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Case Report:

Primary splenic carcinosarcoma with local invasion of chest wall: a rare case*

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Abstract: We herein present a case of carcinosarcoma arising as a primary lesion in the spleen with the presence of local invasion of chest wall prior to widespread metastasis all over the body of a female aged 64 years. The detailed information of therapy and imaging evidences of morphology, histology, and immunohistochemistry are fully provided. To the best of our knowledge, this is the fifth reported case of a primary splenic carcinosarcoma and even the first case to be described with local invasion in the mongoloid. Carcinosarcoma that develops in the spleen with local invasion is extremely rare.

Key words: Spleen; Carcinosarcoma; Chest wall invasion
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1 Introduction

Carcinosarcomas, containing both epithelial and connective tissue components, are rare malignant neoplasms, which commonly arise from the female genital tract (Steeper *et al*., 1983; Gadducci and Romanini, 2001; Cicin *et al*., 2008), and sometimes from extragenital sites (Isimbaldi *et al*., 1996; di Vizio *et al*., 2001). Carcinosarcomas originating in the spleen are extraordinarily rare. There have been no more than four reported cases of primary carcinosarcomas of the spleen in English-language literature. Westra *et al*. (1994) reported the first case of primary splenic carcinosarcoma, which was thought to arise from the mesothelium, reflecting the unique capacity of the female mesothelium for mullerian differentiation. Rao *et al*. (2007) reported a case of splenic carcinosarcoma of a male, which was characterized by the presence of an osteosarcomatous element and raised β human chorionic gonadotropin (β-hCG) levels. Kochar *et al*. (2009) presented a Caucasian man with a high-grade malignant pleomorphic tumor with areas of necrosis, and this case revealed osteosarcomatous differentiation and a spindle and epithelioid morphology. Most recently, Joy *et al*. (2012) reported another case of primary splenic carcinosarcoma. However, no imaging evidence of morphology, histology, or immunohistochemistry was provided. Herein, we report a case of carcinosarcoma arising as a primary lesion in the spleen of a female aged 64 years. The feature of this tumor is the presence of local invasion of the chest wall prior to wide metastasis all over the body. As far as we are aware, this is the fifth reported case of a primary splenic carcinosarcoma and the first case to be described with the local invasion in the mongoloid.

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2 Case presentation

The patient is a 64-year-old mongoloid female who was admitted with persistent dull pain of the left middle trunk, limited to the left upper quadrant and left lower anterior chest wall. She denied any other symptoms, except for occasional shortness of breath. She gave a medical history of hypertension. On physical examination, there was tenderness in the left upper quadrant and left lower anterior chest wall. There were no palpable lymph nodes or mass, and chest examination revealed decreased breath sound of the left lung. Blood analysis showed an elevated white cell count (11.4×10^9 cells/L) and mild anaemia. The analysis of tumor markers showed elevated carcinoembryonic antigen (CEA, 12.95 ng/ml), cancer antigen 125 (CA125, 1041.90 U/ml), and CA153 (119.70 U/ml). The other markers including CA199 and alphafetoprotein (AFP), as well as other hematological and biochemical parameters, were normal. Chest radiograph showed a moderate amount of effusion of the left pleural cavity (Fig. 1a), and percutaneous drainage was performed. Abdominal ultrasound showed a markedly enlarged spleen with a diameter of 22 cm, with a mass of abnormally high echogenicity in the lower splenic pole and areas of low echogenicity within the spleen, but no ascites. Computed tomography (CT) showed a high-density mass in the lower pole of the spleen (Fig. 1b), accompanied by multiple cystic solid mass in the spleen and a 6.1 cm×3.6 cm mass shadow with the bone destruction of the left anterior fifth rib (Fig. 1c). The upper gastrointestinal endoscopy, as well as colonoscopy, was also performed without positive findings. The positron emission tomography/computed tomography (PET/CT) scan confirmed multiple low-density mass and one high-density mass distributed in the spleen, and a soft tissue mass shadow with local rib destruction (Figs. 1d and 1e). There were no other abnormalities found on the PET/CT. Accordingly, primary splenic malignancy was first considered. Then the persistent severe pain caused by the tumors had brought an intolerable burden on her body and mentality. This patient has no pertinent family history, In consideration of the limited distribution of tumors, the palliative splenectomy in combination with resection of the rib tumor was performed. An open radical resection was performed (Yan *et al*., 2015) and the operation showed an enlarged spleen adhesive to the surrounding chest wall, splenic flexure of colon and diaphragm. The other internal organs were entirely normal.

