection of AMMs without a definitive diagnosis.

Results Among 254 patients, 181 were suspected of having a TET based on the serum levels of tumor markers and autoimmune-antibodies and the radiological findings. Of them, 157 patients were deemed resectable and underwent surgical resection without histological confirmation, and 144 (92%) were diagnosed with TETs in the final pathological examinations. In 13 patients with non-TETs, the tumors were difficult to differentiate from TETs by imaging and clinical findings alone.

Conclusions A total of 92% of patients suspected of having a TET and who underwent complete resection without pathological confirmation were accurately diagnosed and properly treated. Surgical resection without a definitive diagnosis was feasible in patients suspected of having a TET when they were considered resectable.

Keywords Thymic epithelial tumor · Thymoma · Preoperative diagnosis · Anterior mediastinum mass

Introduction

Anterior mediastinal masses (AMMs) are the most common group of mediastinal tumors, with 54% of mediastinal masses in the anterior compartment in a large series of patients [1], and 25–50% of AMMs are malignant, such as thymic epithelial tumors (TETs), malignant germ cell tumors (GCTs), and Hodgkin or non-Hodgkin lymphomas [2, 3]. Such malignant lesions require an early diagnosis and treatment. AMMs comprise a diverse group of tumors, and their appearances often vary. Although several articles have described the radiological findings [4–8], detailed studies reviewing the process for the differential diagnosis of AMMs have not yet been reported.

Treatment strategies of AMMs should be selected properly for each kind of tumor. For TETs, including thymoma and thymic carcinoma, excision of the tumor with total thymectomy is considered the mainstay treatment, and complete resection is the most important factor influencing a favorable outcome [9–11]. For benign AMMs such as mature teratoma or cystic diseases, surgical resection of the entire tumor mass is usually recommended, and vital structures such as great vessels should be preserved [12, 13]. In contrast, the treatment approach for patients with malignant GCTs, such as seminoma and nonseminomatous GCT (NSGCT), is different, and multimodal treatment including cisplatin-based chemotherapy followed by surgical resection of residual masses is employed as the standard treatment strategy [14]. Therefore, a pretreatment biopsy

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for histological confirmation is essential for therapeutic decision-making. However, when patients are strongly suspected of having TET according to the clinical features and/or radiological findings, they often undergo surgical resection without histological confirmation [12, 13, 15]. This is because pneumothorax, bleeding, and tumor dissemination associated with a preoperative biopsy should be avoided [16, 17]. The National Comprehensive Cancer Network (NCCN) guideline has also suggested this treatment strategy without a preoperative biopsy [18]. Nevertheless, little evidence concerning this recommendation has been provided.

The purpose of this retrospective study was to assess our diagnostic process for AMMs and to evaluate the validity of radical resection of AMMs without pathological confirmation.

Patients and methods

Patients

This study was a retrospective review of patients with AMMs and was approved by the Institutional Review Board in Nagoya University Hospital (2014-0100). A total of 254 patients underwent surgical resection for AMMs at Nagoya University Hospital between 2004 and 2015. In these patients, 254 AMMs were diagnosed according to the clinical features and radiological findings by board-certified thoracic surgeons and radiologists. Patients suspected of having a mediastinal Hodgkin and non-Hodgkin lymphoma before resection were excluded from this cohort. These clinical features were age; the presence of paraneoplastic syndrome such as myasthenia gravis (MG), pure red cell aplasia (PRCA), and hypogammaglobulinemia; elevation of the serum level of tumor markers such as alpha-fetoprotein (AFP), beta human chorionic gonadotropin (β-hCG), and carcinoembryonic antigen (CEA); and the serum level of antiacetylcholine receptor antibody (ARAb). Concerning paraneoplastic syndrome, the presence of MG was diagnosed by neurologists based on an elevation in the serum level of ARAb ($\geq$0.3 nmol/L), results of electromyogram, and associated symptoms, such as ptosis, double vision, limb muscle weakness, and dysphagia. Titers of serum tumor markers of β-hCG, AFP, and CEA were defined as positive at values over 5 IU/l, 10 ng/ml, and 5 ng/ml, respectively.

Radiological assessment

As radiological examinations, almost all patients underwent contrast-enhanced computed tomography (CT), and magnetic resonance imaging (MRI) was sometimes performed in patients with AMMs that consisted of mainly cystic lesions or who were suspected of having tumor invasion to the adjacent organs. In addition, when contrast-enhanced CT could not be performed because of patients' allergy to contrast agents, MRI was performed alternatively. Fluorine-18 fluorodeoxyglucose positron emission tomography/CT (FDG-PET/CT) was performed in most of the patients who had solid lesions and cystic lesions with thick walls on CT to differentiate not only benign tumors from malignant ones but also thymoma from thymic carcinoma [19, 20]. Supplemental Table 1 shows the clinical features and radiological findings referenced to distinguish AMMs [4–8, 20–27].

