

CT and MRI findings of thymic carcinoid

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Abstract

Objectives: To evaluate the computed tomography (CT) and magnetic resonance imaging (MRI) findings of thymic carcinoid and to compare these findings with previously published findings of thymoma.

Methods: Eleven cases of pathologically proven thymic carcinoid were reviewed retrospectively. Three patients had typical carcinoid and eight patients had atypical carcinoid. The characteristics of the tumours and related thoracic abnormalities were assessed in each case on CT and/or MRI by two chest radiologists. The final decisions on the findings were reached by consensus.

Results: Thymic carcinoids were more likely to have a large mass (ranging from 18-105 mm), irregular contours (n = 8), heterogeneous intensity on T2-weighted images (n = 6; 8 patients undergone MRI), heterogeneous enhancement (n = 9), and local invasion (n = 7). A necrotic or cystic component was identified in seven patients (one typical carcinoid, six atypical carcinoids). Lymphadenopathy was seen in four patients. Septum, capsule, haemorrhage, and calcification were seen in three, two, two, and one patients, respectively, with atypical carcinoid.

Conclusions: Thymic carcinoids tend to have a high prevalence of large masses, irregular contours, heterogeneous intensity on T2-weighted images, heterogeneous enhancement, and local invasion on CT and/or MRI. A necrotic or cystic component is often seen in atypical carcinoid.

Advances in knowledge: Radiologic features of thymic carcinoid mimic those of high-risk thymomas and/or thymic carcinomas.

1. Introduction

Thymic neuroendocrine tumours (NETs) are rare, constituting approximately 2-5% of all thymic epithelial tumours. Thymic carcinoids often behave aggressively, and present as advanced disease due to the invasion of adjacent mediastinal structures, local recurrence, or metastases [1]. Images of thymic carcinoids usually demonstrate a large anterior mediastinal mass. Although only a few reports describing the imaging features of thymic carcinoid have been published, these lesions have been described as masses indistinguishable from thymomas [2, 3].

The aim of our study was to evaluate the CT and MRI findings of thymic carcinoids and to compare these findings with previously published findings of thymomas.

2. Materials and methods

2.1. Patients

Our retrospective multicentre study was approved by our institutional review board (Nagasaki University Hospital), and the requirement for written informed consent was waived. Patient characteristics are shown in TABLE 1. Images were available for retrospective review in eleven patients with thymic carcinoids who underwent CT and/or MRI examinations of the chest at four institutions on a variety of scanners as part of patient evaluations between June 1991 and September 2011. Two of the eleven patients (cases 1 and 2) were diagnosed at biopsy, and the remaining nine patients were diagnosed by thymothymectomy. These eleven patients were comprised of nine men and two women, whose ages ranged from 29 to 71 years (mean, 53.5 years). In six

patients, the presence of thymic carcinoid was discovered incidentally during routine chest radiography. One of the six patients (case 1) had a symptom of hoarseness. In case 3, thymic carcinoid was discovered based on clinical symptoms such as mental disorder and oedema associated with Cushing's syndrome, and had been examined for the presence of an ectopic adrenocorticotrophic hormone (ACTH)-producing tumour. In two patients (cases 9 and 10), the tumour was discovered by an examination performed for chest pain, and in one of them (case 10), serum ACTH level was elevated. In one patient (case 8), thymic carcinoid and spinal metastases were detected on chest CT and lumbar spine MRI during the examination for back pain. The remaining one patient with multiple endocrine neoplasia type 1 (MEN1) (case 11) had a history of surgery for pancreatic insulinoma and parathyroid tumour. The thymic carcinoid was discovered by CT examination when he developed a recurrence in the head of the pancreas and liver metastasis. The patient reported numbness in the lower extremities. During the follow-up period, six patients died due to metastasis and/or local recurrence; three were alive without recurrence; one developed a recurrence, but the status of this patient is unknown, because there has been no data available for the past several years; and one patient died by suicide without local recurrence after 1.2 years of follow-up.

