Metastatic intestinal adenocarcinoma arising within mature teratoma of the mediastinum: report of a surgically-resected case

Yoldez Houcine,[1,2] Chirine Moussa,[2,3] Tarek Abid,[4] Sadok Hammami,[5] Héla Skhiri,[6] Aida Ayadi[1,2]

[1]Pathology Department, Abderrahmen Mammi Hospital, Ariana; [2]Faculty of Medicine, El Manar University, Tunisi; [3]Pneumology Department 1, Abderrahmen Mammi Hospital, Ariana; [4]Pasteur Clinic, Pneumology Department, Tunisi; [5]Pasteur Clinic, Surgery Department, Tunisi; [6]Pasteur Clinic, Oncology Department, Tunisi, Tunisia

Abstract

Intestinal adenocarcinoma spontaneously developing in an anterior mediastinal multilocular teratoma in a 33-year-old female is described. The patient has been experiencing chest distress for several months. On a chest X-ray, a cystic anterior mediastinal mass was identified. A subsequent computed tomography scan revealed a heterogeneous mass measuring 20x15x10 centimeters in the anterior right mediastinum. She underwent a median thoracotomy excision. The histopathologic examination revealed a mature teratoma with intestinal adenocarcinoma metastases associated with pulmonary, cutaneous, and diaphragmatic metastases.

Correspondence: Chirine Moussa, Pneumology Department 1, Abderrahmen Mammi Hospital, Ariana, Tunisia.
E-mail: chirine.moussa22@gmail.com

Key words: mediastinal tumors, teratoma with malignant transformation, adenocarcinoma, metastases.

Contributions: AA conceived the project. AA, TA, SH, HS contributed by providing the data. YH wrote the manuscript. CM, TA, SH, HS revised the manuscript critically for important intellectual content, and AA, CM, ABA gave final approval for the version to be published

Conflict of interest: the authors declare no potential conflict of interest.

Funding: none.

Availability of data and materials: all data underlying the findings are fully available.

Ethics approval and consent to participate: no ethical committee approval was required for this case report by the department, because this article does not contain any studies with human participants or animals. Informed consent was obtained from the patient included in this study. Written informed consent was obtained from the patient to use his personal data for the publication of this case report and any accompanying images.

Received: 19 September 2023.
Accepted: 25 October 2023.
Early view: 25 October 2023.

Chest Disease Reports 2023; 11:11840
doi:10.4081/cdr.2023.11840

Introduction

Mediastinal Teratoma with Malignant Transformation (MTMT) is a rare tumor that most commonly affects young individuals.[1] The diagnosis is founded on the coexistence of a preexisting mediastinal teratoma and a non germ cell malignant tumor. The malignant transformation can develop naturally at either the primary or metastatic site, or both.[2] In up to 41% of cases, it can occur simultaneously with the diagnosis of a mature teratoma, or up to several years later. Adenocarcinoma is one of many forms of malignant transformation.[3]

While the majority of mediastinal mature teratomas are benign and have a favorable prognosis,[4] MTMT has a poor prognosis due to its resistance to chemotherapy and radiation therapy.[5]

Here, we describe a rare surgical case of well-differentiated metastatic intestinal adenocarcinoma arising from a mature cystic teratoma of the mediastinum.

Case Report

A 33-year-old woman was referred to the clinic of Dr. Pasteur for chest pain and dyspnea that had developed over several months. Her previous medical and surgical history was not noteworthy.

On physical examination, her vital signs were stable, and she was afebrile. In her right thorax, weak breath sounds, and dullness to percussion were audible. There were no audible rales, rhonchi, or significant wheeze.

The cranium and forehead exhibited well-circumscribed nodular lesions on clinical examination. A computed tomography scan revealed a 20x15x10 cm heterogeneous mass in the right anterior mediastinum that had invaded the adjacent tissue, the diaphragm, and the thickened pleura. There were pulmonary metastases observed. The adjacent lung was compressed, and the contralateral mediastinum was pushed. No evidence of vessel incursions or entanglements was found. Manifest pleural effusion was observed (Figure 1).