Diagnostic strategy

AMMs likely to be TETs were also classified into resectable or unresectable tumors by experienced thoracic surgeons. We defined resectable TETs as early-stage (stages I and II) tumors or stage III tumors with invasion to the lung and/or pericardium that were technically able to achieve complete resection easily [15, 28, 29]. Patients with resectable TETs underwent upfront resection without a histological diagnosis. In contrast, those with unresectable TETs received a histological diagnosis via a CT-guided needle biopsy or video-assisted thoracic surgical (VATS) biopsy, and they underwent surgical resection following induction chemotherapy or chemo-radiotherapy [29]. Histologic classification was assessed according to the WHO classification system [30]. The extent of disease was defined by the Masaoka-Koga surgico-pathological staging [31]. Patients suspected of having a thymoma without MG, thymic carcinoma or neuroendocrine tumor usually underwent thymectomy, while those suspected of having a thymoma with MG underwent extended thymectomy. When patients were suspected of having a benign AMM such as mature teratoma or cystic diseases, they underwent surgical resection of the entire tumor mass.

Statistical analyses

Clinicopathological variables were tested using Pearson's chi-squared and Fisher's exact tests. Values of $p < 0.05$ were considered to be statistically significant. All analyses were performed using the StatMate-IV software package (ATMS; Tokyo, Japan).

Results

Figure 1 shows the diagnostic tree of the AMMs. At the first process, 254 patients with AMMs were classified into three groups according to the elevation of serum levels of tumor markers and ARAb and/or the presence of MG. Group GCT consisted of 8 patients suspected of having malignant GCTs who had elevated levels of serum tumor markers,

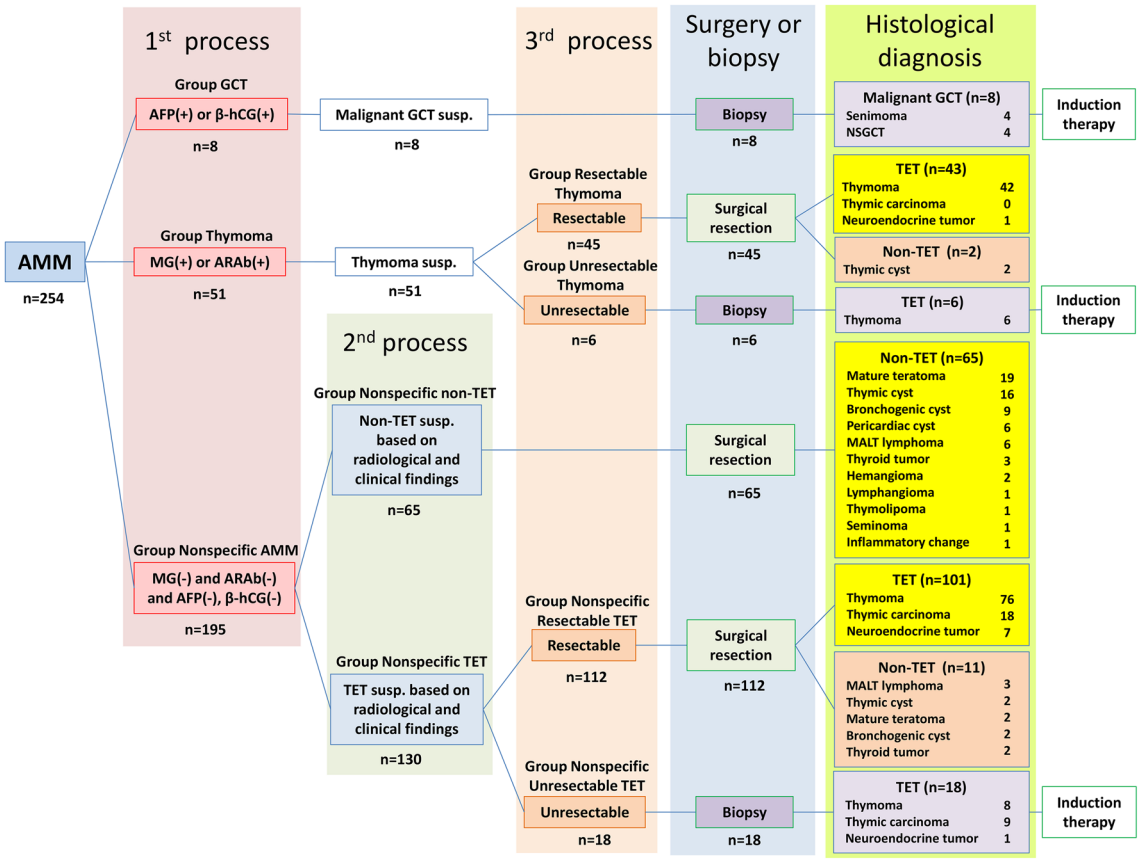

Fig. 1 A schematic illustration of the diagnosis and treatment strategy for AMMs. *AMM* anterior mediastinal mass, *MG* myasthenia gravis, *ARAb* antiacetylcholine receptor antibody, *AFP* alpha-fetoprotein, *β-hCG* beta human chorionic gonadotropin, *GCT* germ cell tumor, *TET* thymic epithelial tumor

such as β-hCG and/or AFP. Group Thymoma consisted of 51 patients suspected of having thymomas. They were diagnosed with MG preoperatively and/or had elevated serum levels of ARAb. Group Nonspecific AMM included the remaining 195 patients.