2.2. Image acquisition and analysis

All patients underwent pre-contrast-enhanced and contrast-enhanced CT scans. The CT images were obtained using a variety of CT scanners, from conventional CT to 64-detector row CT. The CT scans consisted of 1-10 mm collimation sections. Eight

patients underwent MRI examinations, and contrast-enhanced MRI were performed in seven patients. MR images were obtained using 1.5-T MR imaging systems on a variety of scanners.

The CT and MR scans were reviewed retrospectively by two chest radiologists, and the final decisions on the findings were reached by consensus. The imaging findings were assessed on the basis of a previous study by Sadohara et al. [4]. On each pre-contrast-enhanced CT and MRI scan, the size (the longest axis diameter), contour, and internal characteristics of the tumour such as the capsule's perimeter, septum, the presence of haemorrhage, a necrotic or cystic component, and homogeneity were assessed. The presence of calcification within the tumour was evaluated only on pre-contrast-enhanced CT; it was not evaluated on MRI because of its variable signal characteristics [4, 5]. The pattern and degree of tumour enhancement on contrast-enhanced images were also evaluated. In addition, the presence of mediastinal lymphadenopathy, pleural effusion, local invasion (including invasion of the mediastinal fat, lungs, and great vessels), and distant metastases were assessed.

The margins of the tumours were categorized into three types, smooth, lobulated, or irregular. A capsule was judged as present when a low- or high-attenuation rim or a low-intensity rim surrounding the tumour was observed on CT or MRI, respectively. The perimeter of capsule was classified into two types, "almost complete capsule" (visible for more than two-thirds of the tumour perimeter) and "partially visualized capsule" (less than two-thirds of the tumour perimeter). Haemorrhage was hypothesised to be present when an unenhanced area and/or a high attenuation area within the tumour

was seen on non-contrast-enhanced CT, and when a non-enhanced area and/or a high signal intensity area was seen on both T1- and T2-weighted MR images. A necrotic or cystic component was assumed to be present when a low attenuation area was seen within the tumour on CT, or when a non-enhanced area and/or a low signal intensity area was seen on T1-weighted image and a high signal intensity area was seen on T2-weighted image. In terms of the tumour homogeneity, we evaluated whether the tumour was homogeneous or heterogeneous on CT and MR images. The degree of enhancement of the tumour was assessed by visual judgment as less than, equal to, or higher than that of the chest wall muscle.

Tumour vessels were defined as irregularly dilated and tortuous vessels on contrast-enhanced CT and MRI or a signal void on T2-weighted images. Mediastinal lymphadenopathy was considered to be present when the short axis diameter of the lymph nodes was 10 mm or greater. Tumour invasion of the great vessels was judged to be present when the tumour was in contact with them and altered their contour, or when tumour thrombosis and vascular occlusion were seen on CT [4, 6]. In addition, tumour invasion was considered to be present when the vessel wall signal was interrupted or obliterated by the tumour on MR images [4, 7].

If there were differences in the internal characteristics of the tumour between CT and MRI, we used the MR findings for the final decision because MR imaging provides tissue contrast superior to that obtained with CT [8].

3. Results

The tumour size (the longest diameters) and histopathological type in all patients are shown in TABLE 1. The sizes of the thymic carcinoids ranged from 18-105 mm (FIGURES 1-3), and four of them were less than 25 mm in diameter. The tumour in case 3 (FIGURE 1), which was associated with Cushing's syndrome, was 18 mm in diameter. In case 6, a thymic carcinoid measuring 19 mm was located close to a large thymic cyst that was discovered on a chest radiograph. In case 9, the preoperative tumour size was 22 mm in diameter. The tumour in case 11, which was associated with MEN1, was 20 mm in diameter. The remaining seven tumours were larger than 50 mm in diameter. All three patients with typical carcinoid (TC) were men, aged 59 to 71 years (mean, 65.7 years). Six of the eight patients with atypical carcinoid (AC) were men, and together with the two women, they ranged in age from 29 to 69 years (mean, 49.0 years).

