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Ectopic Middle Mediastinal Thymoma: A Rare Case Report and Review of the Literature

Masayuki Sato[1], Hirofumi Nakayama[1], Yoshihiko Fukukura[1], Masayuki Nakajo[1], Toshiyuki Nagata[2], Kazuhiro Tabata[3]

Departments of Radiology[1], General thoracic surgery[2], and Human pathology[3], Kagoshima University Graduate School of Medical and Dental Sciences

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Abstract

We report a case of ectopic middle mediastinal thymoma in an asymptomatic 50-year-old woman.Chest X-ray, CT, MRI and FDG-PET/CT examinations were performed preoperatively. The tumor was removed by video-assisted thoracic surgery, and the pathological diagnosis was type B3 thymoma of the World Health Organization classification and stage II thymoma of the Masaoka clinical staging system.Postoperatively, she received adjuvant radiotherapy of 50 Gy. Ectopic middle mediastinal thymomas are extremely rare with only nine previous case reports. This is the first case of type B3 ectopic middle mediastinal thymoma. Imaging features of our ectopic middle mediastinal thymoma was similar to the usual thymomas in the antero-superior mediastinum except for its very rare location.

Key words: ectopic thymoma, middle mediastinum, CT, MRI, PET/CT

Introduction

Thymomas are the most common neoplasm of the anterior mediastinum. However, they are also known to arise in ectopic locations including the neck, middle or posterior mediastinum, the lung, base of the skull and the pleural cavity[1–9]. Especially, ectopic middle mediastinal thymomas are extremely rare with only 9 previous cases reported in the English literature[1–9]. We report a case of an asymptomatic female with an ectopic middle mediastinal thymoma with review of the literature.

Case Report

A 50–year–old woman was referred to our hospital for further examinations of a mediastinal mass detected on a chest X–ray film during a medical check–up. She denied a history of any disease except middle ear cholesteatoma which was removed 12 years earlier. She had no clinical symptoms, and physical examinations were normal. The results of laboratory data were within normal limits including serum levels of tumor markers (CEA, SCC, NSE, and IL–2R) and acetylcholine receptor antibody.

Chest X–ray revealed a protruding mass on the right side of the mediastinum (Fig. 1). Unenhanced chest CT revealed a solitary lobulated tumor of heterogeneous soft tissue attenuation measuring 3.8×2.5 cm without calcification in the middle mediastinum (Fig. 2a). Contrast enhanced CT revealed the tumor with heterogeneous gradual enhancement at 30, 70 and 300 seconds after injection of contrast medium with focal low attenuation areas, reflecting cystic formation (Fig. 2b–d). The fat plane was not clear between the tumor and the anterior aspect of the trachea to the right main bronchus, posterior aspect of the superior vena cava (SVC), and lateral aspect of the azygos vein. Mild compression of the

Corresponding author: Dr. Masayuki Sato
Department of Radiology, Kagoshima University Graduate School of Medical and Dental Sciences, 8-35-1 Sakuragaoka, Kagoshima-city 890-8544, Japan
Telephone: +81-99-275-5417
Fax: +81-99-265-1106
E-mail: m-satou@m.kufm.kagoshima-u.ac.jp

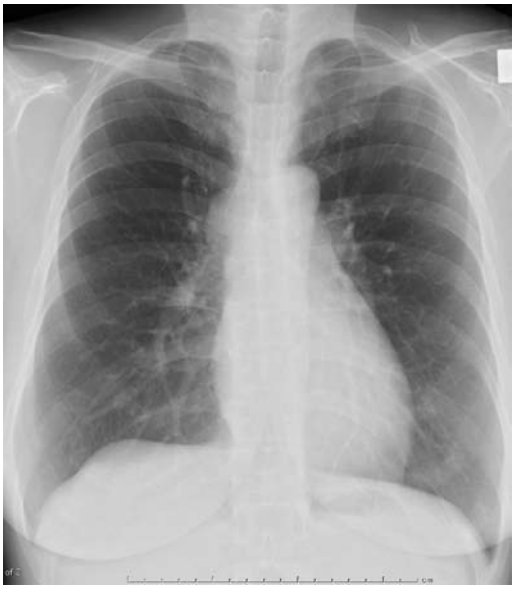

Fig. 1. Posteroanterior chest radiograph shows a protruding mass on the right side of the mediastinum

