Carcinoid tumor of the thymus is a rare neoplasm. It comprises a wide spectrum of lesions ranging from well-differentiated to poorly-differentiated neoplasms. We report a case of anterior mediastinal mass, which is proven to be an atypical thymic carcinoid tumor with a histopathological nature of intermediate-grade moderately-differentiated neuroendocrine carcinoma. We also present the patient’s clinical manifestations, imaging findings and pathological diagnosis. This tumor reveals large area of necrosis in imaging finding, which corresponds with its histopathological differentiation and classification. Since the thymic carcinoid had a tendency of local invasion and distant metastasis, it should be included in the differential diagnosis of anterior mediastinal tumor identified on chest X-ray or CT films. The imaging finding of large necrotic area can be predictable in its histopathological grading.

Key words: Computed tomography, Mediastinum; Neuroendocrine carcinoma; Thymic carcinoid

Carcinoid tumor of the thymus (nowadays known as primary neuroendocrine carcinoma of the thymus) is a rare neoplasm that account for less than 5% of all anterior mediastinal neoplasms [1]. Approximate half of the tumors are associated with endocrine dysfunction, producing Cushing’s syndrome or being part of multiple endocrine neoplasia (MEN) syndrome. Otherwise they may occur as symptomatic or asymptomatic anterior mediastinal masses, and may clinically be indistinguishable from thymoma. At least 30% of thymic carcinoids are regarded as malignant neoplasm, since they have a behavior of local invasion or metastasis, or even both [2]. The term “atypical” is applied on those with a histologically carcinoid architecture and, however, with a malignant nature, i.e. moderate cytological atypia, increased mitotic activity and area of necrosis [1]. We present a case of atypical thymic carcinoid tumor and show the patient’s clinical manifestation, imaging and histopathologic findings.

CASE REPORT

A 37-year-old man was admitted with chief complaint of chest pain and cough for one month. Physical examination and laboratory data were unremarkable. No evidence of endocrinopathy or history of heredofamilial endocrine syndrome could be recognized. The chest X-ray film showed a clearly demarcated and homogeneous opacity arising from and based upon the left hilar region (Fig. 1), measuring 9 cm x 12 cm of diameter. The computed tomography (CT) scan of the chest revealed a well-defined mass lesion arising from left anterior mediastinum with large central necrosis. It was enhanced by contrast agent in the arterial phase, with vascular supply in its peripheral portion (Fig. 2). Vascular washout occurred in the venous phase. The fat planes between the tumor and the pericardium were obliterated (Fig. 2 and 3). No enlarged hilar lymph node or abnormality of both lungs was noted. The findings of abdominal sonography, whole body bone scan and serum tumor markers (CEA, AFP) were unremarkable. Pathological diagnosis via sono-guided biopsy revealed “atypical

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carcinoid tumor of the thymus. The patient received wide excision of the tumor and thymus, as well as involved pericardium, mediastinal pleura, left phrenic nerve and the upper lobe of the left lung. Under histopathological observation, this tumor was composed of monomorphic polyhedral and round cells arranged in trabeculae, cords, lobules, and solid sheets with foci of necrosis and calcification. The tumor cells in the well-differentiated part exhibited monotonous nuclei, with salt-and-pepper chromatin, inconspicuous nucleoli and eosinophilic granular cytoplasm. Whereas those in the solid sheets were more pleomorphic and contained more clumped chromatin (Fig. 4), indicating a rather aggressive mitotic activity, and thus were considered as moderately differentiated pattern. The large area of central

Figure 1. Chest X-ray (posteroanterior view): a clearly demarcated mass lesion arising from left mediastinum with homogeneous radiopacity, measured about 9 cm x 12 cm of size and covering left hilar region.

Figure 2. Contrast-enhanced CT scan of the chest in the arterial phase: a well-defined tumor arising from the left anterior mediastinum, large area of central necrosis with peripheral vascular supply (arrow), obliterated fat planes between the tumor and the pericardium (arrowheads).

Figure 3. Three-dimension (3D) multiplanar reconstruction (MPR) CT images of the chest: a large tumor mass arising from left anterior mediastinum and adhered to pericardium (arrowheads), containing hypoattenuated necrotic area.

