

# Rare primary malignant mixed Müllerian tumor of the mediastinum

## A case report

Chunming Wang, MD<sup>a</sup>, Riqiang Liu, MD<sup>b</sup>, Feifei Huang, MD<sup>c</sup>, Haiming Wei, MD<sup>d</sup>, Lei Yu, MD<sup>a,\*</sup>

### Abstract

**Rationale:** Malignant mixed Müllerian tumor (MMMT) of extragenital organs is rare, especially in male. To our knowledge, this is the first reported case of primary MMMT at the mediastinum in male.

**Patient concerns:** A 54-year-old male was admitted to the hospital due to repeated stimulating dry cough for 2 years. His systemic examination was unremarkable. Laboratory workup revealed that all blood indicators were within normal limits. But subsequent computerized tomography (CT) scans of chest showed an abnormal soft tissue density in the area of its left, measuring approximately 4 cm in anterior-posterior dimension and 7 cm in maximum transverse dimension.

**Diagnoses and Interventions:** The pathogenesis of these tumors remains controversial. The diagnosis is combined with biopsy and immunohistochemical staining. So, the patient underwent radical surgical resection and pathologic examination of the excised specimen was consistent with the diagnosis of MMMT. After surgery, he was treated by sequential chemoradiotherapy.

**Outcomes:** The patient died from tumor recurrence 16 months later.

**Lessons:** MMMT is a rare, highly aggressive tumor associated with interesting embryological origin, a definite diagnosis of which is only confirmed on pathological assessment. Due to its high degree of malignancy and high rate of recurrence, complete macroscopic excision of the tumor is recommended as soon as possible.

**Abbreviations:** CT = computerized tomography, MMMT = malignant mixed mesodermal tumors.

**Keywords:** carcinosarcoma, malignant mixed Müllerian tumor, mediastinum, mesodermal

## 1. Introduction

A malignant mixed Müllerian tumor [also called malignant mixed mesodermal tumors (MMMTs)] is a rare aggressive biphasic neoplasm. MMMT is a carcinosarcoma of uncertain origin most reported in the uterus and ovary.<sup>[1]</sup> There have been few extragenital MMMTs in females, which have been reported in various locations ranging from pelvic peritoneum to

diaphragm peritoneum. And rare examples have also been presented in the prostate and seminal vesicle under various designations in males. Through the literature retrieval, up to date, there has been no any report about the primary MMMT of mediastinum in male. Here, we report the first example on the left side of the anterior mediastinum in a 54-year-old male.<sup>[2,3]</sup>

## 2. Case report

The study was approved by the Biological and Medical Ethics Committee of the People's Hospital of Guangxi Zhuang Autonomous Region, and verbal informed consent was obtained from the patient and his legal surrogate. A 54-year-old male presented to our hospital with repeated stimulating dry cough for 2 years. He had no symptoms such as fever, chest pain, hemoptysis, shortness of breath, and denied any change in his appetite or weight. His medical history was unremarkable except for bronchitis for 1 year. He has got used to smoking about 2 packages and drinking 500 to 1000 mL of liquor per day for 40 years. His systemic examination was unremarkable.

Laboratory workup revealed that all blood tests, including blood routine, urine routine, liver function, blood urea nitrogen, serum creatinine, electrolytes, and tumor markers, were within normal limits. But subsequent computerized tomography (CT) scans of chest showed an abnormal soft tissue density in the area of its left, measuring approximately 4 cm in anterior-posterior dimension and 7 cm in maximum transverse dimension (Fig. 1). No any enlarged lymph node was noted.

In view of the above findings, a surgical consultation was obtained and video-assisted thoracoscopic surgery to resect the mass was performed. A mass measuring about 5 cm, which

Editor: N/A.

CW and RL are first coauthors.

Verbal informed consent in the study was obtained from participant. Ethical approval was given by the Medical Ethics Committee of the People's Hospital of Guangxi Zhuang Autonomous Region with the following reference number: Science-2017-01.

The authors have no conflict of interest.

