Neuroendocrine Carcinoma Arising in a Mediastinal Teratoma with Pulmonary Metastasis: A Case Report and the Chemotherapy Response

So Yeon Lee¹, Young Min Jo², Jaehee Lee¹, Seung Ick Cha¹, Tae In Park² and Chang Ho Kim¹

Abstract

Neuroendocrine carcinoma as a somatic-type malignancy (STM) arising in an extragonadal teratoma is extremely rare. The effect of chemotherapy has been poorly evaluated in such cases contrary to teratomas with other STMs. We herein demonstrate that systemic chemotherapy may be beneficial in a case of neuroendocrine carcinoma arising in a mediastinal teratoma with pulmonary metastasis. A 31-year-old man presented with mediastinal widening visualized on a chest radiograph. Computed tomography showed a huge mediastinal mass with two pulmonary nodules. Surgical resection confirmed the presence of a neuroendocrine carcinoma arising in a mediastinal teratoma and pulmonary metastasis. The patient subsequently received chemotherapy and has had no recurrence during the 28-month follow-up.

Key words: neuroendocrine carcinoma, mediastinal teratoma, malignant transformation


Introduction

Somatic-type malignancy (STM) is defined as a non-germ cell malignant tumor derived from either a primary or metastatic germ cell tumor (GCT) (1). Among STMs arising in GCTs, neuroendocrine carcinoma is extremely rare. In general, advanced STM suggests a poor prognosis because it has been considered resistant to systemic chemotherapy, unlike GCT (2, 3). To the best of our knowledge, only 1 other case of a neuroendocrine carcinoma arising in a mediastinal teratoma has been previously reported (4). However, the effect of systemic chemotherapy has not been established in these extragonadal teratomas with neuroendocrine carcinoma. We herein report another case of a neuroendocrine carcinoma arising in a mediastinal teratoma with pulmonary metastasis which had a good response to systemic chemotherapy.

Case Report

A 31-year-old man presented with abnormal mediastinal widening on a chest radiograph (Fig. 1A). He denied any symptoms. His past medical history and physical examinations were unremarkable. Routine blood tests were within normal ranges excluding an abnormally elevated lactate dehydrogenase level of 517 IU/L (normal range: 240-480 IU/L). Chest computed tomography (CT) showed a 16.7×8.5 cm mass in the anterior mediastinum suggesting a mature teratoma (Fig. 1B). Additionally, two nodular lesions (1.0 cm and 0.8 cm in the long axis) were found in the right middle lobe (RML) and left lower lobe (LLL), respectively (Fig. 1C). Serum tumor markers, including α-fetoprotein, β-human chorionic gonadotropin, and neuron-specific enolase, were normal. A positron emission tomography/CT scan showed lesions with maximum standardized uptake values of 17.9 in the anterior mediastinum, 4.7 in the RML nodule, and 2.6 in the LLL nodule, respectively, and thus suggested...
the possibility of a mediastinal malignant tumor with pulmonary metastasis. The percutaneous needle biopsy specimen of the mediastinal solid mass was suspected to be a malignant neoplasm rather than a mature teratoma. A multidisciplinary decision was made to proceed with surgical resection. Thus, the patient underwent complete excision of the anterior mediastinal mass and wedge resection of the RML nodule.

Macroscopically, the resected mediastinal mass was 15.0×14.0×8.0 cm. The cut surface showed multi-lobulated solid and cystic areas, which composed approximately 90% and 10% of the mass, respectively. The cystic portion was filled with pultaceous material, and the solid portion showed a tan to yellow appearance on the cut surface. A microscopic examination of the cystic portion showed a wide spectrum of tissue types containing fatty tissue, cartilage, respiratory epithelial tissues, bones with marrow cavities, and mature neural tissues, characteristic of a mature teratoma (Fig. 2A). The solid portion showed neuroendocrine features (e.g., an organoid and trabecular pattern) under low magnification. Nests of tumor cells with peripheral palisading, rosette formation between the inter-tumoral septa, and a necrotic focus with karyorrhexis were visible under high magnification of the solid portion (Fig. 2B). According to an immunohistochemical examination, the tumor cells were diffusely and strongly positive for cytokeratin and CD56 (Fig. 2C). A highly aggressive profile was indicated by a Ki67 level of 80% (Fig. 2D). The resected pulmonary nodule was identical to those identified in the solid portion of the primary mediastinal mass. The final pathological diagnosis was a neuroendocrine carcinoma arising in a mediastinal teratoma.

The postoperative course was uneventful. After surgical resection, the patient received 4 cycles of combination chemotherapy with cisplatin and etoposide. The size of the LLL nodule decreased from 0.8 to 0.3 cm. The remaining LLL nodule was planned to be excised, but the patient declined further surgery. Fortunately, no new lesions or change in the remaining nodule in the LLL was detected in the follow-up chest radiography and CT scan taken at 28 months after chemotherapy (Fig. 3). The patient currently remains symptom-free.