The relationship between the CT and MRI findings and the simplified WHO histological classification is shown in TABLE 2. As mentioned above, if there were differences in the internal characteristics of the tumour between CT and MR imaging, we used the MR findings for the final decision. The overall imaging findings are shown in TABLE 2. In our study, thymic carcinoids had irregular contours in two TC and six AC cases. An almost complete capsule was seen in one AC and a partially visualized capsule was seen in another AC (FIGURE 2); the others had no capsule. Septa were seen in three ACs (FIGURES 2, 3). Haemorrhage was present in two ACs (FIGURE 2). Calcification was seen in one AC.

Thymic carcinoids had a high prevalence of heterogeneity on T2-weighted images

(two of the three TCs underwent MRI and four of the five ACs underwent MRI) and post-contrast-enhanced CT or MRI (two TCs and seven ACs) (FIGURES 1-3). The tumours tended to be more enhanced than the chest wall muscle. All TCs and seven of the eight ACs showed higher enhancement than that of muscle on CT and/or MRI (FIGURES 1-3). Tumour vessels on contrast-enhanced CT and MRI and a signal void on T2-weighted images were seen in one TC and one AC case (FIGURE 3), which showed a high degree of enhancement on contrast-enhanced CT and MRI. A necrotic or cystic component was seen in one TC and six ACs (FIGURES 1, 3). Two ACs (cases 2 and 7; FIGURE 2) had a reticular septum within a rich haemorrhagic component.

ACs had a high prevalence of local invasion (six of the eight ACs) (FIGURES 2, 3), infiltrating the mediastinal fat, lungs, and great vessels. The size of all tumours with local invasion was 50 mm or more. Lymphadenopathy was seen in one TC case and in three AC cases (FIGURE 2). Two AC cases had distant metastases, and one of them had lymphadenopathy.

4. Discussion

Thymic NETs are epithelial tumours of the thymus gland that are predominantly or exclusively composed of neuroendocrine cells, which can be shown using immunohistochemical staining [1]. Thymic NETs are rare, constituting 2-5% of all thymic epithelial tumours. In the latest classification of the WHO, the NETs of the thymus are classified into two major categories: well differentiated neuroendocrine tumours comprising typical carcinoid (TC) and atypical carcinoid (AC), and poorly

differentiated neuroendocrine tumours comprising large cell carcinoma and small cell carcinoma [1,9]. The majority of thymic NETs are AC cases. Epidemiological data on TCs are lacking. ACs are mainly tumours of adults (18–82 years; mean 48-55 years in both men and women), and there is a male predominance (M:F = 2-7:1) [9]. In our study, two of the eight patients with AC were women, and the mean age of all AC patients was 49.0 years.

Approximately 50% of patients with thymic carcinoid have endocrine abnormalities, most commonly Cushing's syndrome, due to ectopic ACTH production or MEN syndrome, specifically type 1 MEN [10]. In this study, there were four patients who had endocrine abnormalities; two had type 1 MEN, one had Cushing's syndrome, and another had an elevated serum ACTH level.

Thymic carcinoids often behave aggressively, presenting as advanced disease due to the invasion of adjacent mediastinal structures, local recurrence, or metastases [1, 2]. The prognosis of patients with thymic carcinoids is poor [2]. In our study, seven patients had local invasion, four had lymphadenopathy, and two had distant metastasis at the time of presentation. After surgery or chemotherapy/radiotherapy, new distant metastasis appeared in four patients, and local recurrence developed in two patients.

Some patients with occult or early thymic carcinoids have normal findings on chest radiographs [2, 11, 12]. These individuals may present with clinical evidence of ectopic ACTH production. CT, MRI, and nuclear medicine imaging may be helpful for evaluating these patients (with occult, hormonally active lesions) [2, 11, 12], as seen in case 3 in our study. The lesions in patients with Cushing's syndrome and occult lesions

tended to be smaller in this study. On the other hand, we think that the patients with an incidental thymic mass that was not suspected to be a thymic carcinoid do not need to have biochemical profiling or nuclear medicine imaging.