<sup>a</sup> Departments of Intervention, <sup>b</sup> Departments of Hepatobiliary and Endocrine Surgery, the People's Hospital of Guangxi Zhuang Autonomous Region, <sup>c</sup> Guangxi Medical University Graduate School, <sup>d</sup> Departments of Pathology, the People's Hospital of Guangxi Zhuang Autonomous Region, Nanning, Guangxi, China.

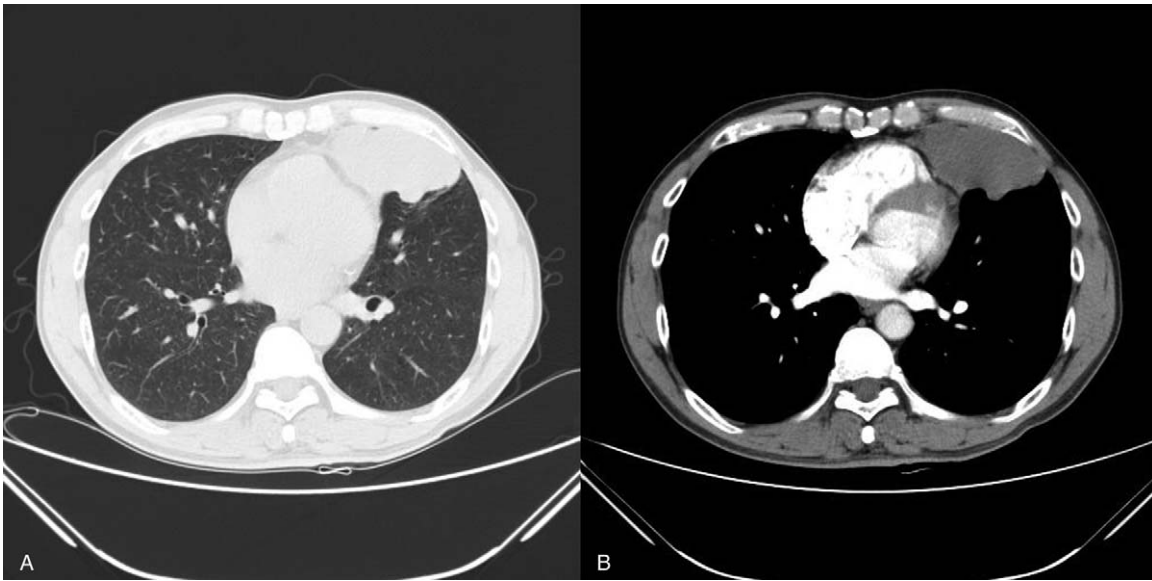
\* Correspondence: Lei Yu, Department of Intervention, The People's Hospital of Guangxi Zhuang Autonomous Region, No.6, Taoyuan Road, Nanning, Guangxi, People's Republic of China (e-mail: yulei@126.com).

Copyright © 2018 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Medicine (2018) 97:42(e12903)

Received: 4 May 2018 / Accepted: 27 September 2018

<http://dx.doi.org/10.1097/MD.00000000000012903>

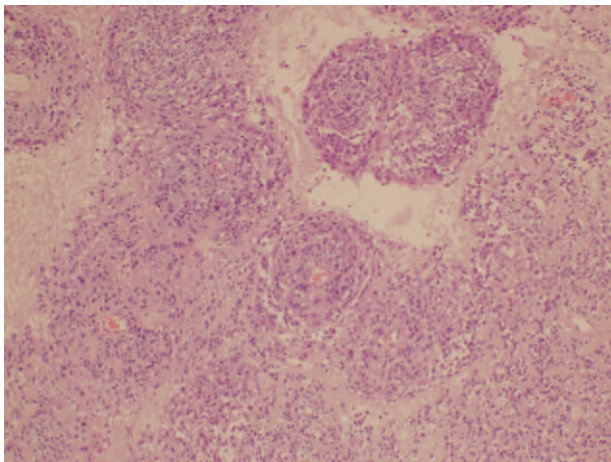


**Figure 1.** (A, B) Computed tomography of the chest showing an abnormal soft tissue density involving the left anterior mediastinum measuring 7 cm × 4 cm.