Most of the patients in the Group GCT were young men with a median age of 28 (range 18–69 years). A histological examination of the biopsied specimen of the eight patients showed four seminomas and four NSGCTs. The 51 patients in the Group Thymoma were suspected of having thymoma according to the presence of MG and/or elevation of the serum levels of ARAb at the first process.

At the second process, the remaining 195 AMMs (Group Nonspecific AMM) were classified into 130 suspected TETs (52%, Group Nonspecific TET) and 65 suspected non-TETs (26%, Group Nonspecific non-TET) based on the clinical features and/or radiological findings (Tables 1, 2 and Supplemental Table 1). All 65 AMMs likely to be non-TETs in the Group Nonspecific non-TET underwent surgical resection without histological confirmation, and they were ultimately diagnosed as non-TET tumors, including 19 mature teratomas, 16 thymic cysts, 9 bronchogenic cysts, 6 pericardial cysts, 6 MALT (mucosa-associated lymphoid tissue) lymphomas, 3 thyroid tumors, and 6 others. Among 19 patients suspected of having a mature teratoma, 12 (63%) were younger than 40 years of age. The 13 teratomas (53%) contained calcification on CT, and 18 (95%) consisted of multi-loculated cystic masses with thickened walls. Concerning cystic diseases, such as thymic cyst, bronchogenic cyst and pericardial cyst, all patients were asymptomatic, and most of the cystic tumors consisted of monolobular nodules with thickened walls (94%) and non-enhancement (97%) on CT. MRI showed water intensity measurement in most cases (84%). Six patients were suspected of having MALT lymphoma, and half of them had Sjögren's syndrome. CT showed that all of them had a solid nodule with multilocular cysts. Eight patients were suspected of having malignant GCTs based on their age and/or the elevation of the serum levels of tumor markers.

At the third process, 51 AMMs suspected of being thymoma in the Group Thymoma and 130 AMMs suspected of being TET in the Group Nonspecific TET were classified into resectable or unresectable tumors. Forty-five AMMs in the Group Thymoma were evaluated as resectable

Table 1 Clinical features and radiological findings of the patients suspected of having non-TETs

	n		*n*	(%)
Mature teratoma	19	Young age (<40 years old)	12	(63)
		CT findings		
		Internal foci of fat	10	(53)
		Calcification	13	(68)
		Multiloculated cystic mass with thickness walls	18	(95)
Cystic disease	31	Asymptomatic	31	(100)
Thymic cyst	16	CT findings		
Bronchogenic cyst	9	Non-enhancement	30	(97)
Pericardial cyst	6	Monolobular nodule with thin walls	29	(94)
		MRI findings		
		Water intensity measurements	26	(84)
MALT lymphoma	6	Sjögren's syndrome	3	(50)
		CT findings		
		Solid nodule with multilocular cysts	6	(100)
		Slight enhancement within solid lesion	3	(50)
Malignant germ cell tumor	9	Young man (<40 years old)	7	(78)
Seminoma	5	Elevation of serum level of AFP, β-hCG	8	(89)
NSGCT	4	Giant mass	6	(67)
		CT findings		
		Heterogeneous enhancement	7	(78)
		FDG-PET findings		
		High accumulation in solid lesion	6	(67)
Thyroid tumor	3	Hypercalcemia	1	(33)
Thyroid goiter	1	CT findings		
Thyroid cyst	1	Connected with thyroid gland	1	(33)
Parathyroid tumor	1	^{99m}Tc-MIBI scintigram findings		
		High accumulation in solid lesion	1	(33)
Hemangioma	2	CT findings		
		Smooth or lobulated with sharp margins	2	(100)
		Heterogeneous enhancement	2	(100)
Lymphangioma	1	CT findings		
		Smooth or lobulated with sharp margins	1	(100)
		Variable-sized cyst, not enhanced	1	(100)