Restrepo et al. [3] reported that thymic carcinoid was seen as an irregular soft tissue mediastinal mass with heterogeneous enhancement on contrast-enhanced CT, which may present with calcifications or invade surrounding normal structures. Rosado de Christenson et al. [2] reported the presence of sharp margins, lobular contours, calcification, mediastinal invasion, and distant metastases on CT imaging as a feature of thymic carcinoid. To our knowledge, there have only been a few reports of the MR findings of thymic carcinoid. A few case reports showed that the MR signal was hypointense on T1-weighted images [13, 14] and hyperintense on T2-weighted images [13]. In our study, thymic carcinoids tended to present as a large mass (1 TC and 6 ACs were larger than 5 cm), irregular contours (2 TCs and 6 ACs), no capsule (3 TCs and 6 ACs), local invasion (1 TC and 6 ACs), and a necrotic or cystic component (1 TC and 6 ACs) on CT or MR imaging. A reticular septum within a rich haemorrhagic component, which was seen in two ACs, seems to be characteristic of AC. Thymic carcinoids appeared to have heterogeneous intensity on T2-weighted images (two of the three TCs underwent MRI and four of the five ACs underwent MRI), and heterogeneous enhancement on CT or MR imaging (2 TCs and 7 ACs). T2-weighted MR imaging was superior to pre-contrast-enhanced CT in the depiction of the internal heterogeneity of the tumour. Razek et al. [15] and Gumustas et al. [16] reported that the mean apparent diffusion coefficient (ADC) of malignant mediastinal masses was significantly lower

than that of benign mediastinal masses. They also mentioned that cystic or necrotic parts interfered with ADC value. In our study, thymic carcinoids tended to have a necrotic or cystic component. In addition, two ACs contained large amounts of haemorrhage. Therefore, we think that it is difficult to evaluate ADC value in thymic carcinoid accurately.

Thymoma or thymic carcinoma is an important disease that should be included as a differential diagnosis of thymic carcinoid. The large size of the tumour and necrotic foci are common characteristics shared between carcinoids and invasive thymomas [3, 17]. The frequency of heterogeneous intensity on T2-weighted images increases from type A tumours to thymic carcinomas [18]. Tomiyama et al. [19] reported that heterogeneous enhancement was present significantly more often in patients with type B3 thymoma and in those with carcinoma. On CT, the thymic carcinomas appear as a large mass with irregular margins with areas of low attenuation related to necrosis, haemorrhage, or cystic degeneration [3]. Sadohara et al. [4] reported that the presence of irregular contours, a necrotic or cystic component, heterogeneous enhancement, lymphadenopathy, and great vessel invasion on CT or MR imaging were strongly suggestive of thymic carcinomas. They also reported that the tumours showing smooth contours, an almost complete capsule, the presence of a septum, and homogeneous enhancement were more likely to be low-risk thymomas (types A, AB, or B1) rather than high-risk thymomas (types B2 or B3) or thymic carcinomas.

According to a few reports of the imaging findings of thymic carcinoid, this tumour is a rare mediastinal mass indistinguishable from thymoma on CT [2, 3]. Our results also

indicate that distinguishing thymic carcinoid from thymoma is very difficult. Although a high degree of enhancement may be characteristic of thymic carcinoid and a reticular septum within a rich haemorrhagic component may be characteristic of AC, these features require further investigation. A solitary anterior mediastinal mass is observed in various other tumours of the thymus, which include mediastinal germ cell tumours, except in mature teratoma and thymic lymphoma.

Our study has several limitations: (a) our study was a retrospective review; (b) the number of patients was low; (c) images were obtained using a variety of scanners and data had variations in the section thickness; (d) some patients did not undergo MRI. However, we believe that these limitations did not greatly influence the main results of our study, and that our findings should be of interest given the previous lack of imaging data regarding thymic carcinoid.