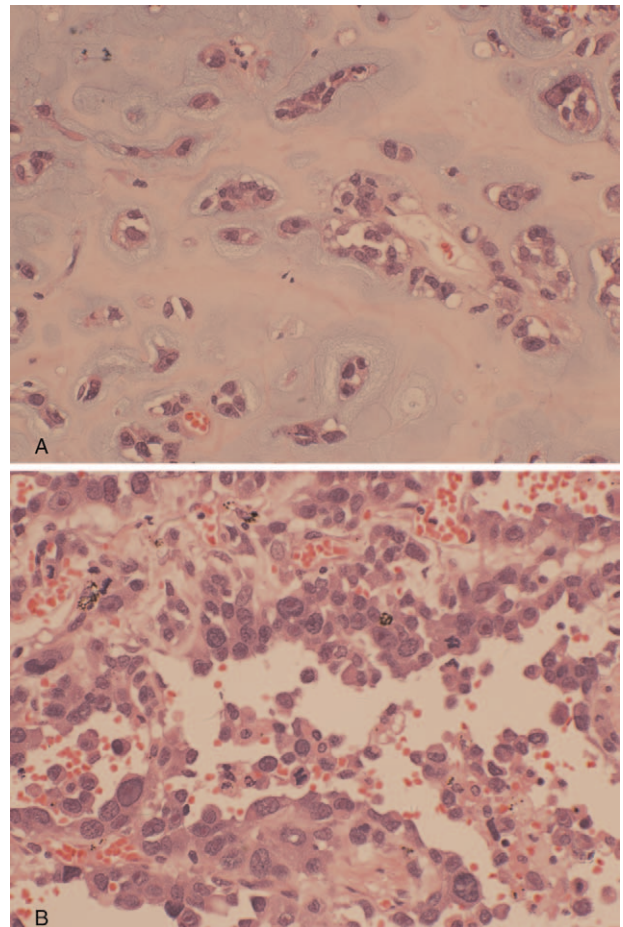
included partial pericardium and lung tissue, was removed completely. Patient tolerated the procedure well and his postoperative period was uneventful.

Histological assessment of the specimen revealed findings consistent with a MMMT. The tumor was composed of variably heterotypic cells. Tumor is variably cellular, consisting of spindle cells, showing prominent nuclear atypia and mitotic activity (Fig. 2). Besides, malignant osteoid and chondroid type of heterologous elements were shown (Fig. 3). Immunohistochemistry revealed neoplastic cells positive for calponin, cytokeratin, S-100, and vimentin (Fig. 4). According to the above, both the combined morphology and immunohistochemical results were of a carcinosarcoma, supporting a Müllerian primary.

Following surgery, patient was treated with 6 cycles of chemotherapy (carboplatin and paclitaxel) followed by 2 irradiation cycles. Unfortunately, the patient died from tumor recurrence 16 months later.