SVC and azygos vein by the tumor was also noted. Chest magnetic resonance (MR) images were also performed (Fig. 3a–c).The tumor showed low signal intensity similar to muscle on T1–weighted images and relatively high signal intensity on T2–weighted images. The tumor had foci of high intensity suggesting cystic formation, and linear low intensities suggesting fibrous septa on T2–weighted images. However, CT and MR examinations did not reveal fibrous capsule of the tumor and mediastinal invasion. ^{18}F–fluoro–deoxyglucose positron emission tomography (FDG–PET) study demonstrated FDG uptake in the tumor with a maximum standardized uptake value (SUV max) of 3.3 at 60 min and 2.8 at 120 min after injection (Fig. 4).

We made a preoperative diagnosis of a benign middle mediastinal tumor, and video–assisted thoracic surgery was performed to remove it. The tumor was surrounded by the SVC, azygos vein, trachea and its bifurcation with

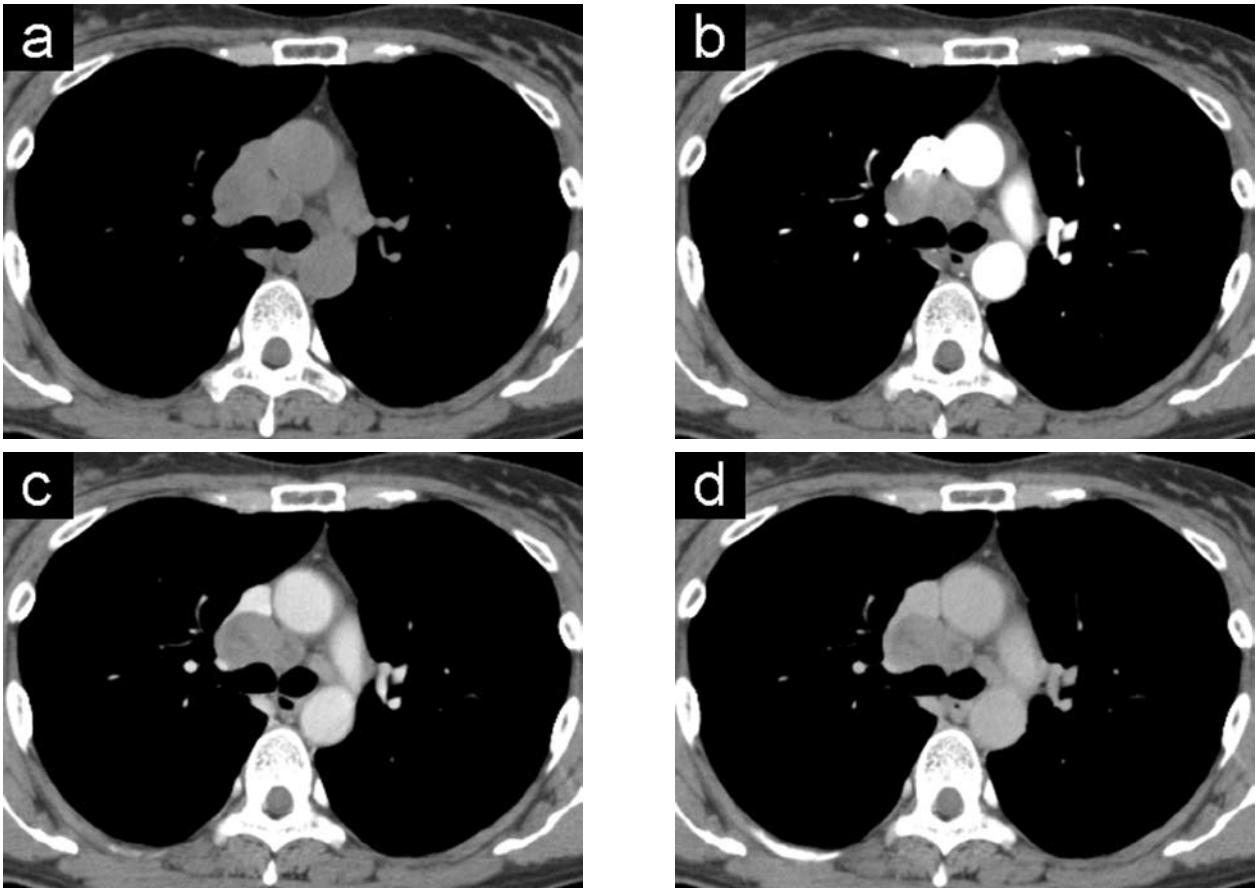

Fig. 2. Unenhanced chest CT (a) shows a solitary lobulated mass with heterogeneous soft tissue attenuation in the middle mediastinum. The tumor is surrounded by the SVC, azygos vein and bifurcation of the trachea.Post-contrast 30 seconds (b), 70 seconds(c) and 300 seconds (d) enhanced images show heterogeneous gradual enhancement with focal low attenuation areas.