5. Conclusion

In conclusion, thymic carcinoids tend to be large masses with irregular contours, no capsule, heterogeneous intensity on T2-weighted images, heterogeneous enhancement, and local invasion on CT or MRI. A necrotic or cystic component was often seen in AC. These radiological features mimic those of high-risk thymomas and/or thymic carcinomas.

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Figure legends

Fig. 1. Case 3: Atypical thymic carcinoid in a 48-year-old woman with Cushing's syndrome.

(a, b) Contrast-enhanced CT images show a heterogeneous anterior mediastinal mass (white arrowhead) with irregular contours, a high degree of enhancement, and a necrotic or cystic component. There is no capsule, septum, haemorrhage, calcification, local invasion, or lymphadenopathy. However, a small mediastinal nodule (white arrow) was pathologically proven to be lymph node metastasis.

(c) Technetium-99m sestamibi (^{99m}Tc -MIBI) scintigram shows a high accumulation in the mass (black arrow).

Fig. 2. Case 7: Atypical thymic carcinoid in a 48-year-old woman.

(a) Contrast-enhanced CT image shows a heterogeneous mass with irregular contours and a high degree of enhancement. An extensive unenhanced area with a reticular septum is seen within the mass. Local invasion, including to the mediastinal fat, is present.

(b-d) Fat-suppressed T1- (b) and T2-weighted (c) and contrast-enhanced T1-weighted subtraction (d) images show a rich haemorrhagic component and a reticular septum. Partial capsule (white arrow) and lymphadenopathy (white arrowhead) are noted.

Fig. 3. Case 10: Atypical thymic carcinoid in a 69-year-old man.

(a-d) Contrast-enhanced CT image (a) and T1- (b) and T2-weighted (c) and

contrast-enhanced MR (d) images show a heterogeneous mass with irregular contours, a high degree of enhancement, a reticular septum, and a necrotic or cystic component (black arrowheads). The tumour vessels (black arrows) are clearly seen. There is no capsule, haemorrhage, calcification, or lymphadenopathy.

Fig. 1

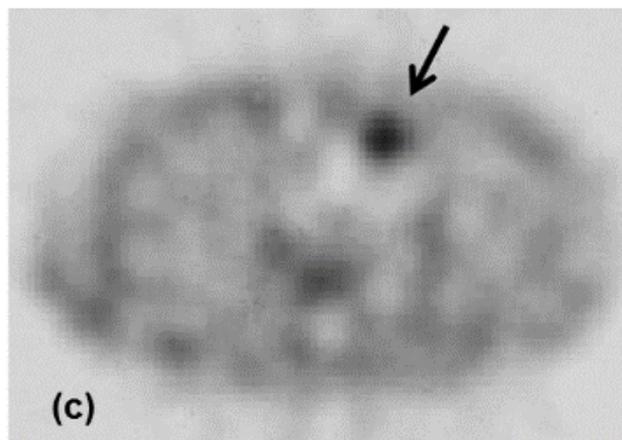
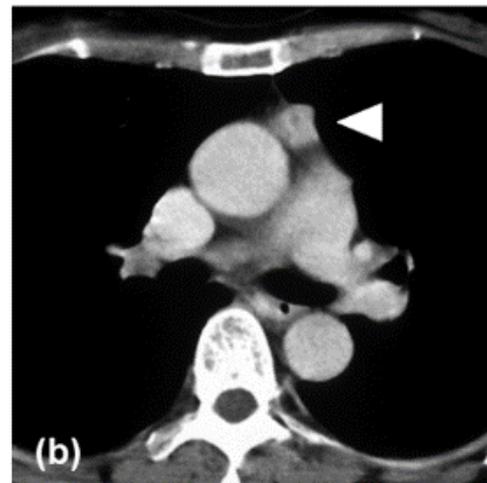
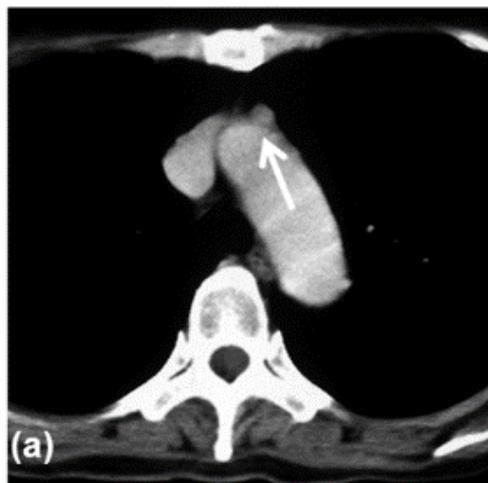