TETs thymic epithelial tumors, *MALT* mucosa-associated lymphoid tissue, *AFP* alpha-fetoprotein, *hCG* human chorionic gonadotropin, *NSGCT* nonseminomatous germ cell tumor, *FDG-PET* fluorine-18 fluorodeoxyglucose positron emission tomography, *^{99m}Tc-MIBI* 99 m-technetium methoxy-isobutyl-isonitrile

thymomas (Group Resectable Thymoma), and 112 AMMs in the Group Nonspecific TET were also judged as resectable TETs (Group Nonspecific Resectable TET). They underwent complete resection without histological confirmation. Consequently, 43 AMMs in the Group Resectable Thymoma and 101 in the Group Nonspecific Resectable TET were diagnosed as TETs; the remaining 2 AMMs in the Group Resectable Thymoma and 11 in the Group Nonspecific Resectable TET were diagnosed as non-TETs. The TETs in the Group Resectable Thymoma consisted of 42 thymomas and 1 neuroendocrine tumor. The subtype of this thymic neuroendocrine tumor was atypical carcinoid, and the patient had slight elevation of serum ARAb but did not have any symptoms of MG. The TETs in the Group Nonspecific Resectable TET consisted of 76 thymomas, 18 thymic carcinomas, and 7 neuroendocrine tumors, which were 6 atypical carcinoids

Table 2 Clinical features and radiological findings of the patients with TETs

	n		*n*	(%)
Thymoma	132	Paraneoplastic syndromes	36	(27)
		MG	32	(24)
		PRCA	4	(3)
		Hypogammaglobulinemia	0	(0)
		Elevation of serum level of ARAb	48	(36)
		Symptoms of compression and/or invasion	19	(14)
		Chest pain	8	(6)
		Cough	5	(3.7)
		Fever up	4	(3)
		SVC syndrome	2	(1.5)
		CT findings	132	(100)
		Oval and lobulated solid mass	132	(100)
		Homogeneous enhancement	131	(99)
		Cyst formation	32	(24)
		Calcification	29	(22)
		Invasion into great vessels and mediastinal structures	13	(9.8)
		Association with pleural dissemination	7	(5.3)
		FDG-PET findings	113	(86)
		FDG accumulation (SUVmax) < 2/2–5/> 5	8/87/18	(7/78/16)
Thymic carcinoma	27	Symptoms of compression and/or invasion	9	(33)
		Chest pain	5	(19)
		Cough	3	(11)
		SVC syndrome	1	(3.7)
		CT findings	27	(100)
		Irregular marginated mass	12	(44)
		Invasion into great vessels and mediastinal structures	16	(59)
		Calcification	6	(22)
		Heterogeneous enhancement suspected of necrosis	10	(37)
		Pleural or pericardial effusion	1	(3.7)
		FDG-PET findings	25	(93)
		FDG accumulation (SUVmax) < 2/2–5/> 5	0/6/19	(0/24/76)
Neuroendocrine tumor	9	Symptoms of compression and/or invasion	4	(44)
		Chest pain	3	(33)
		Hemosputum	1	(11)
		CT findings	9	(100)
		Large (> 5 cm) and lobulated mass	5	(56)
		Heterogeneous enhancement suspected of necrosis	5	(56)
		Invasion into great vessels and mediastinal structures	3	(33)
		FDG-PET findings	7	(78)
		FDG accumulation (SUVmax) < 2/2–5/> 5	0/3/4	(0/43/57)

TETs thymic epithelial tumors, *MG* myasthenia gravis, *PRCA* pure red cell aplasia, *ARAb* antiacetylcholine receptor antibody

and 1 typical carcinoid. Of the 101 patients who belonged to Group Nonspecific Resectable TET and had been diagnosed with TETs pathologically, 78 were suspected of having a thymoma and 67 (86%) actually had a thymoma, 23 were suspected of having thymic carcinoma, and 13 (57%) had thymic carcinoma. No patients were suspected of having thymic carcinoid; however, seven patients were diagnosed with thymic carcinoid. The accuracy rates of the diagnoses of thymoma and thymic cancer were 90% and 85%, respectively.

The remaining 6 AMMs in the Group Thymoma were judged as unresectable thymomas (Group Unresectable Thymoma), and they underwent a CT-guided needle biopsy. All of them were ultimately diagnosed as thymomas and

underwent induction chemotherapy. Among the 130 tumors in the Group Nonspecific TET, 18 were evaluated as unresectable TETs (Group Nonspecific Unresectable TET) and underwent a CT-guided biopsy or VATS biopsy. The histological examinations of the 18 AMMs showed 8 thymomas, 9 thymic carcinomas, and 1 neuroendocrine tumor, which was an atypical carcinoid. All of them underwent induction chemotherapies after histological confirmations. Eleven AMMs suspected of being resectable TETs in the Group Nonspecific TET were proven to be non-TETs, consisting of three MALT lymphomas, two thymic cysts, two mature teratomas, two bronchogenic cysts, and two thyroid tumors (Fig. 2).

