Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://Elsevier.com/locate/radcr

Case Report

Serous cystadenocarcinoma of the spleen

Chung Kuao Chou MD[a,*], Shih-Cheng Chou MD[b]

[a] Department of Radiology, Yuan's General Hospital, No. 162, Cheng-Kung 1st. Rd., Kaohsiung, Taiwan, Republic of China
[b] Department of Pathology, Yuan's General Hospital, Kaohsiung, Taiwan, Republic of China

ARTICLE INFO

Article history:
Received 15 December 2016
Received in revised form
14 January 2017
Accepted 22 January 2017
Available online 24 February 2017

Keywords:
Serous cystadenocarcinoma
Spleen
CT

ABSTRACT

The commonly seen primary malignant neoplasms of the spleen are angiosarcoma and lymphoma. We present a case of serous cystadenocarcinoma of the spleen. It was presumed to be originated from dropped nonmalignant ovarian tissue, which was accidentally implanted to the splenic surface during hysterectomy and bilateral salpingooophorectomies for torsion of right fallopian tube 9 and half years ago and transformed into serous cystadenocarcinoma later. Computed tomography demonstrated a multilocular predominantly cystic tumor with internal soft tissue components in the spleen.

Introduction

Primary neoplasms of the spleen include lymphoma, angiosarcoma, hemangioma, lymphangioma, littoral cell angioma, hamartoma, and inflammatory pseudotumor [1]. Other unusual tumors include lipoma, angiomyolipoma, fibroma, fibrosarcoma, leiomyosarcoma, malignant fibrous histiocytoma, and mucinous cystadenocarcinoma [1,2]. The authors report a serous cystadenocarcinoma solitarily present in the spleen and discuss its probable origin.

Case report

A 65 year-old female consulted the internal medical department with a chief complaint of epigastralgia for several months. She received hysterectomy and bilateral salpingooophorectomies 9 and half years ago due to torsion of right fallopian tube. The gross specimens showed torsion of right fallopian tube with swelling and gangrenous change and congestion of right ovary. Bilateral ovaries and left fallopian tube were of normal outlooking and size. The microscopic examination showed hemorrhagic necrosis of left fallopian tube. It did not reveal any malignancy in the uterus, fallopian tubes, and ovaries. This time, the epigastric pain progressively increased in severity and became constant. An upright abdomen film showed splenomegaly. A subsequent computed tomography examination demonstrated a multilocular cystic tumor, about 16.0 cm in greatest dimension, with irregular internal soft tissue components in the spleen (Figs. 1A and B). The patient was admitted to the surgical ward to receive further evaluation.

Competing Interests: The authors have declared that no competing interests exist.

* *Corresponding author.*
E-mail address: wushungxian@kimo.com (C.K. Chou).

http://dx.doi.org/10.1016/j.radcr.2017.01.018

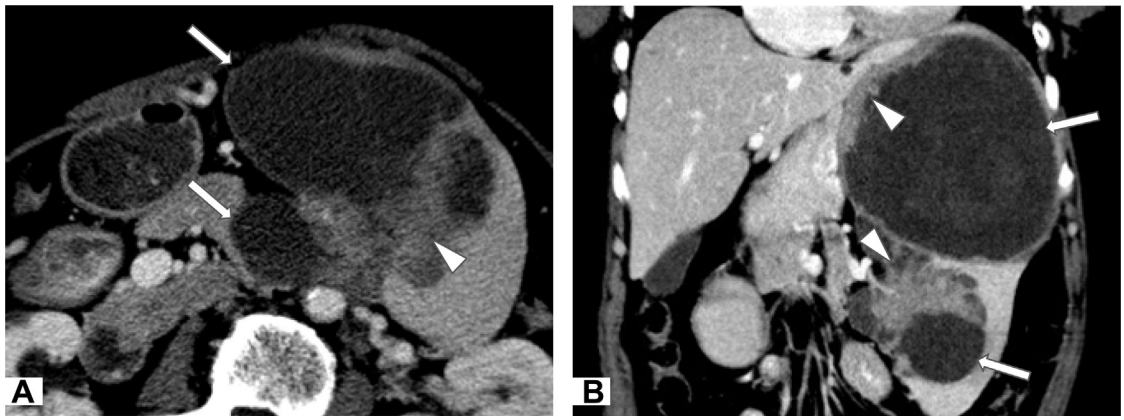

Fig. 1 – (A) Postcontrast axial image and (B) postcontrast reformatted coronal image. A multilocular predominantly cystic tumor with relatively smooth tumor wall (arrows) and internal soft tissue components (arrowheads) was seen.