Fig.2

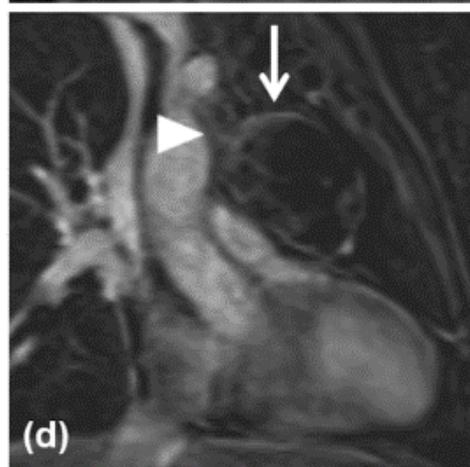
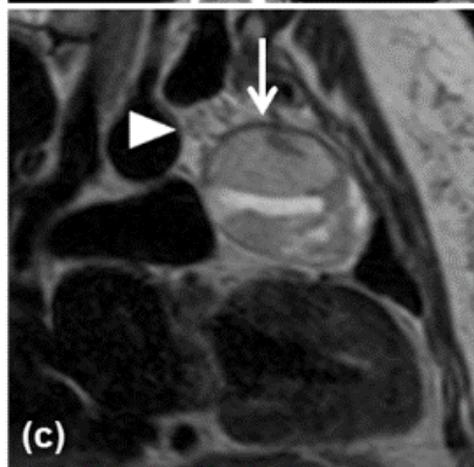
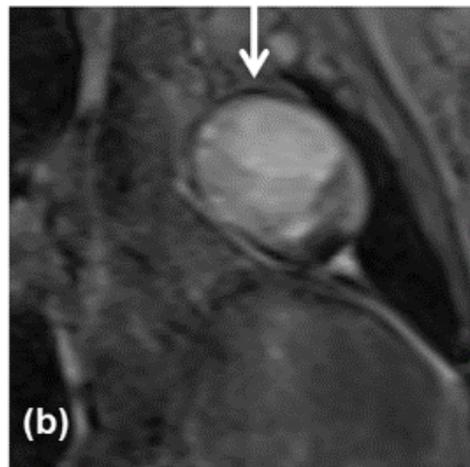
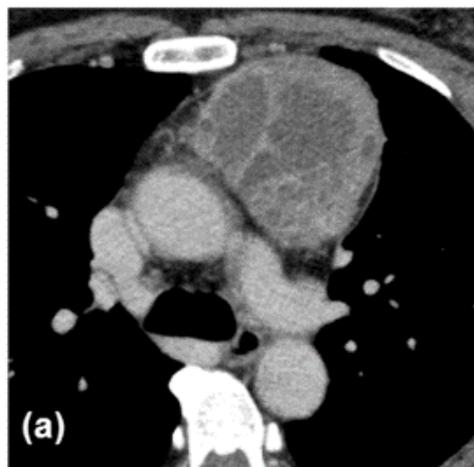