Figure 4. Photomicrograph of the solid portion of atypical thymic carcinoid: cellular atypia with nuclear pleomorphism and increased mitotic activity (arrow) with clumped chromatin (H & E stain, 400 x), recognized as moderately differentiated histological pattern, attributed to moderately differentiated (grade II) atypical carcinoid tumor.
necrosis corresponded to that in imaging findings. Prominent vascular permeation with tumor emboli was noted. The pericardium was also involved. These findings were characteristic of an atypical carcinoid tumor of the thymus. This patient was kept stable after operation and was discharged for further follow up.

**DISCUSSION**

The thymic carcinoid tumors (thymic neuroendocrine carcinomas) are rare tumors which were first described by Rosai and Higa in 1972, and were established as separate neoplasms from conventional thymomas [3]. They originate from the thymic cells of the neuroendocrine system. In a previous report, the intestinal carcinoid tumor accounted for 85% of the total carcinoid tumor, the pulmonary carcinoid for 10%, and elsewhere for 5%. Therefore, the incidence of primary thymic carcinoid is relatively low and only about 100 case reports were seen in literature until 1994 [4, 5]. Thymic neuroendocrine carcinomas predominantly locate in the anterior mediastinum and show a predilection for men (male/female ratio: 3/1). The median age in the reported series is 43 years old. These patients may either be asymptomatic or present with symptoms such as cough, chest pain, or superior vena cava syndrome [1], related to a rapidly-expanding mediastinal mass. This tumor is prone to extend locally to pleura, pericardium, great vessels, phrenic nerve and chest wall. It is also easy to metastasize to mediastinal lymph nodes and distant sites [6].

Thymic neuroendocrine carcinomas are commonly associated clinically with endocrine abnormalities, mainly the multiple endocrine neoplasms (MEN) type I syndrome [7]. Wick et al noted that approximately half of thymic “carcinoids” are functionally active or associated with the MEN syndrome [2]. Other associated conditions include polyarthropathy, proximal myopathy, peripheral neuropathy, hyperparathyroidism, incomplete Sipple syndrome (MEN-II), inappropriate secretion of antidiuretic hormone, Eaton-Lambert syndrome, hypertrophic osteoarthropathy [8] and Cushing syndrome [9, 10].

Its diagnosis can be confirmed by ultrasound- or CT-guided needle biopsy, surgical biopsy, or directly upon surgery. This case did not receive biopsy and only post-surgical histopathological confirmation was obtained. Rosai et al (1976) classified thymic neuroendocrine neoplasms into three categories: grade I, equivalent to conventional carcinoid; grade II, equivalent to atypical carcinoid; and grade III, equivalent to oat (small) cell carcinoma (Table) [11]. The higher the grade, the lower the survival rate would be [12]. The term “atypical carcinoid” was used in previous literature to characterize the carcinoid with a malignant nature of apparent nuclear pleomorphism, excessive mitosis and necrosis, and was regarded as intermediate-grade moderately-differentiated histopathological pattern [3]. This classification was graded relatively to well- (low grade) and poorly- (high grade) differentiated neuroendocrine carcinomas. The former had only minimal mitosis, minimal cytological atypia, and only small necrotic foci whereas the latter had high mitotic activity, marked nuclear atypia and extensive necrosis [1]. In this case, the lesion is considered as a moderately-differentiated pattern (Fig. 4) (Table) and is attributed to grade II neuroendocrine neoplasm due to its rather aggressive mitotic activity and large area of central necrosis. Surgical resection combined with post-surgical radiotherapy or chemotherapy is highly suggested, since the tumor has a high tendency to recur and widely metastasize [2, 13].