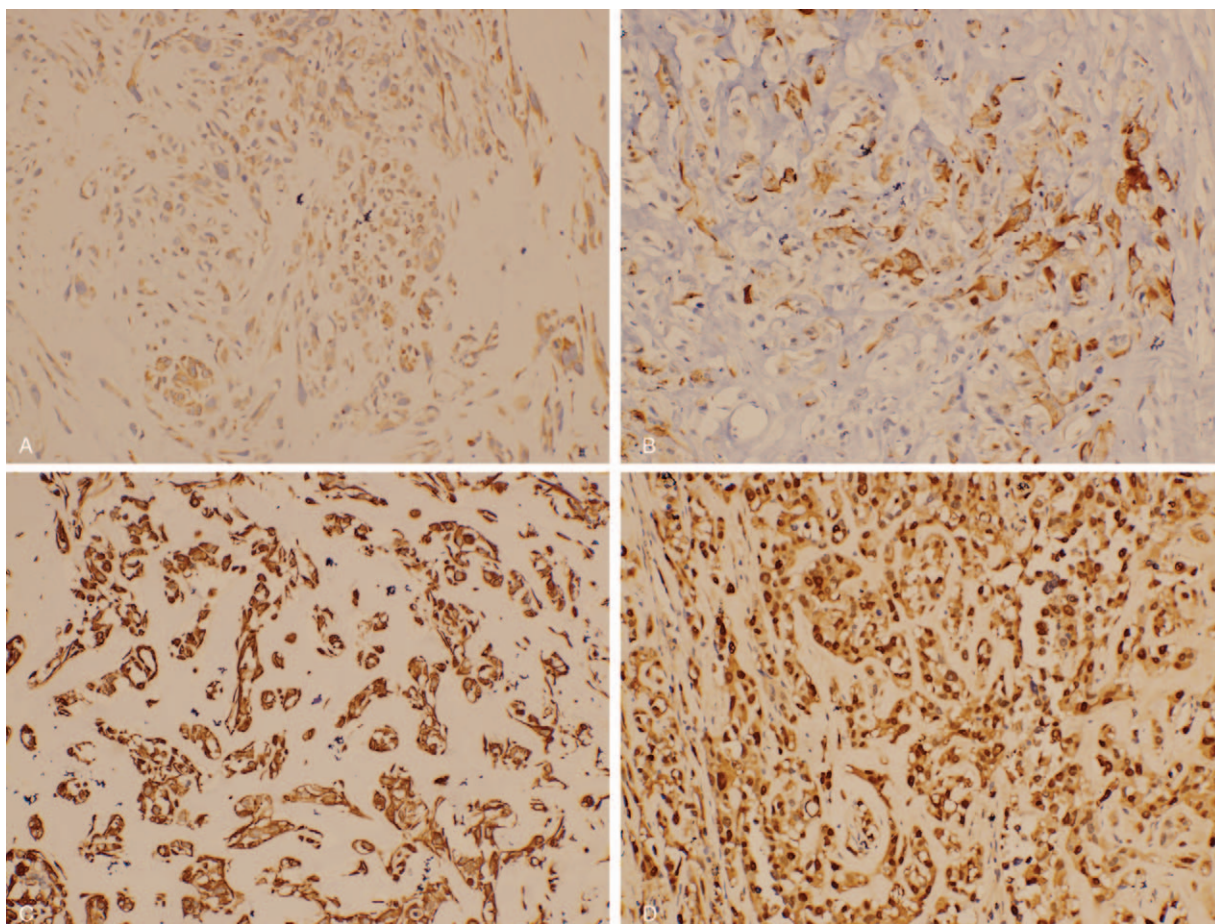


**Figure 2.** Tumor is variably cellular, consisting of spindle cells, showing prominent nuclear atypia and mitotic activity. Varying numbers of thick-walled arterioles are present (H&E, original magnification × 100).



**Figure 3.** H&E high-power view showing both malignant epithelial and mesenchymal elements. (A) (200×) H&E: showing squamous differentiation; (B) (200×) H&E: high power of malignant osteoid.





**Figure 4.** Immunohistochemistry: tumor cells are positive for keratin (A, 200 $\times$ ) and calponin (B, 200 $\times$ ) on the epithelioid components; tumor cells show strong diffuse expression for mesenchymal markers: vimentin (C, 200 $\times$ ) and S-100 (D, 200 $\times$ ).

### 3. Discussion

A “malignant mixed Müllerian tumor” (MMMT) or carcinosarcoma is composed of intimately admixed malignant epithelial and mesenchymal elements. MMMTs most commonly arise in the uterus, which account for 2% to 5% of all malignancies of the uterine corpus, but these tumors can also be found in other parts of the female genital tract such as the cervix, fallopian tubes, vagina, and ovaries, where they have historically termed MMMTs due to their embryological origin.<sup>[4,5]</sup>