The tissue samples were prepared and embedded in paraffin. The paraffin blocks were sectioned to a thickness of 5 μm and stained with hematoxylin and eosin (H&E). Stained sections were visualized under an optical microscope. The procedures of immunohistochemistry were performed on an automated Ventana BenchMark immunostainer (Roche, Basel, Switzerland) at the Department of Pathology, the Second Affiliated Hospital, School of Medicine, Zhejiang University, China.

Postoperatively, the intractable pain was obviously relieved, and even disappeared. One month post operation, follow-up indicated that this patient recovered well without evident recurrence of tumor and could do some housework.

The patient was then reviewed by an oncologist who advised treatment with palliative chemotherapy, consisting of cisplatin and etoposide.

3 Results

3.1 Gross observation

The spleen was enlarged, weighing 2980 g and measuring 25 cm×15 cm×15 cm. The external surface was bosselated, and the cut surface revealed an undefined, heterogenous soft mass in the lower pole, measuring up to 9.0 cm×8.0 cm×4.2 cm (Fig. 2a). The dividing line was not clear all round the mass, and there was no obvious coating observed. The multiple cystic solid mass proved to be hematoncus.

The rib mass appeared as a soft grayish-white mass with the size of 4.0 cm×3.0 cm×2.0 cm, and adhered seriously to the surrounding bone and intercostal muscles.

3.2 Optical microscopy

Histological images showed a low-grade malignant tumor of patchy distribution, accompanied by areas of necrosis. The neoplasm without coating invaded the normal tissue of the spleen. There were distinct areas of necrotic tissue. The rest of the tumor showed a spindle and epithelioid morphology on optical microscopy. The spindle tumor cells showed no distinctive atypia and fewer mitoses, while the epithelioid cells varied in size and shape, and had a