The mass appeared to be an enormous teratoma. The concentrations of alpha foetoprotein and Human Choriogonadotropin (HCG) were within the normal range.

The patient was subsequently resected via thoracotomy. The tumor was located on the anterior and right thorax intraoperatively

and appeared to originate from the thymus (Figure 2). Extensive portions of the pleura and diaphragm were also removed for the removal of pulmonary nodules and cutaneous lesions.

Materials and Methods

There were mediastinal tumors, pleural tissue, cutaneous lesions, diaphragmatic, and pulmonary nodules among the specimens. All specimens were fixed in 10% formalin before undergoing a conventional histological examination. Sections stained with Hematoxylin and Eosin (H&E) were analyzed. Using an automatic slide stainer, immunohistochemistry was performed.

Pathologic findings

Macroscopic examination

The resected mediastinum measured 19x13x8 cm and weighed 1149 grams. The cut surface was multilocular with cysts of mucinous, gelatinous, or serous material altering with a variable solid component that appeared infiltrative (Figure 3). Occasionally, the content of a cyst may contain a viscous substance composed of keratin and hair.

There was no vegetation on the interior or exterior.

The nodules of the diaphragm and lungs were whitish and robust with an infiltrative appearance. They had maximum diameters of 4 cm and 6 mm, respectively.

Both skin lesions were confined to the hypodermis and measured 1 cm in diameter.

Examining by microscope

On a microscopic level, the cyst was lined by respiratory epithelium, gastric epithelium, and occasionally denuded cutaneous tissue. The subepithelial tissue consisted of dense fibrotic tissue that contained hair follicles, sebaceous glands, and perspiration glands. Within the cystic walls, mature glial, cartilage, smooth muscle, adipocytic, and gastric organs were observed.

No rudimentary teratomatous elements or other germ cell components were detected. Solid areas, however, corresponded to a malignant proliferation composed of non-ciliated atypical columnar epithelial cells with abundant eosinophilic cytoplasm that proliferated with a tubular or trabecular pattern (Figure 4). This was considered a moderately differentiated adenocarcinoma. With four mitoses per fifty High-Power Fields (HPF), mitotic figures were uncommon. Occasionally, prominent nucleoli were seen. The stroma contained fibers. Multiple tumor emboli and perineural infiltration were observed.

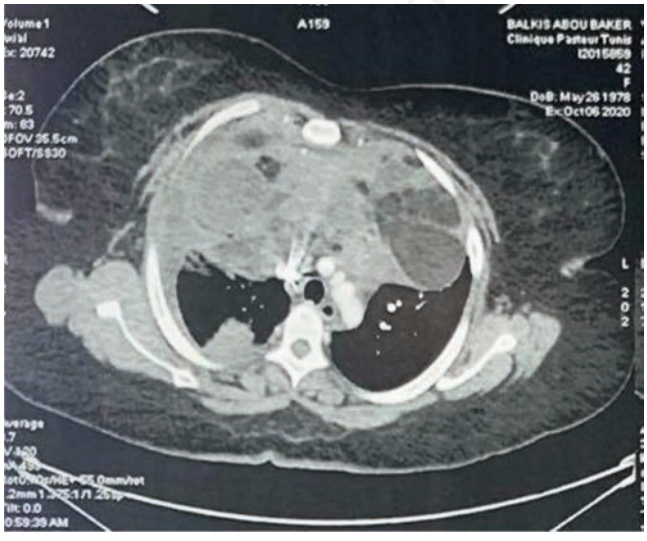

Figure 1. A giant and heterogeneous mass in the right anterior mediastinum with multilocular cystic spaces alternating with extensive solid areas.