Discussion

STM occurs in approximately 3% of all patients with GCT (5). STM is most commonly derived from a teratoma in the gonads and, therefore, was previously referred to as a teratoma with malignant transformation (1). Reported STMs include various types of sarcoma, epithelial malignancies (e.g., adeno-, squamous cell, adenosquamous, and undifferentiated carcinoma), and hematological malignancies (2, 3). Neuroendocrine carcinoma arising in a teratoma is rarely reported. Thus, the role of chemotherapy has not been fully established in teratomas with malignant neuroendocrine transformation. To the best of our knowledge, our case is the first to report that systemic chemotherapy may be effective in a neuroendocrine carcinoma arising from a mediastinal teratoma.

Complete surgical resection has been the mainstay of therapy when malignant transformation is found at a single site (3). Unresectable or metastatic settings will generally require multimodal therapy including both chemotherapy and locoregional approaches (6). However, while GCT is sensitive to platinum-based chemotherapy, STM arising from GCT has been traditionally thought to be unresponsive to platinum-based chemotherapy (1). Therefore, the presence of a metastatic STM implies a poor prognosis (2, 3). Nevertheless, Donadio et al. (6) showed that systemic chemotherapy may be effective for teratomas with STM limited to a single-cell type. It is recommended that the choice of chemotherapy regimens in such cases should be dictated by the transformed histology rather than the GCT (2, 6).

In a neuroendocrine carcinoma arising in a teratoma, few data concerning the role of chemotherapy are available due

Figure 1. Chest radiograph and computed tomography (CT) findings. (A) A huge mediastinal widening is noted on the chest radiograph. (B) CT reveals an approximately 16.7×8.5 cm mass in the anterior mediastinum, containing multiple calcifications and a low-density area, suggesting a mature teratoma. (C) Two pulmonary nodules (arrow) are present in the right middle lobe and left lower lobe.
to a very low incidence. A recent review revealed that in 6 cases, a neuroendocrine carcinoma arising in an ovarian teratoma had an exceedingly poor prognosis with progressive disease despite administering systemic chemotherapy (7). In another 6 cases of neuroendocrine tumors arising in an extragonadal retroperitoneum/pelvis teratoma, the prognosis was better due to detection at an early stage and a low malignant potential of the tumors, including carcinoid tumors (8-13), in contrast to ovarian neuroendocrine carcinomas which were mostly diagnosed at an advanced stage with other malignant components (14, 15). The first case of a neuroendocrine carcinoma arising in a mediastinal teratoma, as reported by Schaefer et al. (4), was confined to the mediastinum, and the patient did not receive adjuvant chemotherapy after surgical resection. Thus, the response to chemotherapy has not been properly evaluated in neuroendocrine carcinomas arising in teratomas at extragonadal sites such as the mediastinum, retroperitoneum, and pelvis. Our case had a high malignant potential based on the presence of metastatic pulmonary nodules and a Ki67 labeling index of 80% (16). Combination chemotherapy with cisplatin and etoposide was effective for controlling local recurrence and distant metastasis in our patient, although the nodule in the LLL was not pathologically confirmed.

In the present case, surgical resection of the mediastinal mass and the pulmonary nodule preceded systemic chemotherapy. This approach made it possible to make a definitive
pathological diagnosis and also confirm the metastasis, which led to the selection of chemotherapy regimens appropriate for disease control. Systemic chemotherapy followed by surgical resection may also be chosen. However, there are no unique clinical characteristics for the diagnosis of a teratoma with STM. Typically, this histology is incidentally found at the time of surgery (6). Thus, an exact pathological diagnosis may be difficult and there is a risk of disease progression if the selected chemotherapy regimens are not effective. Therefore, it may be better to perform surgical resection followed by a pathological confirmation, if the patient is capable of undergoing surgery, so that subsequent chemotherapy is dictated by the transformed histology.

Contrary to previous reports of neuroendocrine carcinomas arising from ovarian teratomas (7), the present case showed platinum-based chemotherapy to be effective. Even though the carcinomas were similarly advanced, it is doubtful that a difference in the primary site affects the response to chemotherapy. Ovarian teratomas with a neuroendocrine malignant transformation have been frequently associated with other malignant components such as mucinous adenocarcinoma (14, 15). More data must be accumulated to explain these differences, although an exact transformed histology seems to be more important for the prognosis than the primary site.

In conclusion, a neuroendocrine carcinoma arising in a mediastinal teratoma and pulmonary metastasis responded to systemic chemotherapy following surgical resection. Chemotherapy dictated by an exact histology may thus be beneficial for cases of neuroendocrine carcinoma arising in a mediastinal teratoma compared to an ovarian teratoma with a similar transformation. This case may be helpful for making therapeutic decisions when such a case is encountered in clinical practice.

The authors state that they have no Conflict of Interest (COI).

References