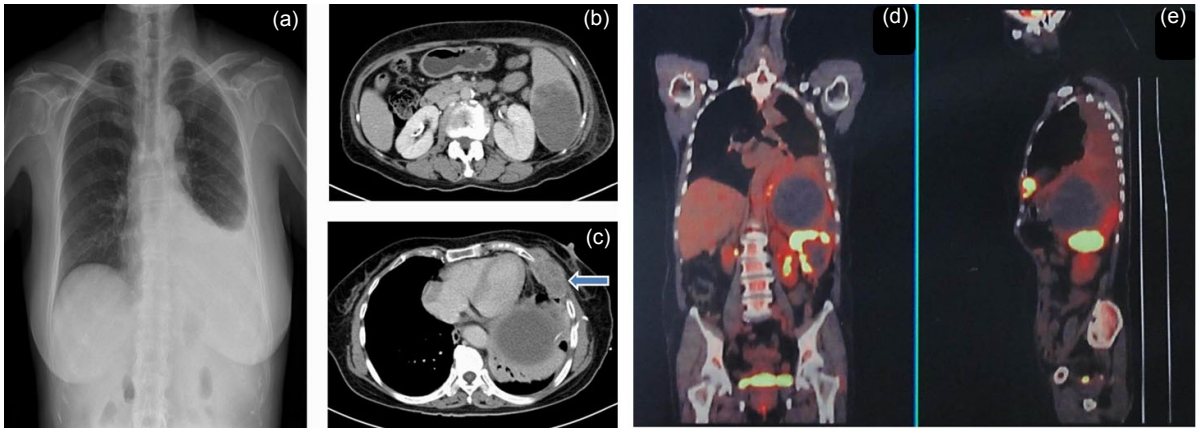

Fig. 1 Imaging diagnosis

(a) Chest radiograph showed a moderate amount of effusion of the left pleural cavity. (b, c) Computed tomography (CT) showed a high-density mass in the lower pole of the spleen (b), accompanied by multiple cystic solid mass in the spleen and a 6.1 cm×3.6 cm mass shadow with the bone destruction of the left anterior fifth rib (blue arrow) (c). (d, e) The positron emission tomography/computed tomography (PET/CT) scan confirmed multiple low-density mass and one high-density mass distributed in the spleen, and a soft tissue mass shadow with local rib destruction. There were no other abnormalities found on the PET/CT