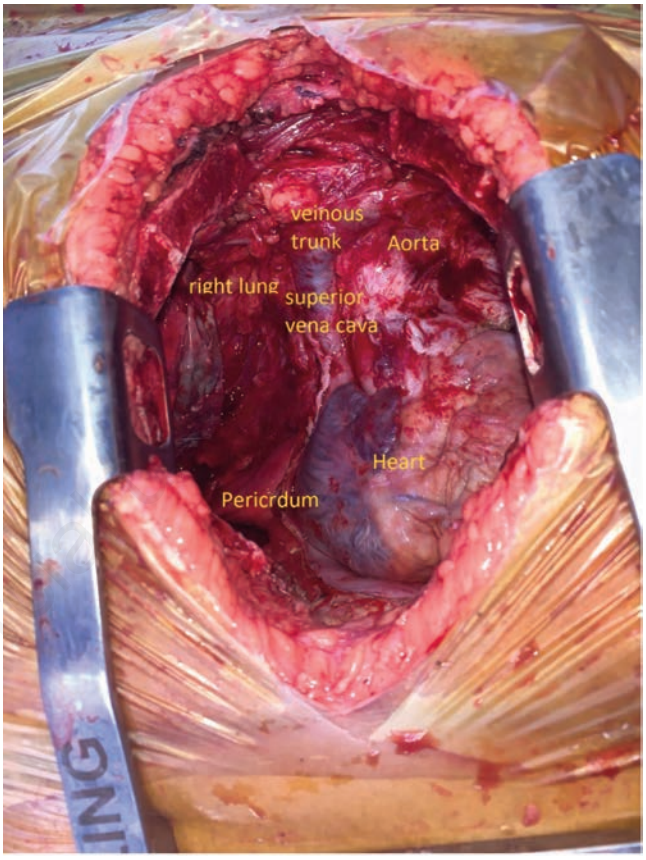

Figure 2. The right mediastinal organs were compressed and pushed to the other side.

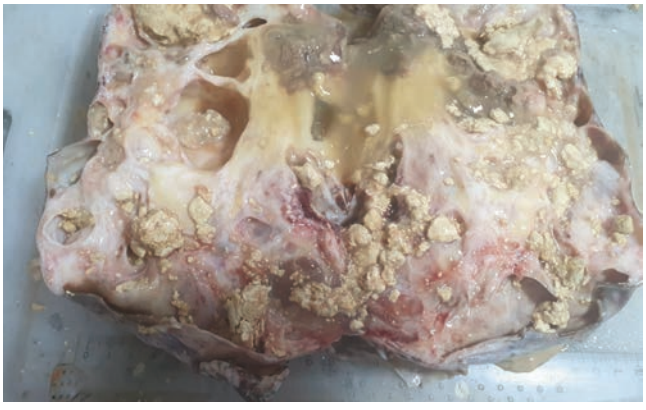

Figure 3. The tumor was multilocular with cysts of mucinous, gelatinous, or serous material alternating with variable solid component.

A thymic parenchyma remnant was observed at the periphery.

This adenocarcinoma infiltrated the peripheral fibrous capsule extensively and invaded the mediastinal fat and pleura. This cancerous compound covered 30% of the tumor's surface.

Figure 5 depicts skin lesions, diaphragmatic nodules, and pulmonary nodules composed of the same malignant epithelial proliferation, confirming the diagnosis of metastatic lesions.

Immunohistochemistry A panel of immunohistochemical tests was conducted, and only CK7 was positive (Figure 6). Germ cell tumor was ruled out because tumor cells were negative for CD30, Placental-Like Alkaline Phosphatase (PLAP), and alpha-feto protein. They were also negative for CK20, which ruled out gastric adenocarcinoma as a diagnosis.

Follow up

The postoperative course did not show any particular issue.

Given the aggressive nature of the diagnosis, adjuvant chemotherapy, including fluoropyrimidine, was initiated following surgical resection.

The patient had no evidence of recurrences 4 months after the operation.