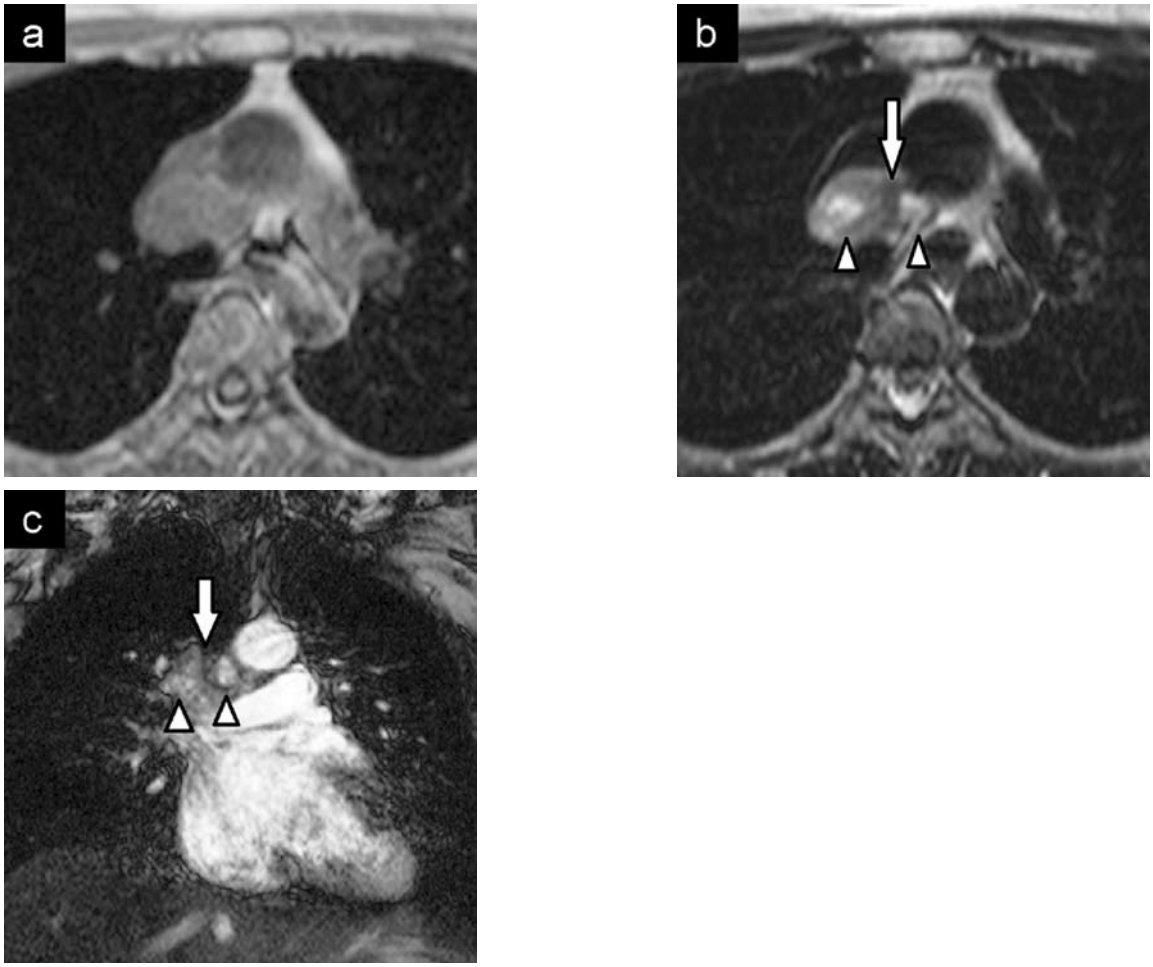

Fig. 3. The tumor shows low signal intensity similar to muscle on T1-weighted image (a) and relatively high signal intensity on T2-weighted images (b). It has foci with high intensity suggesting cystic formation (arrowheads), and linear low intensities (arrows)suggesting fibrous septa on both T2-weighted axial (b) and fat saturation T2-weighted coronal (c) images.

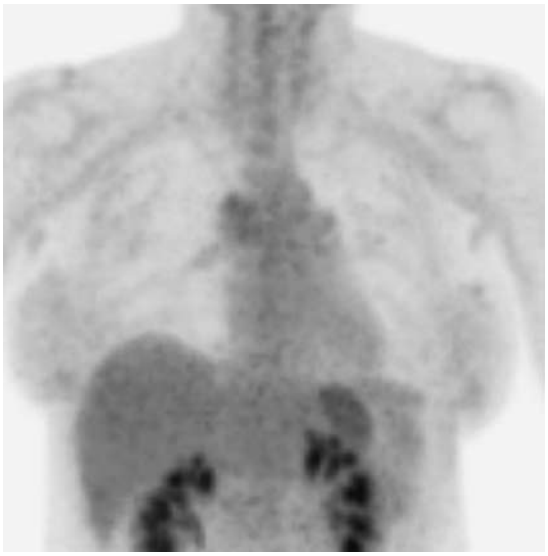

Fig. 4. FDG-PET study shows moderate FDG uptake in the tumor.

partly dense adherence to surrounding connective tissue. Maroscopic findings of the resected specimen showed a dark–red and yellowish–white tumor measuring 4.0×3.5×1.8 cm, consisted of cystic and solid components with a partial fibrous capsule.

Histologically, the tumor showed expanding lobular growth pattern with fibrous septa. The tumor cells were partially infiltrating into surrounding connective tissue, but further invasion was not observed (Fig. 5a). The predominantly observed tumor cells were medium–sized polygonal epithelial cells with mild atypia. There were a small number of intraepithelial lymphocytes (Fig. 5b). Immunohistochemical examinations revealed the epithelial cells were diffusely positive for AE1/3 and CAM5.2, and partially positive for EMA, but negative for CD5, CD56, chromogranin, and TTF–1. Infiltrating lymphocytes were positive for CD5 (Fig. 5c). MIB–