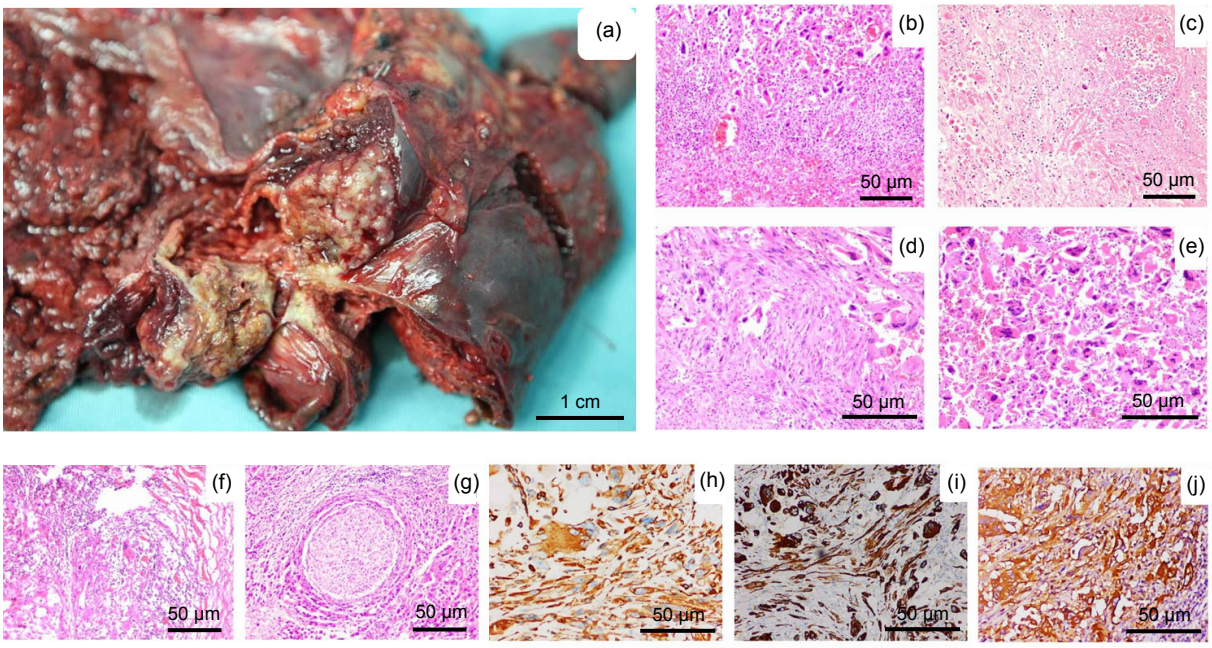

Fig. 2 Pathological diagnosis

(a) Gross section of spleen showing tumor nodule located in the lower pole. (b–e) Histological appearance of splenic carcinosarcoma: (b) shows the coexistence of tumor tissue and normal splenic tissue; (c) shows lots of necrotic tissues in the central region of the tumor; (d) shows the sarcomatous component composed of uniform spindle cells arranged in a fascicular pattern; (e) shows the carcinomatous component composed of irregular granular cells, showing frequent megakaryocytes. (f–g) Histological appearance of the metastatic tumor of the chest wall: (f) shows the tumor tissue invading the striated muscle; (g) shows the tumor tissue encompassing the nerve fiber. (h–j) Splenic carcinosarcoma immunohistochemistry: (h) indicates that sarcomatous areas show strong immunostaining for vimentin; (i) indicates that carcinomatous areas reveal strong positive staining for cytokeratin (CK; pan); (j) shows positive epithelial membrane antigen (EMA) immumohistochemistry

vague boundary (Figs. 2b–2e). The neoplasm of chest wall also showed cellular morphologies similar to the splenic malignancy. The tumor tissue, invading the surrounding striated muscle and encompassing the nerve fiber, was also observed (Figs. 2f and 2g). There was no evidence of any glandular or squamous differentiation. There were no features of any other sarcoma.

The tissue samples resected from splenic flexure of the colon and diaphragm proved histologically to be tissue hyperplasia caused by chronic inflammation.

3.3 Immunohistochemistry

For immunohistochemical analysis, the tumor cells revealed strong immunoreactivity for vimentin (Fig. 2h). There was patchy but convincing positivity for cytokeratin (CK; pan) and epithelial membrane antigen (EMA) (Figs. 2i and 2j). The tumor cells were negative for F8, CD31, CD34, SMA, Desmin, S100, HMB-45, Calretinin, HBME-1, and TTF-1, and focally weakly positive for CD68.

To summarize, this was a poorly differentiated malignant tumor with essentially 2 components, i.e. the spindle and epithelioid components. This is consistent with a carcinosarcoma showing heterologous differentiation.

4 Discussion

Carcinosarcomas are rare biphasic malignant tumors. Histological analysis of tumors has shown characteristics of epithelial carcinoma and mesenchymal differentiation. They occurred in many anatomical locations such as the female genital tract (Dave *et al*., 2011; Kanthan and Senger, 2011), pelvic peritoneum (Ko *et al*., 2005), breast (Cornette *et al*., 2005), stomach (Iezzoni and Mills, 1993), colon (Isimbaldi *et al*., 1996), pancreas (Darvishian *et al*., 2002; Chmiel *et al*., 2005), head and neck, respiratory system, hepatobiliary system, thyroid, thymus, and skin. A malignant mass arising within the spleen is most commonly of a lymphoreticular origin (Kochar *et al*., 2009). The finding of carcinosarcoma in the spleen is very rare. In this case, sarcomatous areas consisted of uniform spindle cells, while carcinomatous areas were composed of irregular granular cells with frequent megakaryocytes.

The signs and symptoms for primary splenic malignancy lack specificity. Many preoperative and/or postoperative examinations, such as physical examination, abdominal ultrasound, CT scan, and endoscopic examination of the gastrointestinal tract, have to be conducted to exclude the metastatic neoplasms prior to the diagnosis of primary splenic tumor (Kochar *et al*., 2009). In our limited experience, PET/CT could be helpful to the above procedures. In addition, the collision tumor representing synchronous carcinoma and sarcoma from separate sources (Thompson *et al*., 1996), and endometriosis-associated extragenital carcinosarcomas (Booth *et al*., 2004), should also be differentially diagnosed from primary carcinosarcoma of the spleen.