Discussion

MTMTs are uncommon malignancies. Somatic Type Cancer (STM) appears to be more prevalent in mediastinal teratoma than in gonadal primitive tumors. It most commonly occurs in the anterior mediastinum. It is unknown what causes malignant transformation. Numerous authors believe that malignant germ cell tumor cells exhibit remarkable plasticity and pluripotency, which could explain the emergence of cells that differentiate into somatic tissue types.[6] Typically, STM originates from one of the epithelial components. The most common histologic type (75%) is squamous cell carcinoma, followed by adenocarcinoma, as in our case, and carcinoid; other malignancies are rare.[7] According to our literature review, 22 cases of mediastinal mature teratoma with malignant transformation to adenocarcinoma have been reported prior to this case (*Supplementary Table 1.*). The prevalence of MTMT is highest in males, with fourteen males, seven females, and one unclassified patient. The median age was 39, with extremes of 20 and 66 years of age. MTMT exhibit the same local symptoms as other mediastinal germ cell tumors, but are more symptomatic than pure teratoma. In the preponderance of instances, STM occurs concurrently with the maturing teratoma, as was the case in ours. In some instances, the adenocarcinoma transformation occurs between 6 months and 14 years later. The extent of the tumor ranges from 3 to 36 cm. In some instances, serum levels of alpha-fetoprotein and beta-subunit of human chorionic gonadotropin are elevated. In this case, there were 12 instances of metastatic disease and 7 instances of multiple metastatic locations. In seven cases, the most common metastatic sites were pleural or pulmonary sites. On the basis of a CT scan or magnetic resonance imaging, MST may be suspected. Imaging studies typically disclose a solid mass (representing the MST) accompanied by a cystic teratomatous structure or a heterogeneously attenuating lesion. Frequent occurrences of calcification and massive necrosis are observed. MTMT infiltrates the mediastinal structures, diaphragm, and lung frequently.[8] Metastases can manifest anywhere in the body, including regional lymph nodes,[9] the lungs,[10-14] the pleura,[15-22] and the subcutaneous region.[23-26] The cut surface of the tumor is partially cystic and heterogeneous, with focally calcified or necrotic areas. The somatic malignancy is solid and whitish, with occasionally hemorrhagic or necrotic regions. On microscopic examination, the cystic component of a mature teratoma is surrounded by epithelium of ectodermal origin, such as keratinizing squamous epithelium or sebaceous glands, endodermal epithelium, such as stratified ciliated columnar epithelium, or mesodermal derivatives, such as adipose, smooth muscle, or fibrous tissues.[27] The mature teratoma may contain numerous mature organoid tissues.[28-31] Typically, the malignant transformation occurs within the tumor's wall.[9] Giannatempo *et al.* conducted a study involving 320 MTMT patients. 15.7% were adenocarcino-

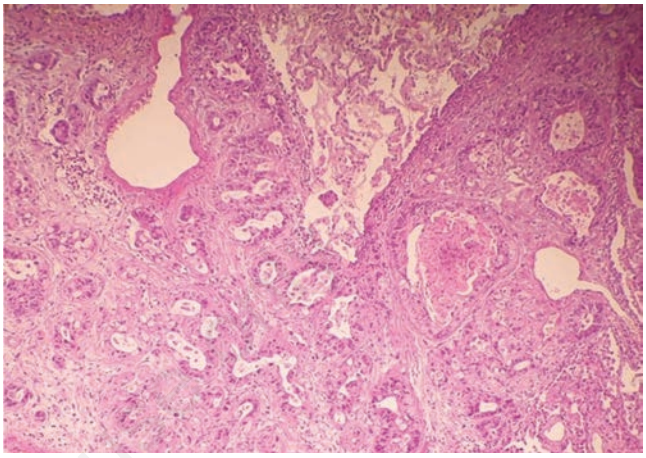

Figure 4. Well-differentiated intestinal teratoma proliferating with the cystic teratoma (HEx20).