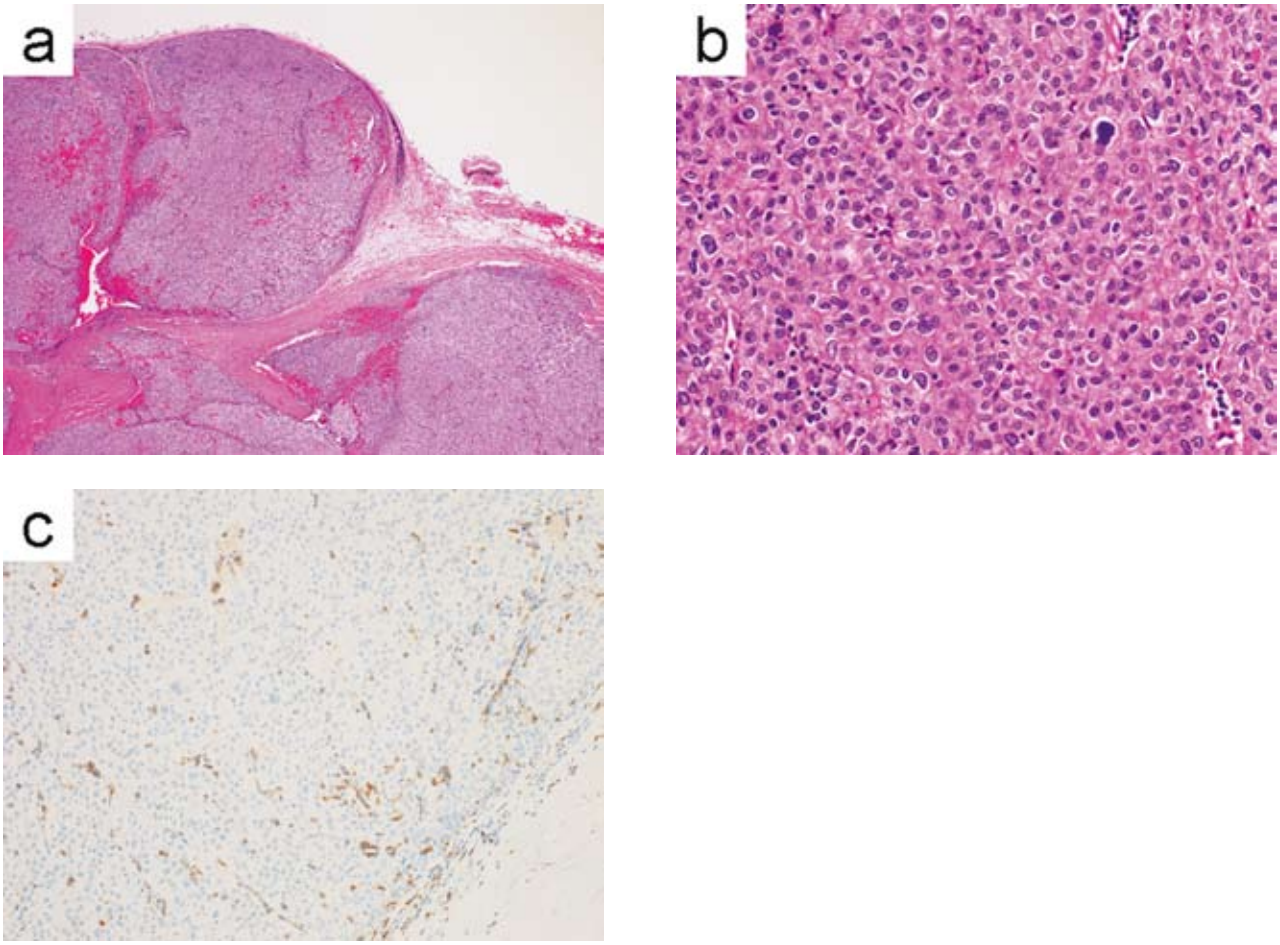

Fig. 5. The tumor shows expanding lobular growth pattern with fibrous septa. The tumor cells are infiltrating into surrounding connective tissue (a: H&E stain, 2×). The predominantly observed tumor cells are medium-sized polygonal epithelial cells with mild atypia. There are a small number of intraepithelial lymphocytes (b: H&E stain, 20×). CD5 staining shows positivity for infiltrating lymphocytes (c: Immunohistochemical staining for CD5, 10×).

1 labeling index was 8%. The pathological diagnosis was type B3 thymoma defined by the World Health Organization classification[10], and stage II in the Masaoka clinical staging system[11].

Postoperatively, she received adjuvant radiotherapy of 50 Gy. She is alive and well with no recurrence 12 months after surgical excision.