Table 2 shows the clinical features and radiological findings of the 168 patients who were ultimately diagnosed with TETs. They consisted of 132 patients with thymoma in the Groups Thymoma and Nonspecific TET and 27 patients with thymic carcinoma and 9 patients with neuroendocrine tumor in the Groups Thymoma and Nonspecific TET. Among the 132 patients with thymoma, 32 (24%) had MG, 4 (3%) had PRCA, and none had hypogammaglobulinemia. Forty-eight patients (36%) with thymoma had elevated serum levels of ARAb. In contrast, 94% of patients with MG and/or elevated serum levels of ARAb in the Group Thymoma were diagnosed with thymomas in the final histological examinations. Two tumors in the Group Resectable Thymoma were found to be thymic cysts. These two patients had slightly elevated serum ARAb titers (0.3 and 3.7 nmol/L), but they had no MG symptoms. Among the patients with thymoma, 14% had symptoms associated with tumor compression and/or invasion to neighboring organs, while 33% patients with thymic carcinoma had any symptoms. Almost all of the thymomas were oval and lobular solid masses that were enhanced homogeneously on CT, while 44% of thymic carcinomas showed an irregular delineated mass, 59% showed invasion into the great vessels and mediastinal structures, and 37% had heterogeneous enhancement with areas of necrosis. Thirty-two thymomas (24%) were accompanied by cystic lesions, and 29 (22%) had calcification. The frequency of thymomas with calcification was same as thymic carcinomas (22%). PET/CT revealed that 87 thymomas (78%) had an intermediate accumulation [maximum standardized uptake value (SUVmax): 2–5], while 76% of the thymic carcinomas had a high accumulation of FDG (SUVmax: > 5). The clinical features and radiological findings of the neuroendocrine tumors were similar to those of the thymic carcinomas. The patients with neuroendocrine tumors had chest pain and masses associated with necrosis and/or invasion into neighboring structures. On PET/CT, the tumors showed an intermediate accumulation.

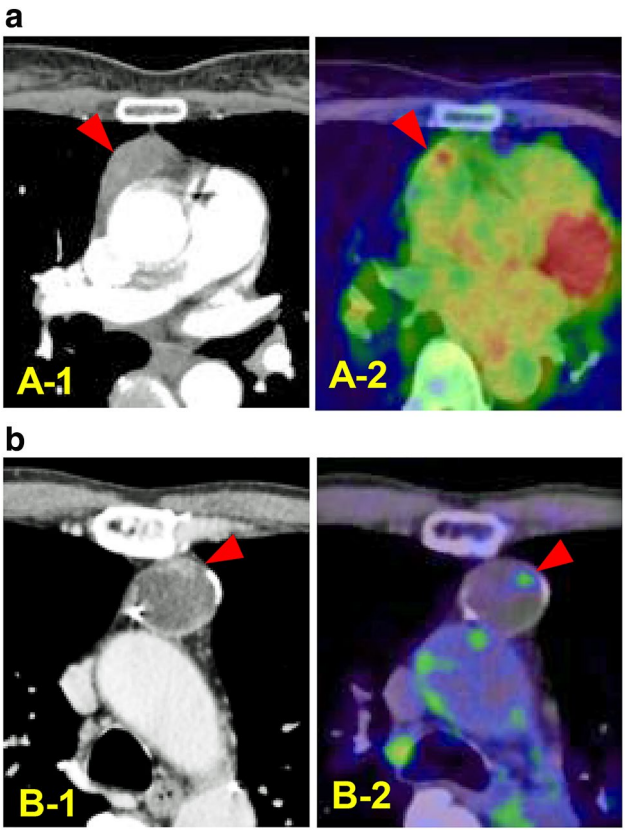

Fig. 2 Non-TETs. **a** Contrast-enhanced CT showed that an oval nodule was an enhanced solid lesion monotonously (A-1), and PET-CT revealed the intermediate accumulation of FDG in the nodule (A-2). Thymoma was suspected based on these radiographic findings. However, a pathological examination showed that it was a MALT lymphoma. **b** CT showed an oval cystic nodule that had a partially thickened wall (B-1), and PET-CT revealed the slight accumulation of FDG in the wall (B-2). Cystic thymoma was suspected based on these radiographic findings. However, a pathological examination showed that it was a thymic cyst

Table 3 shows histological features and pathological stage of the patients with TETs, and compared the oncological outcomes between two groups with/without preoperative biopsy. Concerning thymoma, the patients with biopsy were significantly associated with type B2 or B3 tumor ($p = 0.014$) and with pathological stage III or IV (< 0.001). About thymic carcinoma, the patients with biopsy were correlated with pathological stage III or IV ($p = 0.03$). Therefore, we confirmed that the patients with more advanced stage and more malignant histological subtype were selected properly and underwent preoperative biopsy.