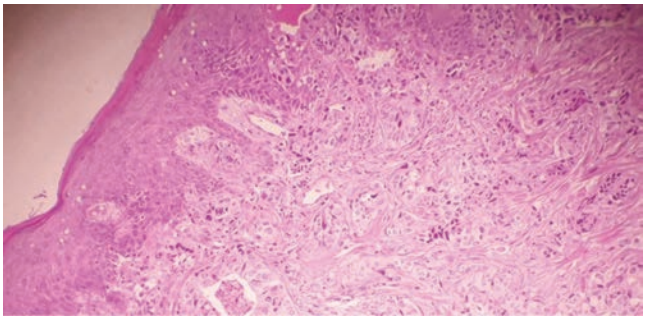

Figure 5. Well-differentiated intestinal teratoma proliferating with the cystic teratoma (HEx20).

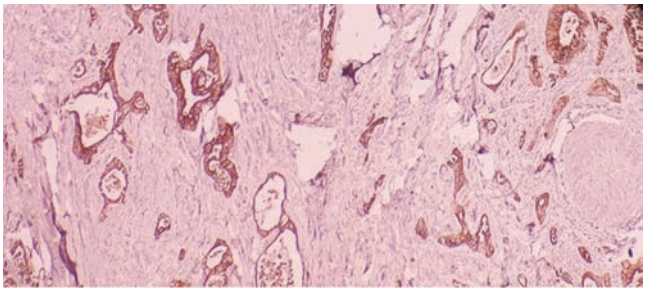

Figure 6. Malignant tumor cells arranged in glandular structures are positive for CK7, malignant glands surrounding the sheath nerve (Immunohistochemistry x 20).

mas, 13.5% were rhabdomyosarcomas, 23.3% were sarcomas, 30.8% were peripheral neuroectodermal tumors, and 16.7% had combined histologies.[32]

Due to the rarity of this condition, treatment is not standardized. Commonly, surgery is used to remove the entire tumor, especially in cases of localized disease and singular tumor sites.[33,34] The application of adjuvant chemotherapy is not standardized and varies from case to case.

Administering adjuvant treatment was extremely beneficial and efficient in our circumstance. Chemotherapy yielded extraordinary results. It had eliminated most of the remaining lesions.

Due to the presence of numerous histological components, the diagnosis of intestinal adenocarcinoma within a mature teratoma presents numerous obstacles. Using specific diagnostic markers, such as CK20 and CK7, the presence of intestinal adenocarcinoma within the teratoma was confirmed. As intestinal adenocarcinomas are known to have distinct molecular characteristics and therapeutic considerations compared to other mediastinal tumors, this finding has clinical significance.

This case was significantly impacted by the presence of intestinal adenocarcinoma within the teratoma. Due to the aggressive character of intestinal adenocarcinomas, adjuvant chemotherapy was administered to the primary tumor site after surgical resection. The prevalence of intestinal adenocarcinoma (30%) necessitated a stricter surveillance plan and consideration of the possibility of metastasis.

The prognosis for MTMT is dismal, and MST appears to be an independent prognostic factor.[32] However, chemotherapy and surgery can lead to long-term survival.[35] In the study by Giannatempo *et al.*,[32] the aggregate 5-year survival rates for metastatic patients ranged from 47.9 to 69.8 percent. In Comiter *et al.*'s series of 21 patients with malignant transformation of teratoma, 94% had metastases, and 81% had a recurrence at a median time of 6 months.[35] In these two series, the primary tumor site, the number of prior chemotherapies, and the type of transformed histology are prognostic factors.[32,35] MST expansions are a natural progression of the teratoma or a transformation induced by chemotherapy or radiation therapy. In 19 cases of MTMT in adenocarcinoma (*Supplementary Table 1*), the transformation appears to be the consequence of the teratoma's natural evolution. However, it appeared to delay initial treatment in three patients: in one case 14 years after radiotherapy plus chemotherapy,[15] and in two cases 6 months[18] and 10 years[28] after chemotherapy. MTMT is a rare disorder with a dismal prognosis and no standard treatment. Complete surgery appears to be the standard of care. The pathologic examination of the mass tumor and a comprehensive immunohistochemical analysis are crucial to establishing this uncommon and difficult diagnosis. Managing early recurrence and metastases requires a long-term follow-up.