The histogenesis and biological behavior of carcinosarcoma are not fully understood. Surface mesothelium has been proposed as the origin of splenic epithelial tumors (Rao *et al*., 2007). Some people stated that such tumors arose from invaginated mesothelium of malignant transformation or a preexisting embryonic rest (Morinaga *et al*., 1992; Rao *et al*., 2007). We are more inclined to believe that the neoplasm in this case probably arose directly from the spleen, in the absence of evidence to support metastasis from other sites. So far, the survival time of splenic carcinosarcoma patients post operation ranged from 3 to 12 months (Westra *et al*., 1994; Rao *et al*., 2007; Kochar *et al*., 2009; Joy *et al*., 2012). This may be because of the rapid spread and highly invasive nature of these lesions (Rao *et al*., 2007). The metastatic paths of carcinosarcoma could include the bloodstream and lymphatic metastasis, local spread, and so on. In our case, only local metastasis of the chest wall occurred, and resulted in severe pain, which could be related to the early stage of this tumor. Follow-up observation will determine whether other metastasis happened subsequently.

To date, there are no guidelines available for the treatment of splenic carcinosarcoma. It is generally agreed that complete macroscopic excision of the malignancy may provide the best chance of survival (Kochar *et al*., 2009). Postoperatively, adjuvant treatments, such as chemotherapy and radiotherapy, should be under consideration to further kill the tumor cells and improve the prognosis of patients. For chemotherapy, both the carcinomatous and the sarcomatous components have to be addressed. There is no consensus

concerning optimal chemotherapeutic regimes (Kochar *et al*., 2009). Ifosfamide and cisplatin combination therapy has been reported to offer a better survival rate (Ko *et al*., 2005). Cyclophosphamide-doxorubicin-containing chemotherapy has been suggested for breast carcinosarcoma (Cornette *et al*., 2005). Some researchers stated that carcinosarcomas responded better to cisplatin-based regimes (Gadducci and Romanini, 2001). Some other regimens, such as ovarian-type chemotherapeutic regimens combining cisplatin, etoposide, cyclophosphamide, doxorubicin and paclitaxel, sarcoma-type regimens combining doxorubicin, ifosfamide, and dacarbazine, were also reported for carcinosarcomas (Resnik *et al*., 1995; Cass *et al*., 1996; Cicin *et al*., 2008). For splenic carcinosarcoma, Kochar *et al*. (2009) applied cisplatin and etoposide combination therapy to treat a 60-year-old Caucasian man, who died 7 months after diagnosis attributed to the wide metastasis. Although various combinations of chemotherapy have been explored, an optimal therapeutic modality is yet to be determined (Kanthan and Senger, 2011).

Adjuvant radiotherapy has been used to treat carcinosarcoma (Park *et al*., 2011). However, its value in addition to systemic treatment remains ill-defined (Dave *et al*., 2011). Park *et al*. (2011) investigated the influence of adjuvant radiotherapy on patterns of failure and survivals in uterine carcinosarcoma, and indicated that adjuvant radiotherapy after surgical resection was effective in decreasing loco-regional recurrence, and most treatment failures were due to distant metastasis. The combined chemo-radiotherapeutic approach has also been adopted and has shown survival benefit for uterine carcinosarcoma patients (Galaal *et al*., 2009). In brief, multimodal therapy including surgery, radiotherapy, and chemotherapy might be an optimal treatment. Ko *et al*. (2005) reported a case of a primary carcinosarcoma of the pelvic peritoneum with five-year disease-free survival after managing the patient with surgery, chemotherapy, and radiotherapy.

Evidence gained from the above regimens for carcinosarcomas of different original sites may be beneficial for the treatment of the splenic tumor. It seems unlikely to be able to conduct any trial to test different regimes, because these tumors are so rare. Regardless of the treatment, the prognosis of carcinosarcoma is universally poor.

5 Conclusions

Splenic carcinosarcoma is a rare tumor with embryological origin. There have been just four previously reported cases of primary splenic carcinosarcoma. Every effort should be made to carefully exclude other primary sites before reaching the diagnosis of primary carcinosarcoma. There is no consensus regarding the optimal treatment strategy for this disease. Multimodal therapy including surgery, radiotherapy, and chemotherapy might be an optimal treatment. The prognosis of carcinosarcoma is universally poor.