These results showed that 222 AMMs suspected of being resectable TETs in the Groups Resectable Thymoma and Nonspecific Resectable TET and non-TETs in Group Nonspecific non-TET underwent complete resection without histological confirmation. Among them, the 209 (94%) shown in the yellow box in Fig. 1 were diagnosed correctly before surgical resection according to our diagnostic process. For the TETs alone, 144 (92%) of the 157 patients suspected of

Table 3 Histological type and pathological stage of the patients with TETs

		n	With biopsy (%)	Without biopsy (%)	*p* value
Thymoma	Total	132	14 (11)	118 (89)	
Histological type	A/AB/B1	72	3 (21)	69 (58)	0.014
	B2/B3	54	11 (79)	43 (36)	
	Others	6	0 (0)	6 (5.1)	
p-Masaoka-Koga stage	I/II	110	5 (36)	105 (89)	< 0.001
	III/IV	22	9 (64)	13 (11)	
Thymic carcinoma	Total	27	9 (33)	18 (67)	
Histological type	Sq	27	9 (100)	18 (100)	
p-Masaoka-Koga stage	I/II	9	0 (0)	9 (50)	0.03
	III/IV	18	9 (100)	9 (50)	
Neuroendocrine tumor	Total	9	1 (11)	8 (89)	
Histological type	Typical carcinoid	1	0 (0)	1 (13)	0.71
	Atypical cartinoid	8	1 (100)	7 (88)	
p-Masaoka-Koga stage	I/II	4	0 (0)	4 (50)	0.34
	III/IV	5	1 (100)	4 (50)	

Sq squamous cell carcinoma

having TETs were accurately diagnosed, and they underwent complete resection without histological confirmation.

Discussion

The NCCN guidelines recommend that a surgical biopsy be avoided if resectable thymoma is strongly suspected based on clinical and radiological features [18]. However, the outcomes of surgical resection of AMMs likely to be TETs without a preoperative defined diagnosis have seldom been reported. To our knowledge, this is the first study reviewing patients suspected of having TETs who underwent resection without a preoperative diagnosis. The 222 patients suspected of having TETs or non-TETs underwent upfront resection without a preoperative diagnosis, and 209 (94%) were accurately diagnosed according to our diagnostic process and achieved complete resection. In addition, there have been no reports regarding the accuracy of the diagnosis of AMM with a statistical analysis, it is, therefore, difficult to assess the acceptability of this diagnostic approach. However, Morrissey et al. reported that the accuracy of a fine-needle aspiration biopsy for AMM was 88% [32]. Therefore, we consider that 94% of AMMs without pathological confirmation were accurately diagnosed, suggesting that surgical resection without a definitive diagnosis may be feasible.

Concerning the diagnostic process, we classified AMMs into three groups at the first process based on previous reports that 90% of NSGCTs were associated with elevated serum level of AFP and/or β-hCG [33–36] and that AMMs with MG and/or elevation of serum ARAb titer were almost always thymomas (about 98%) [21]. Most of the patients, whose serum AFP and/or β-hCG were marked elevated, were suspected of having GCT and they underwent CT-guided biopsy because all cases were not considered urgent cases based on their physical conditions and radiological findings. Concerning the elevation of serum ARAb titer, previous reports were consistent with the results of this study [21]. In addition, we classified the AMMs in Group Nonspecific AMM into suspected TETs and non-TETs at the second process. All cases of suspected non-TET were confirmed to not be TETs; however, 11 (8.5%) cases of suspected TETs in Group Nonspecific TET were found to be non-TETs. MRI is considered to be the most useful imaging modality for distinguishing cystic from solid lesions [8]. However, in the present study, we found it difficult to distinguish cystic non-TETs from cystic thymoma based on the radiological findings alone. The distinction of cystic AMMs with thick walls remains an issue to be resolved.

Resection of AMMs deemed likely to be TETs without a preoperative biopsy is thought to be reasonable for four reasons. First, the accuracy of the radiological diagnosis of AMMs containing TETs has been improved by the widespread use of detection tools such as multi-slice spiral CT, MRI, and PET-CT in recent years. Travani et al. reported that PET-CT and helical multidetector CT (MDCT) were useful for the differential diagnosis between TETs and benign lesions [37]. They found that PET-CT showed a positive predictive value (PPV) and negative predictive value (NPV) relative to the malignant or benign nature of the lesion of 92.3% and 100%, respectively. MDCT showed a PPV and NPV of 100% and 80%, respectively. Second, not undergoing a preoperative routine biopsy can avoid complications such as pneumothorax, bleeding, and tumor dissemination. Pneumothorax after a CT-guided percutaneous biopsy has a reported incidence of 10–60%

[16]. Some cases of tumor dissemination after a biopsy have also been reported [17]. Therefore, a biopsy of a possible TET should avoid a transpleural approach. Third, the adult thymus shows involution with fat replacement and is thought to be non-functional for human activity of daily life [38]. In addition, the surgical approach via thymectomy has become less invasive with the recent introduction of VATS and robotic-assisted thoracoscopic surgery [39]. Finally, according to a survey of current practice among members of the European Society of Thoracic Surgeons (ESTS) in 44 centers, 91% of institutions did not routinely confirm the histological diagnosis when thymoma was suspected [15]. This report indicates that many thoracic surgeons with experience agree with resection thymoma without histological confirmation.