Fig. 3

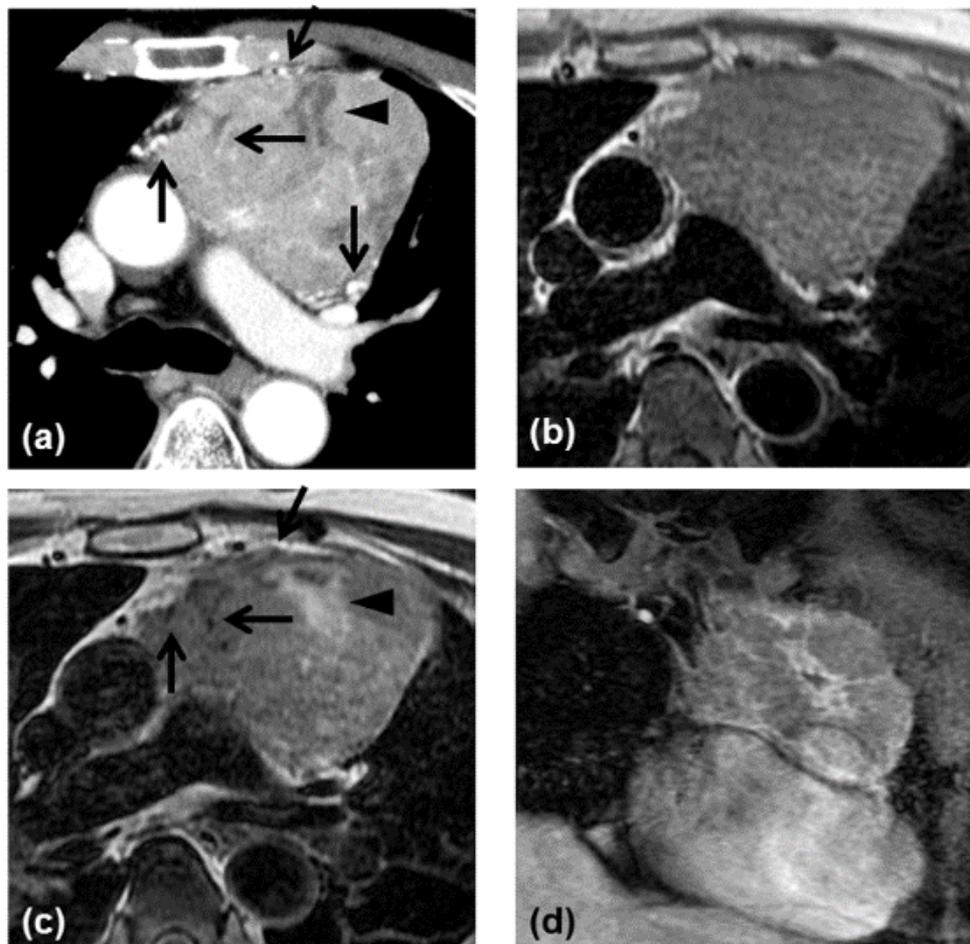


Table 1. Patient characteristics

Patient no.	Age, sex	Reason for discovery	Clinical findings at diagnosis	Endocrine disorder	Tumour size (mm)	Diagnostic method	Histopathological type	Follow-up data after diagnosis
1	29, M	Routine chest radiograph	Hoarseness	Normal	105	Fine needle aspiration biopsy	Atypical	Death with bone metastasis after 4.7 years
2	57, M	Routine chest radiograph	Normal	MEN1	78	Open biopsy	Atypical	Death with local progression, lung metastasis, and carcinomatous pleurisy after 4.5 years
3	48, F	Examination of ectopic ACTH	Mental disorder, oedema	Cushing's syndrome	18	Thymothymectomy	Atypical	Death with local recurrence after 3.7 years
4	41, M	Routine chest radiograph	Normal	Normal	68	Thymothymectomy	Atypical	Death with lung and bone metastasis after 10 years
5	67, M	Routine chest radiograph	Normal	Normal	59	Thymothymectomy	Typical	Unknown survival, local recurrence invading the heart after 8.5 years
6	59, M	Routine chest radiograph	Normal	Normal	19	Thymothymectomy	Typical	Alive without recurrence after 7.9 years
7	48, F	Routine chest radiograph	Normal	Normal	68	Thymothymectomy	Atypical	Death with bone and lung metastasis after 4.9 years
8	55, M	Examination for back pain	Back pain	Normal	50	Palliative thymectomy	Atypical	Death with bone, liver, lung, and lymph node metastasis after 7 years
9	71, M	Examination for chest pain	Chest pain	Normal	22	Thymothymectomy	Typical	Alive without recurrence after 4 years
10	69, M	Examination for chest pain	Chest pain	Elevated ACTH	100	Thymothymectomy	Atypical	Death by suicide with depression, without local recurrence after 1.2 years