Extragenital MMMTs such as female peritoneum, stomach, colon, hepatobiliary system, urinary tract, thyroid, spleen, and breast, have been reported in the literature, but they are uncommon, especially in male.<sup>[6–8]</sup> In males, only a few of similar tumors have been described in the prostate, testis, and seminal vesicles.<sup>[6,9,10]</sup> The tumor we present arising in the anterior mediastinum is morphologically similar to mesodermal (Müllerian) adenosarcoma of the uterus.<sup>[2]</sup> The finding of MMMT in this location is extremely rare. To the best of our knowledge, there are only 2 cases in female patients reported by Gale et al<sup>[11]</sup> and this is the first reported case of a primary anterior mediastinum MMMT in a male patient. In this case, there was a single mass replacing part of the anterior mediastinum substance. And there was no primary neoplasm shown in other positions of the body by related examinations such as the preoperative and postoperative CT scans, surgical examination of the chest, endoscopic examination of the gastrointestinal tract, and testicular ultrasound.

The pathogenesis of carcinosarcoma is uncertain. The explanation for the origin of the histological features of these tumors focuses almost entirely on the 3 following theories. The “conversion” theory postulates that these tumors develop as a result of the metaplastic transformation of one neoplastic cell type into another. The “combination” theory postulates that both populations would originate from a common undifferentiated, totipotent neoplastic cell precursor. The “collision” theory proposes that these tumors arise from a mixture of 2 distinct separate and independent neoplastic populations, that is, a carcinoma and a sarcoma. According to recent ultrastructural and immunohistochemical findings reported by Gorstein and Anderson<sup>[12]</sup> and De Brito et al,<sup>[13]</sup> which showed the simultaneous coexpression of markers (especially keratin and vimentin) in the epithelial and the mesenchymal-like components, the conversion or the combination theories were more supported. As we know by now, both carcinosarcomas in the female genital tract and those that arise outside the genital tract in females are included in the category of endometrioid neoplasms. In males, rare Müllerian-derived lesions have been described and they have been reported to occur only in the genital area. However, although a theoretical possibility, given that matter evidence of it in the examined tissues, endometriosis cannot constitute the origin of carcinosarcoma in our patient.<sup>[6,9]</sup>

Both epithelial and mesenchymal elements in a carcinosarcoma are malignant. The mesenchymal elements in our case are

chondrosarcoma, which are similar to their more frequent counterparts in the female genital tract.<sup>[14]</sup> But the epithelial component-malignant myoepithelioma in our case is scarce. Various immunohistochemical stains, thought to be useful in the diagnosis of a carcinosarcoma, have been widely investigated. The malignant epithelial elements show a generalized immunoreactivity for anticytokeratin antibodies and epithelial membrane antigen (EMA). Immunohistochemistry revealed the mesenchymal elements positive for vimentin.<sup>[15]</sup> The neoplasm in our case expresses both epithelial markers (keratin and calponin) and mesenchymal markers (vimentin and S-100).

The differential diagnosis in this case should be made with immature teratoma. Immature teratoma arising from a primordial germ cell usually occurs in much younger patients, which comprises embryonal neuroectodermal elements and typically shows endodermal derivatives. But there is no evidence to suggest that the tumor we describe is a teratoma because no teratomous elements are seen after thorough sampling and testicular tumor markers are normal in this case.

Due to the limited number of cases reported, no guidelines have been established with regard to the standard treatment for MMMTs. The mainstay of treatment is complete macroscopic excision of the tumor, which may provide the best chance of survival, but most tumors are metastatic at the time of diagnosis, making radical resection difficult. There is no consensus concerning optimal chemotherapeutic regimens, because these tumors are so rare. Various chemotherapeutic agents have been used in the past for treating MMMTs. So far, combination of platinum-based chemotherapy and paclitaxel appears to be superior to other chemotherapy regimens in terms of toxicity and patient tolerance.<sup>[16]</sup> Unfortunately, regardless of the treatment, the prognosis of the neoplasm is generally poor. The median survival time for these patients has been demonstrated: the 2-year survival rate for stage I disease is 53%, which decreases to 8.5% in stages II and III.<sup>[1]</sup> Our patient died within 16 months of diagnosis.