References

1. Chen C, Zheng H, Jiang S. An Unusual Case of Giant Mediastinal Teratoma With Malignant Transformation. Ann Thorac Surg 2008;86:302-4.
2. Motzer RJ, Amsterdam A, Prieto V, et al. Teratoma with malignant transformation: diverse malignant histologies arising in men with germ cell tumors. J Urol 1998;159:133-8.
3. Habougit C, Yvorel V, Sulaiman A, et al. Mediastinal mature teratoma with malignant carcinomatous transformation (somatic-type malignancy with metastatic course). Int J Surg Pathol 2015;23:682-4.
4. Chetaille B, Massard G, Falcoz P-E. Mediastinal germ cell tumors: anatomopathology, classification, teratomas and malignant tumors. Rev Pneumol Clin 2010;66:63-70.
5. Shimizu K, Nakata M, Hirami Y, et al. Teratoma with malignant transformation in the anterior mediastinum. J Thorac Cardiovasc Surg 2008;136:225-7.
6. Honecker F, Stoop H, Mayer F, et al. Germ cell lineage differentiation in non seminomatous germ cell tumor. J Pathom 2006;208:395-400.
7. Curling OM, Potsides PN, Hundson CN. Malignant change in benign cystic teratoma of the ovary. Br J Obstet Gynecol 1979;86:399-402.
8. Morinaga S, Nomori H, Kobayashi R, Atsumi Y. Well-differentiated adenocarcinoma arising from mature cystic teratoma of the mediastinum (teratoma with malignant transformation). Report of a surgical case. Am J Clin Pathol 1994;101:531-4.
9. Jung JI, Park SH, Park JG, et al. Teratoma with malignant transformation in the anterior mediastinum: a case report. Korean J Radiol 2000;1:162-4.
10. Popp G, Dragnev K. Secondary malignant transformation of a primary mediastinal germ cell tumor with diffuse lymphangitic spread to the lungs. South Med J 2003;96:696-8.
11. Michel M, Pratt JW. Anterior mediastinal nonseminomatous germ cell tumor with malignant transformation: a case report. Curr Surg 2004;61:576-9.
12. Seki Y, Imaizumi M, Shigemitsu K, et al. Mucinous adenocarcinoma of the anterior mediastinum. Kyobu Geka 2004;57:413
13. Chang Y-L, Wu C-T, Lee Y-C. Mediastinal and retroperitoneal teratoma with focal gastrointestinal adenocarcinoma. J Thorac Oncol 2006;1:729-31.
14. Duran I, Riveros L, Berthold DR, et al. Eyelid metastasis from mediastinal teratoma with malignant transformation. Acta Oncol 2007;46:1200-1.
15. El Mesbahi O, Terrier-Lacombe M-J, Rebischung C, et al. Chemotherapy in patients with teratoma with malignant transformation. Eur Urol 2007;51:1306-11.
16. Chen C, Zheng H, Jiang S. An unusual case of giant mediastinal teratoma with malignant transformation. Ann Thorac Surg 2008;86:302-4.
17. Saitou M, Niitsuma K. A case of teratoma with malignant transformation in the anterior mediastinum. Nihon Kokyuki - Gakkai Zasshi 2008;46:526-9.
18. Sakurai H, Miyashita Y, Oyama T. Adenocarcinoma arising in anterior mediastinal mature cystic teratoma: report of a case. Surg Today 2008;38:348-51.
19. Shimizu K, Nakata M, Hirami Y, et al. Teratoma with malignant transformation in the anterior mediastinum. J Thorac Cardiovasc Surg 2008;136:225-7.
20. Khurana A, Mehta A, Kamboj M. Colonic-type adenocarcinoma (somatic-type malignancy) arising in a mediastinal mature cystic teratoma: a case report of a rare entity. Indian J Pathol Microbiol 2011;54:199-200.
21. Muramatsu T, Nishii T, Ohmori K, Shiono M. Mature cystic teratoma with malignant transformation to adenocarcinoma. Ann Thorac Surg 2011;91:1971-3.
22. Kim J-Y, Lee C-H, Park W-Y, et al. Adenocarcinoma with sarcomatous dedifferentiation arising from mature cystic teratoma of the anterior mediastinum. Pathol Res Pract 2012;208:741-5.
23. Dechaphunkul A, Bigras G, Sawyer M. Response to 5-fluorouracil-based chemotherapy in a patient with metastatic colonic-type adenocarcinoma arising in a primary mediastinal-teratoma. Case Rep Oncol Med 2012;2012:729278.
24. Paliwal N, Gupta K, Dewan RK, Mullick S. Adenocarcinoma (somatic-typemalignancy) in mature teratoma of anterior mediastinum. Indian J Chest Dis Allied Sci 2013;55:39-41.

