Metastatic Thymic Adenocarcinoma from Colorectal Cancer

Mina Lee, M.D. 1, Suk Jin Choi, M.D. 2, Yong Han Yoon, M.D. 1, Joung-Tack Kim, M.D. 1, Wan Ki Baek, M.D. 1, Young Sam Kim, M.D. 1

This report describes the case of a 57-year-old man with an anterior mediastinal tumor. Four years previously, he underwent laparoscopic anterior resection for sigmoid colon cancer. Thirty months after that procedure, bilateral pulmonary metastasectomy was performed. Twelve months later, follow-up computed tomography revealed a 1-cm pulmonary nodule on the upper lobe of the right lung and a solid mass on the anterior mediastinum, and the patient was also observed to have an elevated serum carcinoembryonic antigen (CEA) level. Repeated pulmonary nodule resection and total thymectomy were performed. Immunohistochemical staining of the anterior mediastinal tumor revealed adenocarcinoma, and his serum CEA level returned to normal after the operation. These findings strongly suggested metastatic thymic adenocarcinoma from a colorectal cancer.


CASE REPORT

A 57-year-old male patient was referred for the treatment of an anterior mediastinal tumor and a small pulmonary nodule on the right upper lung. Four years previously, he underwent laparoscopic anterior resection with lymphadenectomy for sigmoid colon cancer, which pathological analysis showed to be pT3N0M0. After sigmoid colon cancer surgery, adjuvant chemotherapy was performed with leucovorin and 5-fluorouracil (5-FU). Thirty months after the initial sigmoid colon resection, bilateral multiple pulmonary nodules were found on follow-up chest computed tomography (CT), suggesting hematogenous pulmonary metastasis from colon cancer. Additional chemotherapy was administered, consisting of irinotecan, leucovorin, and 5-FU, followed by bilateral thoracoscopic resection of the pulmonary nodules. The histopathologic and immunohistochemical features of the resected pulmonary nodules suggest metastasis from previously resected sigmoid cancer.

Twelve months after the patient underwent bilateral metastasectomy, a follow-up chest CT revealed a 1-cm pulmonary nodule on the upper lobe of the right lung (RUL), and a 6.7×3.8×8-cm solid mass on the anterior mediastinum. A fluorne-18-fluorodeoxyglucose-positron emission tomography/CT scan showed an abnormal hypermetabolic mass in the anterior mediastinum and right upper pulmonary nodule (Fig. 1), and...
Fig. 1. (A) Chest computed tomography revealed a pulmonary nodule on the right upper lung (line) and an anterior mediastinal tumor (arrow). (B) Fluorine-18-fluorodeoxyglucose-positron emission tomography/computed tomography showed an abnormal hypermetabolic mass in the anterior mediastinum and right upper pulmonary parenchyma, which we concluded were metastatic nodules from a primary colorectal tumor.

Fig. 2. (A) Cut sections of the resected thymus revealed a well-demarcated, solid, and partly cystic mass with extensive necrosis. (B) The degenerative, cystic, and distended thymic epithelium was partially involved with the tumor, as shown by the area of dirty necrosis (arrow). The histomorphologic findings of the thymic tumor were equivalent to those of the colon cancer (inlet) (H&E, ×40).

Mina Lee, et al

an elevated serum carcinoembryonic antigen (CEA) level of 6.75 ng/mL was observed (normal range, 0.00 to 4.7 ng/mL). On this basis, we hypothesized that the pulmonary nodule in the RUL was metastatic colon cancer, and that the anterior mediastinal tumor was a thymic malignancy, such as thymoma or thymic carcinoma.

We planned to perform simultaneous pulmonary wedge resection and mediastinal tumor resection. Due to tight pleural adhesion, wedge resection of the RUL nodule was performed via a right lateral thoracotomy. The tight plural adhesion and the resulting prolonged operation time led us to postpone surgery for the anterior mediastinal tumor. The histopathologic and immunohistochemical features of the resected pulmonary nodule from the RUL indicated that it was metastatic adenocarcinoma from the colon. Four weeks later, total thymectomy to remove the anterior mediastinal tumor was performed via a median sternotomy. The tumor was firmly adherent to the pericardium, but did not invade it. Complete resection of
Metastatic Thymic Adenocarcinoma

Fig. 3. (A–D) Immunohistochemical staining of the anterior mediastinal tumor revealed that the neoplastic epithelium was diffusely and strongly positive for (A) caudal type homeobox2 (CDX2, ×40) and (C) cytokeratin 20 (CK20, ×40), which is a major regulator of intestine-specific genes, whereas the thymic tissue with cystic degeneration was negative for CDX2 and CK20, and the neoplastic epithelium was negative for (B) cytokeratin 7 (CK7, ×40) and (D) CD5 (CD5, ×40) which are usually expressed in thymic carcinoma.

The tumor was performed without resecting the pericardium.

The cut section of the resected thymus revealed a well-demarcated, solid, and partly cystic mass with extensive necrosis. The mass in the thymus consisted of large cystic glandular spaces with extensive confluent dirty necrosis, intracystic papillary growth, and pericystic infiltrations. The thymic epithelium had been partly invaded by the necrotic portion of the tumor (Fig. 2B).