11	45, M	Check for metastasis of pancreatic tumour	Numbness in the lower extremities	MEN1	20	Thymothymectomy	Atypical	Alive without recurrence after 7.6 years
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ACTH; adrenocorticotrophic hormone, MEN1; multiple endocrine neoplasia type 1

Table 2. Relationship between the CT and MRI findings and the simplified World Health Organization (WHO) histological classification

CT and MRI findings	Typical (n = 3)	Atypical (n = 8)	Total (n = 11)
	CT 3/ MRI 3/ overall 3	CT 8/ MRI 5/ overall 8	CT 11/ MRI 8/ overall 11
Size	19-59 [33.3]	18-105 [63.4]	18-105 [55.2]
Contour			
Smooth	1 / 1 / 1 (33)	1 / 1 / 1 (13)	2 / 2 / 2 (18)
Lobulated	0 / 0 / 0 (0)	1 / 0 / 1 (13)	1 / 0 / 1 (9)
Irregular	2 / 2 / 2 (67)	6 / 4 / 6 (75)	8 / 6 / 8 (73)
Capsule			
Almost complete	0 / 0 / 0 (0)	1 / 1 / 1 (13)	1 / 1 / 1 (9)
Partial	0 / 0 / 0 (0)	1 / 1 / 1 (13)	1 / 1 / 1 (9)
None	3 / 3 / 3 (100)	6 / 3 / 6 (75)	9 / 6 / 9 (82)
Homogeneity (pre-contrast-enhanced CT, T2WI)			
Homogeneous	3 / 1 / 1 (33)	3 / 1 / 3 (38)	6 / 2 / 4 (36)
Heterogeneous	0 / 2 / 2 (67)	5 / 4 / 5 (63)	5 / 6 / 7 (64)
Septum	0 / 0 / 0 (0)	3 / 3 / 3 (38)	3 / 3 / 3 (27)
Necrotic or cystic component	0 / 1 / 1 (33)	6 / 4 / 6 (75)	6 / 5 / 7 (64)
Haemorrhage	0 / 0 / 0 (0)	1 / 2 / 2 (25)	1 / 2 / 2 (18)
Calcification	0 / - / 0 (0)	1 / - / 1 (13)	1 / - / 1 (9)
Degree of enhancement			
Less than chest wall muscle	0 / 0 / 0 (0)	0 / 0 / 0 (0)	0 / 0 / 0 (0)
Equal to chest wall muscle	1 / 0 / 0 (0)	3 / 0 / 1 (13)	4 / 0 / 1 (9)
Greater than chest wall muscle	2 / 3 / 3 (100)	5 / 4 / 7 (88)	7 / 7 / 10 (91)
Enhancement pattern			
Homogeneous	2 / 1 / 1 (33)	2 / 0 / 1 (13)	4 / 1 / 2 (18)
Heterogeneous	1 / 2 / 2 (67)	6 / 4 / 7 (88)	7 / 6 / 9 (82)
Tumour vessel	1 / 1 / 1 (33)	1 / 1 / 1 (13)	2 / 2 / 2 (18)
Local invasion	1 / 1 / 1 (33)	6 / 4 / 6 (75)	7 / 5 / 7 (64)
Distant metastasis	0 / 0 / 0 (0)	2 / 2 / 2 (25)	2 / 2 / 2 (18)
Lymphadenopathy	1 / 1 / 1 (33)	3 / 3 / 3 (38)	4 / 4 / 4 (36)
Pleural effusion	0 / 0 / 0 (0)	0 / 0 / 0 (0)	0 / 0 / 0 (0)