Discussion

Embryologically, thymic epithelium arises bilaterally from the third and probably fourth bronchial pouches and migrates into the antero–superior mediastinum[12]. Ectopic occurrence of thymoma results from failure of this migration. According to previous reports[13], ectopic thymic tissue may be present in the retro–innominate–vein area, and adipose tissue surrounding the thymus which occasionally contains some thymic tissue, often has continuity with pleural or hilar adipose tissue. Thus, it is possible for thymoma to be located in the middle mediastinum.

Ectopic middle mediastinal thymomas are extremely rare. To date, only 10 patients including the present case have been reported since the first report by Kojima et al. in 2002[1]. Details of these cases and the present case are shown in Table 1. These 10 patients were 6 women and 4 men with a mean age of 60 years (range, 47 to 71 years). Two patients had clinical symptoms: one had precordial discomfort and the other had left chest pain with unproductive cough and shortness of breath. One patient had myasthenia gravis. The mean size of tumors was 6.7 cm (range, 3.5 to 10.0 cm). Histologically, the tumors were diagnosed as type A thymoma in 2 patients, type AB in 6, and one was rare histological

Table 1. Previous reports of ectopic middle mediastinal thymoma (from Refs. 1-9) and the present report

Reference	Age/ Gender	Symptoms	Size (cm)	Type/ Stage	Radiotherapy/ Dose	Image/ Findings
Kojima K et al. 2002[1]	60/F	Nil	5.5×3.5×2.8	AB/ II	(＋)/50 Gy	CT/Heterogeneously enhanced mass MR/T1 low, T2 high
Minnti S et al. 2004[2]	53/M	No symptoms Myasthenia gravis(+)	7	AB/ Unknown	Unknown	CT/Soft tissue mass MR/T1 intermediate
Kanzaki M et al. 2004[3]	60/F	Nil	6.0×5.5×4.1	AB/ I	(－)	CT/Heterogeneously enhanced mass, and calcification MR/T1 low, T2 slightly high mass
Venavaga K et al. 2005[4]	47/M	Left chest pain Unproductive cough Shortness of breath	10×7.5×7	AB/ II	(＋)/Unknown	CT
Kuzdzal J et al. 2006[5]	69/F	Nil	10×10×7	Metastatic thymoma/ Unknown	(－)	CT
Nakamura H et al. 2007[6]	69/F	Precordial discomfort	7.5×4.8×3.2	A/ I	(－)	CT MR/Heterogeneous mass
Huang TW et al. 2007[7]	71/F	Nil	7×6×4	A/ I	(－)	CT/Soft tissue density mass
Sakurai H et al. 2009[8]	61/M	Nil	3.5	AB/ I	(－)	CT/Soft tissue density mass MR/T1 iso and T2 low mass, and septal enhancement ^{18}F-FDG PET/Slightly positive mass ^{11}C-acetate PET/Highly positive mass
Shikada Y et al. 2012[9]	56/M	Nil	6.5×4.5×3.5	AB/ II	(＋)/50 Gy	CT/Solid and uniform mass, and slight enhancement MR/T1 iso and T2 heterogenous mass, and slight enhancement
Present case 2012	50/F	Nil	4.0×3.5×1.8	B3/ II	(＋)/50 Gy	CT/Soft tissue density and heterogeneously enhanced mass MR/ T1 low, T2 relatively high and, heterogeneously enhanced mass ^{18}F-FDG PET/Moderately positive mass

type (metaplastic thymoma) according to the WHO histological criteria. The present case was type B3 thymoma, which was the first case of type B thymoma. The tumor stage according to the Masaoka classification was stage I in 4 cases, stage II in 4, and the other two cases were unknown. Four patients of stage II disease received postoperative radiotherapy.