Immunohistochemical analysis of the anterior mediastinal tumor showed that it was diffuse and strongly positive for caudal type homeobox 2 (CDX2) in the neoplastic epithelium (Fig. 3A). In addition, this tissue was negative for cytokeratin 7 (CK7) (Fig. 3B), and showed patchy positive staining for cytokeratin 20 (CK20) (Fig. 3C). Both the neoplastic and thymic epithelium were negative for CD5 (Fig. 3D).

Three months after thymectomy, the patient’s serum CEA level fell back to within the normal range (4.34 ng/mL). Currently, the patient is at the one-year follow-up point after thymectomy, and continues to be treated with palliative chemotherapy for sigmoid colon cancer. His latest chest CT scan showed no evidence of definitive metastasis in the anterior mediastinum and/or the lung.
DISCUSSION

The venous blood from the colorectal tract is drained via the portal venous system, and thus distant hematogenous metastasis from colorectal cancer usually occurs in the liver. In contrast, the venous blood from the distal rectum is drained via the inferior vena cava, meaning that hematogenous pulmonary metastasis from the distal rectum usually occurs in the lung parenchyma [1].

Thymic neoplasm is one of the most common primary neoplasms of the anterior mediastinum, although thymic neoplasm itself is a very rare malignancy. The overall incidence of thymoma in the U.S. is only 0.13 cases per 100,000 person-years [2].

Thymoma is associated with an increased risk of secondary malignancy. Welsh et al. [3] reported the prevalence of additional malignancies to be 8%–21% in thymoma patients, and Tanakaya et al. [4] reviewed five cases of metachronous colorectal carcinoma associated with thymoma. However, they did not determine the precise mechanism of the development of extrathymic malignancies associated with thymoma [4]. Although Yeo et al. [5] reported a case of metastasis of colon carcinoma to the mediastinal thyroid, we have not found any reports of metastasis to the thymus from colon cancer.

Thymic carcinoma is rare, and usually occurs as squamous cell carcinoma or lymphoepithelioma-like carcinoma. Primary thymic adenocarcinoma itself is extraordinarily rare, and to our knowledge, fewer than 50 cases have been reported. Jung et al. [6] reported a case of primary tubular adenocarcinoma of the thymus with an enteric immunophenotype, and Moser et al. [7] reported two cases of mucinous adenocarcinoma of the thymus. In both of these cases, no evidence of other malignancies was found, and the authors finally diagnosed the thymic tumors as primary thymic adenocarcinomas that showed enteric differentiation based on immunohistochemical studies. They proposed that enteric-type thymic adenocarcinoma represents a novel subtype of thymic carcinoma, and this suggestion has been included in the 2015 World Health Organization classification of thymus tumors. In this classification system, thymic adenocarcinomas form a single subgroup and are labeled according to their hematoxylin and eosin (H&E) histology, abandoning the previous subdivision of thymic adenocarcinoma into papillary and non-papillary types [8]. Thymic adenocarcinoma with enteric differentiation is now considered a novel subtype of thymic adenocarcinoma.

It is difficult to distinguish between metastasis of colon cancer to the thymus and primary thymic carcinoma with enteric differentiation, as they show similar histopathologic features. In our case, both sigmoid colon cancer and the mediastinal tumor had the same histopathological features on H&E staining. However, immunohistochemical staining of the anterior mediastinal tumor revealed that the neoplastic epithelium was strongly positive for CDX2, which is a major regulator of intestine-specific genes, whereas the thymic tissue with cystic degeneration was negative for CDX2. Furthermore, the neoplastic epithelium showed patchy positivity for CK20, which is predominantly expressed in the gastrointestinal tract epithelium, whereas it was negative for CK7, which is expressed by thymic tissue with cystic degeneration. Both the neoplastic and thymic epithelia were negative for CD5, which is usually expressed by thymic carcinoma. In addition to these immunohistochemical findings, the patient’s elevated serum CEA level was normalized after thymectomy. Previously reported cases of primary thymic adenocarcinoma with no history of colon cancer showed similar histopathologic features, but the patient in this case had a previous history of treatment for colon cancer, and a thymic tumor was not found when the sigmoid colon cancer was initially diagnosed. Four years after first undergoing surgery for sigmoid colon cancer, metastatic pulmonary nodules and an anterior mediastinal tumor were found on chest CT and positron emission tomography-CT scans. Unfortunately, the immunohistochemical findings of this patient’s colon cancer were not available, so we could not directly compare the immunohistochemical findings of the thymic lesion to those of the patient’s original colon cancer. However, the histomorphologic and immunohistochemical features of the thymic lesion were compatible with colonic adenocarcinoma. Furthermore, the patient’s CEA level normalized postoperatively. Based on these clinical and histomorphologic findings, we conclude that the thymic tumor was a metastatic lesion from a primary colorectal adenocarcinoma.

To our knowledge, this is the first reported case of metastatic thymic adenocarcinoma from a primary colorectal tumor.
CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGMENTS

This work was supported by INHA UNIVERSITY Research Grant.

REFERENCES