A percutaneous biopsy revealed clusters of moderately differentiated neoplastic cells bearing hyperchromatic nuclei, prominent nucleoli, and vacuolated cytoplasm and arranged in focal papillary pattern. The mucicarmine stain was positive. Immunohistochemically, the tumor cells were positive for cytokeratin (CK) 7, but not for CK20, CDX2, and thyroid transcription factor (TTF)-1. The results suggested a metastatic adenocarcinoma. The serum levels of cancer antigen (CA) 15-3 and CA 125 were 69.3 U/mL (normal <31.3U/mL) and 2352.8 U/mL (normal <35U/mL), respectively. Those of carcinoembryonic antigen (CEA) and CA 19-9 were within normal range. The following surveys in chest, breast, and upper and lower gastrointestinal tracts did not detect any possible primary malignancy. A surgical intervention was performed to remove the spleen. During operation, the spleen was easily isolated and resected without any adhesion to the adjacent organs. The gross specimen (Fig. 2) revealed a multilocular cystic tumor with internal soft tissue components, necrotic tissue, and hemorrhage. There was no detectable mucin content within the tumor. The microscopic examination (Figs. 3A and B) demonstrated clusters of moderately differentiated neoplastic cells bearing hyperchromatic and pleomorphic nuclei, prominent nucleoli, and eosinophilic cytoplasm, which were arranged in papillary pattern. There were multiple psammoma bodies disseminated in the tumor. No mucin-secreted epithelium was found. Immunohistochemically, these tumor cells were positive for CK-7 (Fig. 3C) and Ber-EP4 but negative for CK-20 (Fig. 3D), CDX2, and TTF-1. These results were consistent with serous cystadenocarcinoma [3]. A positron emission tomography examination 1 month later did not detect any other possible malignancy. Based on these findings, a diagnosis of serous cystadenocarcinoma of the spleen was made. The patient was regularly followed up in outpatient department. One and a half year later, a palpable left neck lymph node was noted. The biopsy showed malignant cells with same immunochemical stains, including positive CK-7, negative TTF-1, CK-20, and CD20 stains, as that of splenic serous cystadenocarcinoma. The result was judged as lymph node metastasis. The patient received local adjuvant radiotherapy of the neck and regular follow-up.

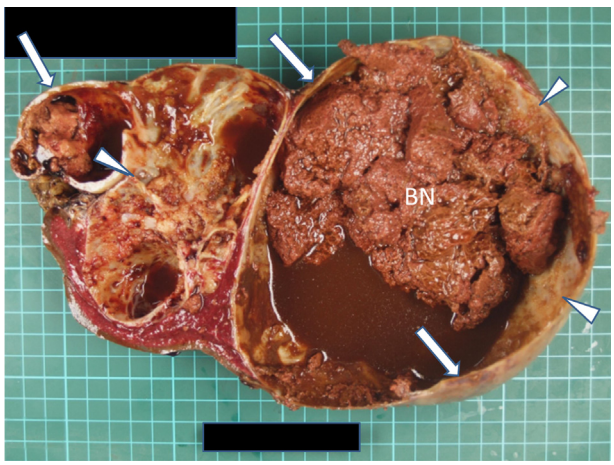

Fig. 2 – The gross specimen showed the cystic tumor wall (arrows), internal soft tissue components (arrowheads), and a mixture of blood and necrotic tissue (BN).

Discussion

Primary neoplasms of the spleen include lymphoma from lymphoid tissue and hemangioma, lymphangiom, hamartoma, littoral cell angioma , hemangioendothelioma, hemangiopericytoma, and angiosarcoma from vascular element [1]. Primary cystadenocarcinoma of the spleen is extremely rare. All the reported cases were mucinous type [2,4–9]. The hypothesized origins of these tumors include (1) ectopic pancreatic tissue; (2) ectopic intestinal tissue; and (3) invaginated mesothelium of the splenic capsule [2,6]. In contrast to the mucinous type, the current case might represent a different entity. The patient received hysterectomy and bilateral salpingooophorectomies 9 and half years ago due to torsion of right fallopian tube. Neither gross