In general, thymomas present as sharply demarcated round or oval soft tissue attenuation masses with mild to moderate contrast enhancement on CT[14]. Occasionally, focal low attenuation areas are identified within tumors reflecting hemorrhage, necrosis, or cyst formation. Rarely, thymomas appear entirely cystic lesions. Linear or ring–like calcifications are occasionally seen in any types. On MR images, thymomas typically appear as round, oval, or lobulated masses with low signal intensity similar to muscle on T1–weighted images, and relatively high signal intensity on T2–weighted images. T2–weighted images occasionally show scattered high signal intensity areas and lobulated internal architectures within the tumors, which correspond to cystic portions and fibrous septa, respectively. On T1–weighted images, the signal intensity of the cystic regions was variable, depending on protein content of the cyst fluid or the presence of hemorrhage. According to the report by Tomiyama et al.[15], the smooth contour and round shape are most suggestive of type A thymoma, the irregular contour is most suggestive of thymic carcinoma, and calcification is suggestive of type B thymoma, but CT is of limited value in differentiation among type AB, B1, B2, and B3 thymomas. Sadohara et al.[16] have reported that the irregular contour, necrosis, cystic component, heterogeneous enhancement, lymphadenopathy and great vessel invasion are strongly

suggestive of thymic carcinomas on CT or MR imaging. The findings of smooth contour, complete or almost complete capsule, presence of septum, and homogenous enhancement on MR imaging are helpful in distinguishing low–risk (type A, AB, and B1) thymomas from high–risk (type B2 and B3) thymomas or thymic carcinomas. On PET images, the usefulness of FDG uptake for predicting the malignant nature of thymic epithelial tumors was reported[17].

Review of the 9 reported cases shows that, there are no definite imaging findings of ectopic mediastinal thymoma. CT study was performed in all cases, and the tumors were showed as soft tissue density masses. Contrast effect was heterogeneous enhancement (2 cases) or slight enhancement (1 case). Calcification was seen in one case. MR study was performed in 5 cases. The tumors showed low to intermediate intensity on T1–weighted images, and low to high intensity on T2–weighted images. Heterogeneity (2 cases) and septal enhancement (1 case) were also seen. PET study was performed in only one case. PET using FDG and ^{11}C–acetate showed slightly positive FDG uptake and highly positive acetate uptake in the lesion. Imaging findings of all reported ectopic middle mediastinal thymomas including the present case were similar to those of the antero–superior mediastinal thymomas.

Differential diagnosis of middle mediastinal masses includes lymphadenopathy (malignant lymphoma, sarcoidosis, Castleman's disease, and metastasis), aortic arch aneurysm, enlarged pulmonary artery, foregut duplication cysts (bronchogenic, esophageal, and neurenteric), pericardial cyst and tracheal lesions. Neurogenic tumors and mediastinal goiters can also occur in the middle mediastinum[18].

In conclusion, thymomas can arise in the middle mediastinum. The imaging features of ectopic middle mediastinal thymomas may be similar to those of the usual antero–superior mediastinal thymomas. Although extremely rare, they should be included in the differential diagnosis of middle mediastinal tumors.

References

1) Kojima K, Yokoi K, Matsuguma H, Kondo T, Kamiyama Y, Mori K, et al. Middle mediastinal thymoma. J Thorac Cardiovasc Surg 2002; 124: 639–640.

2) Minniti S, Valentini M, Pinali L, Malago R, Lestani M, Procacci C.Thymic masses of the middle mediastinum. J Thorac Imaging 2004; 19: 192–195.

3) Kanzaki M, Oyama K, Ikeda T, Yoshida T, Murasugi M, Onuki T.Noninvasive thymoma in the middle mediastinum. Ann Thorac Surg 2004; 77: 209–210.

4) Venayaga K, Ooi JS, Shabir B. A rare case of middle mediastinal thymoma mimicking left lower lobe lung tumor. Med J Malaysia 2005; 60: 508–510.

5) Kużdżal J, Zieliński M, Papla B, Szlubowski A. Middle mediastinal thymoma of unusual pathologic type. Ann Thorac Cardiovasc Surg 2006; 12: 200–202.