In the present study, the 11 patients (8.5%) suspected of having TETs in Group Nonspecific TET underwent resection and were found to have non-TETs. These nodules, which include cystic lesions and MALT lymphomas, are sometimes difficult to distinguish from TETs based solely on radiological findings because of the thick wall around the nodule or the heterogeneous accumulation of FDG in the nodule (Fig. 2). For the six patients with thymic cyst or bronchogenic cyst, in particular, surgical resection was likely unnecessary and resulted in overtreatment. However, Morrissey et al. reported that the diagnostic accuracy of a percutaneous biopsy for a mediastinal mass was 77–94% [32]. If those six patients with cystic non-TETs had undergone a preoperative biopsy, it seemed difficult that they were diagnosed correctly and avoided unnecessary surgical treatment.

There are some limitations associated with our retrospective study. First, the number of study cohorts was not very large, and this study was performed at a single institution. Second, this study did not include patients with mediastinal lymphoma. Those patients underwent only a percutaneous biopsy of the tumor to plan chemotherapy, no surgical resection. Therefore, the clinical features and/or radiological findings of lymphoma in the anterior mediastinum were not examined in this study.

In conclusion, our analysis suggests that 94% of the patients with AMMs suspected of being TETs or non-TETs who underwent complete resection without a biopsy were accurately evaluated according to our diagnostic process. We, therefore, consider the recommendation of the NCCN guideline feasible provided the preoperative information is evaluated properly.

Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest in association with this study.

References

1. Davis RD Jr, Oldham HN Jr, Sabiston DC Jr (1987) Primary cysts and neoplasms of the mediastinum: recent changes in clinical presentation, methods of diagnosis, management, and results. Ann Thorac Surg 44:229–237
2. Oldham HN Jr (1971) Mediastinal tumors and cysts. Ann Thorac Surg 11:246–275
3. Wychulis AR, Payne WS, Clagett OT et al (1971) Surgical treatment of mediastinal tumors: a 40 year experience. J Thorac Cardiovasc Surg 62:379–392
4. Strollo DC, Rosado de Christenson ML, Jett JR (1997) Primary mediastinal tumors. Part 1: tumors of the anterior mediastinum. Chest 112:511–522
5. Marc VG (2006) Mediastinum. In: Jud WG (ed) Diagnostic imaging. Chest, 1st edn. Amirsys Inc, Salt Lake City, pp 1–66
6. Souza CA, Muller NL (2008) Imaging of the mediastinum. In: Patterson GA, Cooper JD, Deslauriers J et al (eds) Pearson's thoracic and esophageal surgery, 3rd edn. Elsevier Inc, Amsterdam, pp 1477–1505
7. Carter BW, Okumura M, Detterbeck FC et al (2014) Approaching the patient with an anterior mediastinal mass: a guide for radiologists. J Thorac Oncol 9:S110–S118
8. Carter BW, Benveniste MF, Madan R et al (2017) ITMIG classification of mediastinal compartments and multidisciplinary approach to mediastinal masses. Radiographics 37:413–436
9. Kondo K, Monden Y (2003) Therapy for thymic epithelial tumors: a clinical study of 1320 patients from Japan. Ann Thorac Surg 76:878–884
10. Nicholson AG, Detterbeck FC, Marino M et al (2014) The IASLC/ITMIG Thymic Epithelial Tumors Staging Project: proposals for the T component for the forthcoming (8th) edition of the TNM classification of malignant tumors. J Thorac Oncol 9:S73–S80
11. Ruffini E, Detterbeck F, Van Raemdonck D et al (2014) Tumours of the thymus: a cohort study of prognostic factors from the European society of thoracic surgeons database. Eur J Cardiothorac Surg 46:361–368
12. Christian Stremmel BP (2015) Mediastinal cysts and duplications. In: Kuzdzal J, Asamura H, Detterbeck F et al (eds) ESTS textbook of thoracic surgery. Medycyna Praktyczna, Cracow, pp 245–255
13. Allen MS (2002) Presentation and management of benign mediastinal teratomas. Chest Surg Clin N Am 12:659–664
14. Yokoi K, Usami N, Kawaguchi K (2015) Mediastinal germ cell tumors. In: Kuzdzal J, Asamura H, Detterbeck F et al (eds) ESTS textbook of thoracic surgery. Medycyna Praktyczna, Cracow, pp 267–307
15. Ruffini E, Van Raemdonck D, Detterbeck F et al (2011) Management of thymic tumors: a survey of current practice among members of the European society of thoracic surgeons. J Thorac Oncol 6:614–623
16. Gupta S, Seaberg K, Wallace MJ et al (2005) Imaging-guided percutaneous biopsy of mediastinal lesions: different approaches and anatomic considerations. Radiographics 25:763–786
17. Kattach H, Hasan S, Clelland C et al (2005) Seeding of stage I thymoma into the chest wall 12 years after needle biopsy. Ann Thorac Surg 79:323–324
18. David SE, Gregory JR, Wallace A (2013) NCCN clinical practice guidelines in oncology (NCCN Guidelines®) thymomas and thymic carcinomas. J Natl Compr Cancer Netw 11:562–576
19. Sasaki M, Kuwabara Y, Ichiya Y et al (1999) Differential diagnosis of thymic tumors using a combination of 11C-methionine PET and FDG PET. J Nucl Med 40:1595–1601
20. Rankin S (2010) [(18)F]2-fluoro-2-deoxy-D-glucose PET/CT in mediastinal masses. Cancer Imaging 10(Spec no A):S156–S160