25. Abid H, Neji H, Haddar S, et al. Mediastinal mature teratoma with spontaneous malignant transformation. Rev Mal Respir 2013;30:424-8.
26. Habougit C, Yvorel V, Sulaiman A, et al. Mediastinal mature teratoma with malignant carcinomatous transformation (somatic-type malignancy) with metastatic course. Int J Surg Pathol 2015;23:682-4.
27. Lin C, Du Y, Li Y, et al. Superior mediastinal mature cystic teratoma with gastrointestinal adenocarcinoma transformation: Report of a case. Oncotarget 2016;7:38392-7.
28. Le Fèvre C, Vigneron C, Schuster H, et al. Metastatic mediastinal mature teratoma with malignant transformation in a young man with an adenocarcinoma in a Klinefelter's syndrome: Case report and review of the literature. Cancer Radiother 2018;22:255-63.
29. Murakami K, Hamaji M, Yoshizawa A, Date H. Sub-centimeter adenocarcinoma arising from mature mediastinal teratoma during 11 years of follow-up. Gen Thorac Cardiovasc Surg 2020;68:1543-6.
30. Athanasiou A, Vanel D, El Mesbahi O, et al. Non-germ cell tumors arising in germ cell tumors (teratoma with malignant transformation) in men: CT and MR findings. Eur J Radiol 2009;69:230-5.
31. Wick MR, Ulbright TM, Moreira AL, et al. Germ cell tumors with somatic-type malignancy. In: Travis WD, Brambilla É, Müller-Hermelink HK, Harris CC, editors. World Health Organization classification of tumors. Pathology and genetics of tumours of the lung, pleura, thymus, and heart. Lyon, France: IARC Press; 2015.
32. Giannatempo P, Pond GR, Sonpavde G, et al. Treatment and clinical outcomes of patients with teratoma with somatic-type malignant transformation: an international collaboration. J Urol 2016;196:95-100.
33. Chovanec M, Oravcova I, Demitrovicova L, et al. Malignant transformation of teratoma to adenocarcinoma with complete remission with all-trans retinoic acid-based treatment and surgery. Clin Genitourin Cancer 2016;14:e131-3.
34. Chang CC, Chang YL, Lee YC. Cystic malignant teratoma with early recurrence after intraoperative spillage. Ann Thorac Surg 2008;86:1971-3.
35. Comiter CV, Kibel AS, Richie JP, et al. Prognostic features of teratomas with malignant transformation: a clinicopathological study of 21 cases. J Urol 1998;159:859-63.

Online supplementary material:

Supplementary Table 1. Cases of mediastinal mature teratoma with malignant transformation with adenocarcinoma.