6) Nakamura H, Adachi Y, Fujioka S, Miwa K, Haruki T, Taniguchi Y. Thoracoscopic resection of middle mediastinal noninvasive thymoma: report of a case. Surg Today 2007; 37: 787–789.

7) Huang TW, Cheng YL, Tzao C, Chang H, Tsai WC, Lee SC. Middle mediastinal thymoma. Respirology 2007; 12: 934–936.

8) Sakurai H, Kaji M, Suemasu K. Thymoma of the middle mediastinum: ^{11}C–acetate positron emission tomography imaging. Ann Thorac Surg 2009; 87: 1271–1274.

9) Shikada Y, Katsura M, Takenaka T, Takeo S. A case of middle mediastinal thymoma. Gen Thorac Cardiovasc Surg 2012; 60: 664–667.

10) Travis WD, Brambilla E, Müller–Hermelink HK, Harris CC. WHO classification of tumors. Pathology and genetics of tumors of the lung, pleura, thymus and heart. Lyon: IARC Press; 2004.

11) Masaoka A, Monden Y, Nakahara K, Tanioka T. Follow–up study of thymomas with special reference to their clinical stages. Cancer 1981; 48: 2485–2492.

12) Shimosato Y, Mukai K, Matsuno Y. Anatomy and anatomic compartments of the mediastinum. In: Silverberg SG, editor. Tumors of the mediastinum, AFIP atlas of tumor pathology, 4th Series Fascicle 11. Washington, DC: Armed Forces Institute of Pathology; 2010. pp.1–18.

13) Ashour M. Prevalence of ectopic thymic tissues in myasthenia gravis and its clinical significance. J Thorac Cardiovasc Surg 1995; 109: 632–635.

14) Takahashi K, Al–Janabi NJ.Computed tomography and magnetic resonance imaging of mediastinal tumors. J Magn Reson Imaging 2010; 32: 1325–1339.

15) Tomiyama N, Johkoh T, Mihara N, Honda O, Kozuka T, Koyama M, et al. Using the World Health Organization classification of thymic epithelial neoplasms to describe CT findings. AJR 2002; 179:

881–886.

16) Sadohara J, Fujimoto K, Muller NL, Kato S, Takamori S, Ohkuma K, et al. Thymic epithelial tumors: comparison of CT and MR imaging findings of low–risk thymomas, high–risk thymomas, and thymic carcinomas. Eur J Radiol 2006; 60: 70–79.

17) Endo M, Nakagawa K, Ohde Y, Okumura T, Kondo H, Igawa S, et al. Utility of ^{18}FDG–PET for differentiating the grade of malignancy in thymic epithelial tumors. Lung Cancer 2008; 61: 350–355.

18) Whitten CR, Khan S, Munneke GJ, Grubnic S. A diagnostic approach to mediastinal abnormalities. Radio Graphics 2007; 27: 657–671.

中縦隔原発の異所性胸腺腫の一例

佐藤昌之[1)]，中山博史[1)]，福倉良彦[1)]，中條政敬[1)]，永田俊行[2)]，田畑和宏[3)]

[1)] 大学院医歯学総合研究科　先進治療科学専攻　腫瘍学講座　放射線診断治療学,
[2)] 同循環器・呼吸器病学講座　呼吸器外科学, [3)] 同腫瘍学講座　人体がん病理学

稀な中縦隔原発異所性胸腺腫の一例を経験したので，文献的考察を加えて報告する．症例は無症状の50歳代女性で，検診時の胸部X線写真にて異常が指摘され，精査加療目的に紹介受診された．術前にCT，MRI，FDG-PET/CTによる精査が施行された．胸腔鏡下手術（VATS）が施行され，WHO分類type B3，正岡病期分類Ⅱ期の異所性胸腺腫の最終診断となった．術後には50 Gyの放射線治療が追加された．過去の文献では中縦隔原発異所性胸腺腫は９例の英文報告があるのみで，type B3 胸腺腫の報告はない．存在部位は非常に稀であるが，本症例を含め，画像的な特徴は通常の前縦隔原発の胸腺腫と同様であった．