Contributors

Yun ZHANG carried out the work of diagnosis and treatment; Ting SUN and Gui-feng WANG wrote and revised the paper.

Compliance with ethics guidelines

Ting SUN, Gui-feng WANG, and Yun ZHANG declare that they have no conflict of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from the patient for being included in the study.

References

Booth, C., Zahn, C.M., McBroom, J., *et al*., 2004. Retroperitoneal müllerian carcinosarcoma associated with endometriosis: a case report. *Gynecol. Oncol*., **93**(2):546-549. http://dx.doi.org/10.1016/j.ygyno.2004.01.018

Cass, I., Resnik, E., Chambers, J.T., *et al*., 1996. Combination chemotherapy with etoposide, cisplatin, and doxorubicin in mixed müllerian tumors of the adnexa. *Gynecol. Oncol*., **61**(3):309-314. http://dx.doi.org/10.1006/gyno.1996.0148

Chmiel, B., Wodolazski, A., Kozaczka, A., 2005. Carcinosarcoma of the pancreas—case report and literature review. *Wiad. Lek*., **58**(3-4):243-246 (in Polish).

Cicin, I., Saip, P., Eralp, Y., *et al*., 2008. Ovarian carcinosarcomas: clinicopathological prognostic factors and evaluation of chemotherapy regimens containing platinum. *Gynecol. Oncol*., **108**(1):136-140. http://dx.doi.org/10.1016/j.ygyno.2007.09.003

Cornette, J., Tjalma, W.A., Buytaert, P., 2005. Biphasic sarcomatoid carcinoma or carcinosarcoma of the breast: prognosis and therapy. *Eur. J. Gynaecol. Oncol*., **26**(5):514-516.

Darvishian, F., Sullivan, J., Teichberg, S., *et al*., 2002. Carcinosarcoma of the pancreas: a case report and review of the

literature. *Arch. Pathol. Lab. Med.*, **126**(9):1114-1117. http://dx.doi.org/10.1043/0003-9985(2002)126<1114:COTP>2.0.CO;2

Dave, K.S., Chauhan, A., Bhansali, R., *et al*., 2011. Uterine carcinosarcomas: 8-year single center experience of 25 cases. *Indian J. Med. Paediatr. Oncol*., **32**(3):149-153. http://dx.doi.org/10.4103/0971-5851.92814

di Vizio, D., Insabato, L., Conzo, G., *et al*., 2001. Sarcomatoid carcinoma of the colon: a case report with literature review. *Tumori*, **87**(6):431-435.

Gadducci, A., Romanini, A., 2001. Adjuvant chemotherapy in early stage uterine sarcomas: an open question. *Eur. J. Gynaecol. Oncol*., **22**(5):352-357.

Galaal, K., Kew, F.M., Tam, K.F., *et al*., 2009. Evaluation of prognostic factors and treatment outcomes in uterine carcinosarcoma. *Eur. J. Obstet. Gynecol. Reprod. Biol*., **143**(2):88-92. http://dx.doi.org/10.1016/j.ejogrb.2008.12.014

Iezzoni, J.C., Mills, S.E., 1993. Sarcomatoid carcinomas (carcinosarcomas) of the gastrointestinal tract: a review. *Semin. Diagn. Pathol*., **10**(2):176-187.

Isimbaldi, G., Sironi, M., Assi, A., 1996. Sarcomatoid carcinoma of the colon: report of the second case with immunohistochemical study. *Pathol. Res. Pract*., **192**(5):483-487. http://dx.doi.org/10.1016/S0344-0338(96)80015-X

Joy, E.R., Cornish, J.A., Bootun, R., *et al*., 2012. Primary carcinosarcoma of the spleen. *J. Surg. Case Rep*., **2012**(7):3. http://dx.doi.org/10.1093/jscr/2012.7.3