21. Nakajima J, Okumura M, Yano M et al (2016) Myasthenia gravis with thymic epithelial tumour: a retrospective analysis of a Japanese database. Eur J Cardiothorac Surg 49:1510–1515
22. Bukowski RM, Wolf M, Kulander BG et al (1993) Alternating combination chemotherapy in patients with extragonadal germ cell tumors. A Southwest oncology group study. Cancer 71:2631–2638
23. Nichols CR (1991) Mediastinal germ cell tumors. Clinical features and biologic correlates. Chest 99:472–479
24. Marom EM (2010) Imaging thymoma. J Thorac Oncol 5:S296–S303
25. Inagaki H, Chan JK, Ng JW et al (2002) Primary thymic extranodal marginal-zone B-cell lymphoma of mucosa-associated lymphoid tissue type exhibits distinctive clinicopathological and molecular features. Am J Pathol 160:1435–1443
26. Nakajima J, Murakawa T, Fukami T et al (2008) Postthymectomy myasthenia gravis: relationship with thymoma and antiacetylcholine receptor antibody. Ann Thorac Surg 86:941–945
27. Lee KS, Im JG, Han CH et al (1989) Malignant primary germ cell tumors of the mediastinum: CT features. Am J Roentgenol 153:947–951
28. Yamada Y, Yoshino I, Nakajima J et al (2015) Surgical outcomes of patients with stage III thymoma in the Japanese nationwide database. Ann Thorac Surg 100:961–967
29. Kim ES, Putnam JB, Komaki R et al (2004) Phase II study of a multidisciplinary approach with induction chemotherapy, followed by surgical resection, radiation therapy, and consolidation chemotherapy for unresectable malignant thymomas: final report. Lung Cancer 44:369–379
30. Travis WD, Brambilla E, Burke AP et al (2015) WHO classification of tumors of the lung, pleura, thymus and heart, 4th edn. IARC press, Lyon
31. Koga K, Matsuno Y, Noguchi M et al (1994) A review of 79 thymomas: modification of staging system and reappraisal of conventional division into invasive and non-invasive thymoma. Pathol Int 44:359–367
32. Morrissey B, Adams H, Gibbs AR et al (1993) Percutaneous needle biopsy of the mediastinum: review of 94 procedures. Thorax 48:632–637
33. Wright CD, Kesler KA, Nichols CR et al (1990) Primary mediastinal nonseminomatous germ cell tumors. Results of a multimodality approach. J Thorac Cardiovasc Surg 99:210–217
34. Bokemeyer C, Nichols CR, Droz JP et al (2002) Extragonadal germ cell tumors of the mediastinum and retroperitoneum: results from an international analysis. J Clin Oncol 20:1864–1873
35. Lemarie E, Assouline PS, Diot P et al (1992) Primary mediastinal germ cell tumors. Results of a French retrospective study. Chest 102:1477–1483
36. Kesler KA, Rieger KM, Ganjoo KN et al (1999) Primary mediastinal nonseminomatous germ cell tumors: the influence of postchemotherapy pathology on long-term survival after surgery. J Thorac Cardiovasc Surg 118:692–700
37. Travaini LL, Petralia G, Trifiro G et al (2008) [18F]FDG positron emission tomography/computed tomography and multidetector computed tomography roles in thymic lesion treatment planning. Lung Cancer 61:362–368
38. Shimosato Y, Mukai K, Matsuno Y (2010) Tumors of the mediastinum. In: Steven GS, William AG, Leslie HS et al (eds) AFIP atlas of tumor pathology, 4th edn. American Registry of Pathology, Washington, DC, pp 16–18
39. Augustin F, Schmid T, Sieb M et al (2008) Video-assisted thoracoscopic surgery versus robotic-assisted thoracoscopic surgery thymectomy. Ann Thorac Surg 85:S768–S771