#### 4. Conclusion

MMMT is a rare, highly aggressive tumor associated with interesting embryological origin. Preoperative diagnosis under imaging examinations was uncertain and making a definite diagnosis was only confirmed on pathological assessment. The optimal management is still under debate, from surgical approach to postoperative adjuvant treatment with sequential radiation and chemotherapy. Although MMMTs carry a dismal prognosis, but morphologically similar tumors in other sites generally have a better prognosis when completely excised with negative margins. So, wide surgical excision as early as possible is

recommended as the preferred treatment option, regardless of the adjuvant therapy used.

#### Author contributions

**Conceptualization:** Lei Yu.

**Formal analysis:** Haiming Wei.

**Investigation:** Feifei Huang.

**Supervision:** Lei Yu.

**Writing – original draft:** Chunming Wang.

**Writing – review & editing:** Riqiang Liu, Lei Yu.

#### References

- [1] Kanthan R, Senger JL, Diudea D. Malignant mixed Müllerian tumors of the uterus: histopathological evaluation of cell cycle and apoptotic regulatory proteins. *World J Surg Oncol* 2010;8:60.
- [2] Eichhorn JH, Young RH, Clement PB, Scully RE. Mesodermal (Müllerian) adenosarcoma of the ovary: a clinicopathologic analysis of 40 cases and a review of literature. *Am J Surg Pathol* 2002;26:1243–58.
- [3] Williamson JM, Stevens M, Mahon D. Metachronous small bowel metastasis from a mixed Müllerian mesodermal tumour. *Ann R Coll Surg Engl* 2016;98:26–8.
- [4] Silverberg SG, Major FJ, Blessing JA, et al. Carcinosarcoma (malignant mixed mesodermal tumor) of the uterus. A Gynecologic Oncology Group pathologic study of 203 cases. *Int Gynecol Pathol* 1990;9:1–9.
- [5] Costa MJ, Tidd C, Willis D. Cervicovaginal cytology in carcinosarcoma [malignant mixed müllerian (mesodermal) tumor] of the uterus. *Diagn Cytopathol* 1992;8:33–40.
- [6] Laurila P, Leivo I, Makisalo H, et al. Müllerian adenosarcoma-like tumor of the seminal vesicle. *Arch Pathol Lab Med* 1992;116:1072–6.
- [7] Shah S, Kim DH, Harster G, Hossain A. Carcinosarcoma of the colon and spleen: a fleshy purple mass on colonoscopy. *Dig Dis Sci* 2001;46:106–8.
- [8] Tsekouras DK, Katsaragakis S, Theodorou D, et al. Rectal carcinosarcoma: a case report and review of literature. *World J Gastroenterol* 2006;12:1481–4.
- [9] Manivel C, Shenoy BV, Wick MR, Dehner LP. Cystosarcoma phyllodes of the prostate. A pathologic and immunohistochemical study. *Arch Pathol Lab Med* 1986;110:534–8.
- [10] Mazur MT, Myers JL, Maddox WA. Cystic epithelial-stromal tumor of the seminal vesicle. *Am J Surg Pathol* 1987;11:210–7.
- [11] Gale JT, Mendelson DS, Cohen BA, Teirstein AS. Benign mixed tumor of salivary gland origin presenting as a mediastinal mass. *J Comput Tomogr* 1986;10:23–5.
- [12] Gorstein F, Anderson TL. Malignant mixed mesodermal tumors: carcinoma, sarcoma, or both? *Hum Pathol* 1991;22:207–9.
- [13] De Brito PA, Silverberg SG, Orenstein JM. Carcinosarcoma (malignant mixed müllerian (mesodermal) tumor) of the female genital tract: immunohistochemical and ultrastructural analysis of 28 cases. *Hum Pathol* 1993;24:132–42.
- [14] Singh R. Review literature on uterine carcinosarcoma. *J Cancer Res Ther* 2014;10:461–8.
- [15] Artioli G, Wabersich J, Ludwig K, et al. Rare uterine cancer: carcinosarcomas. Review from histology to treatment. *Crit Rev Oncol Hematol* 2015;94:98–104.
- [16] Duska LR, Garrett A, Eltabbakh GH, et al. Paclitaxel and platinum chemotherapy for malignant mixed müllerian tumors of the ovary. *Gynecol Oncol* 2002;85:459–63.