Kanthan, R., Senger, J.L., 2011. Uterine carcinosarcomas (malignant mixed Müllerian tumours): a review with special emphasis on the controversies in management. *Obstet. Gynecol. Int*., **2011**:470795. http://dx.doi.org/10.1155/2011/470795

Ko, M.L., Jeng, C.J., Huang, S.H., *et al*., 2005. Primary peritoneal carcinosarcoma (malignant mixed mullerian tumor): report of a case with five-year disease free survival after surgery and chemoradiation and a review of literature. *Acta Oncol*., **44**(7):756-760. http://dx.doi.org/10.1080/02841860500252016

Kochar, K., Vijayasekar, C., Pandey, U., *et al*., 2009. Primary carcinosarcoma of the spleen: case report of a rare tumor and review of the literature. *Int. J. Surg. Pathol*., **17**(1):72-77. http://dx.doi.org/10.1177/1066896908316070

Morinaga, S., Ohyama, R., Koizumi, J., 1992. Low-grade mucinous cystadenocarcinoma in the spleen. *Am. J. Surg. Pathol*., **16**(9):903-908.

Park, H.J., Kim, H.J., Wu, H.G., *et al*., 2011. The influence of adjuvant radiotherapy on patterns of failure and survivals in uterine carcinosarcoma. *Radiation Oncol. J*., **29**(4):228-235. http://dx.doi.org/10.3857/roj.2011.29.4.228

Rao, A., Mathew, G., Marimuthu, K., *et al*., 2007. Carcinosarcoma of the spleen: literature review of a very rare tumour. *Open Med.*, **2**(2):230-235. http://dx.doi.org/10.2478/s11536-007-0011-9

Resnik, E., Chambers, S.K., Carcangiu, M.L., *et al*., 1995. A phase II study of etoposide, cisplatin, and doxorubicin chemotherapy in mixed Müllerian tumors (MMT) of the uterus. *Gynecol. Oncol*., **56**(3):370-375. http://dx.doi.org/10.1006/gyno.1995.1065

Steeper, T.A., Piscioli, F., Rosai, J., 1983. Squamous cell carcinoma with sarcoma-like stroma of the female genital tract. Clinicopathologic study of four cases. *Cancer*, **52**(5):890-898. http://dx.doi.org/10.1002/1097-0142(19830901)52:5<890::AID-CNCR2820520525>3.0.CO;2-T

Thompson, L., Chang, B., Barsky, S.H., 1996. Monoclonal origins of malignant mixed tumors (carcinosarcomas): evidence for a divergent histogenesis. *Am. J. Surg. Pathol*., **20**(3):277-285.

Westra, W.H., Anderson, B.O., Klimstra, D.S., 1994. Carcinosarcoma of the spleen: an extragenital malignant mixed müllerian tumor? *Am. J. Surg. Pathol*., **18**(3):309-315.

Yan, J.F., Kuang, T.T., Ji, D.Y., *et al*., 2015. Laparoscopic versus open distal pancreatectomy for benign or premalignant pancreatic neoplasms: a two-center comparative study. *J. Zhejiang Univ.-Sci. B (Biomed. & Biotechnol.)*, **16**(7):573-579. http://dx.doi.org/10.1631/jzus.B1400257

中文概要

题　目：一例脾脏原发性肉瘤侵犯胸壁的病例报道

概　要：本文报道了一例伴有胸壁局部侵犯的脾脏原发性肉瘤的 64 岁女性病例。在采用正电子发射计算机断层显像（PET/CT）等先进方法对肿瘤及转移灶进行了及时准确的诊断后，患者接受了根治性手术。同时标本经过苏木精-伊红染色法（H&E）和免疫组化等检查进一步明确了脾脏原发性肉瘤的病理学诊断结果。据我们所知，这是目前世界上第五例原发性脾脏肉瘤的报道，同时也是第一例伴有局部胸壁侵犯并获得手术根治的脾脏肉瘤的报道。

关键词：脾脏；肉瘤；胸壁侵犯