Routine roentgenograms of the chest in case of thymic neuroendocrine carcinoma usually demonstrate slightly lobulated, rounded masses with uniform opacity in the anterior mediastinum, and may project over the pulmonary hilum. In this case, the lesion is a round bulky mediastinal mass in appearance. Previous literatures revealed that the thymic carcinoids with Cushing’s syndrome would have a small size, whereas those without the syndrome might be larger [5, 13, 14]. In this case, the tumor is as large as 9 cm x 12 cm of diameter in size and no evidence of endocrine dysfunction is detected, which is consistent with previous experience. Delicate internal calcification is sometimes noted on conventional planar tomograms [15], whereas in this case no significant calcification can be observed in imaging findings, although microscopic calcifications do be present in histopathological interpretation. CT is superior than conventional chest film in defining small (< 3cm) lesions and in demonstrating invasion of the surrounding structures such as

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**Table 1. Comparison of Various Proposed Terms for Thymic Neuroendocrine Neoplasms**

<table>
<thead>
<tr>
<th>Conventional Terminology</th>
<th>Rosai et al</th>
<th>Moran and Suster</th>
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<tbody>
<tr>
<td>Carcinoid</td>
<td>Carcinoid type (grade) I</td>
<td>Well-differentiated (low grade) neuroendocrine carcinoma</td>
</tr>
<tr>
<td>Atypical carcinoid</td>
<td>Carcinoid type (grade) II</td>
<td>Moderately-differentiated (intermediate grade) neuroendocrine carcinoma</td>
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<tr>
<td>Small-cell carcinoma</td>
<td>Carcinoid type (grade) III</td>
<td>Poorly-differentiated (high grade) neuroendocrine carcinoma</td>
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The differential diagnosis of mediastinal mass is based on both clinical and imaging information. Among all mediastinal masses, primary anterior mediastinal tumors account for about 50% of proportion. They comprise a diverse group of tumors, e.g. thymoma (benign or invasive), thymolipoma, germ cell tumor, lymphangioma, intrathoracic goiter and thymic carcinoma. Thymomas are the most common entity, which is locally invasive and sometimes associated with myasthenia gravis, hypogammaglobulinemia, and pure red cell aplasia. They may sometimes contain hypoattenuated area(s) of necrosis and are difficultly differentiated from the carcinoid tumor. Thymolipomas are essentially benign in nature and their fatty content can be helpful for differential diagnosis. Germ cell tumors are a heterogeneous group of neoplasm, which may be either benign or malignant in nature, either solid or cystic in appearance, and either unique or mixed in germ layer composition. Lymphangiomas are rather rare, mostly occurring in young children. They, if occur locally, usually appear as cystic lesions, while they are sometimes difficultly to be differentiated from a thymic cyst. Intrathoracic goiters, in contrast, often occur in adult. They characteristically show prominent and prolonged enhancement, sometimes with inhomogeneous cystic degeneration, and lack of necrotic area, which can be all helpful for differentiating thymic carcinoid.

Although the imaging pattern of the solid matrix provides limited information in mitotic activity and cellular atypia, actually a large area of necrosis may be helpful to predict a relatively high grade neoplasm with a relatively aggressive invasive behavior. Therefore we need to collect more cases to obtain a statistically predictable and reliable database.

**CONCLUSION**

Thymic carcinoid tumor is a rare disease entity in mediastinum, with tendency of local spreading and distant metastasis. The possibility of thymic carcinoid tumor should be considered in addition to other common mediastinal tumors whenever dealing with anterior mediastinal mass detected by plain chest film and/or CT scan study, especially when there is associated clinical and/or laboratory findings of endocrine dysfunction or Cushing’s syndrome. The syndrome may not be present if the tumor is quite large in size. However, when a large area of necrosis is observed, a relatively high grade neoplasm with a relatively aggressive invasive behavior should be considered.

**REFERENCES**

非典型胸腺類癌：一病例報告

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胸腺類癌（即原發性神經內分泌胸腺瘤）為一種罕見腫瘤，其細胞分化良惡之間涵蓋甚廣。茲報導一例前縱膈腔腫瘤，證實為非典型胸腺類癌，並具有「中等程度分化的非典型神經內分泌癌」之組織病理特性。同時也討論該例之其臨床表徵、影像學發現與病理學診斷。本例在影像學上表現大區域壞死，更可印證組織病理分化等級，較為特殊。由於胸腺類癌具有局部侵犯及遠處轉移之傾向，當X光或電腦斷層（CT）片辨識出前縱膈腔腫瘤時，必須將其納入鑑別診斷。並期待大區域壞死之影像特徵能預測此類腫瘤的組織病理分級。

關鍵詞：胸腺類腫瘤，神經內分泌腫瘤，縱膈腔，電腦斷層攝影