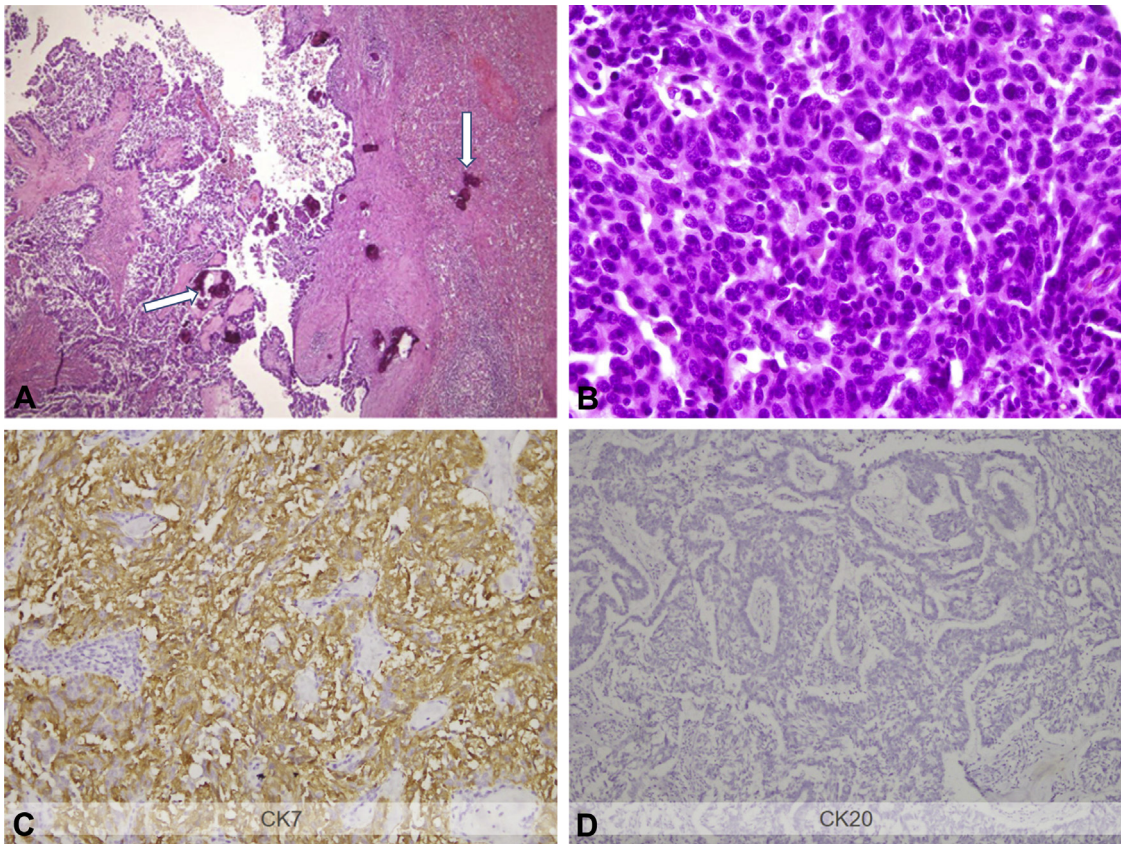

Fig. 3 – (A) A 40× microscopic picture showed neoplastic cells arranged in a papillary pattern. Multiple psammoma bodies (arrows) were seen. (B) A 400× microscopic picture showed clusters of moderately differentiated neoplastic cells bearing hyperchromatic and pleomorphic nuclei, prominent nucleoli, and eosinophilic cytoplasm. (C) The immunohistochemical stain demonstrated diffuse cytoplasmic CK7 expression. (D) The immunohistochemical stain did not demonstrate CK20 expression.

specimens, including normal endometrial thickness and ovarian sizes, nor microscopic examinations revealed any evidence of gynecologic malignancy. This time, she was found to have a multilocular predominantly cystic tumor with internal soft tissue components in the spleen. Immunohistochemically, the neoplastic epithelial cells were positive for CK-7 and negative for CK-20, suggestive of a serous cystadenocarcinoma [3]. A CK7+/CK20− expression was seen in most serous ovarian cystadenocarcinoma [3,10,11]. On the other hand, mucinous ovarian carcinoma tends to have an 80% of CK20+ expression [3,12]. Microscopically, the hyperchromatic and pleomorphic neoplastic cells and psammoma bodies were compatible with serous carcinoma. Combining the gross tumor appearance, immunohistochemical stains, and histomorphological pictures together, serous cystadenocarcinoma is most likely. The remaining issue is whether the tumor was primary or metastatic. Histologically, the splenic parenchyma is composed of lymphoid and vascular tissues. Neither of them has a serous-secreting function. The patient had normal serum CEA and CA 19-9 levels, which indicated lower possibility of intestinal or pancreatic adenocarcinoma. A positive Ber-EP4 immunochemical stain almost excluded a mesothelium-origin malignancy [13]. The presumed tumor origins of mucinous cystadenocarcinoma of the spleen were not applicable in our case. It seemed metastasis would be more likely. However, the patient did not have any previously confirmed or currently detected malignancy after a thorough clinical and imaging survey. Then, the previous operation history suggested a very unusual possibility that minute nonmalignant tissue from an intra-abdominal organ such as ovary, stomach, colon, pancreas, or others might be dropped and accidentally implanted to the splenic surface during the surgery and transformed into cancer later. Generally, simultaneous elevation of serum levels of both CA 125 and CA 15-3, like in this patient, favors an ovarian carcinoma [14]. On the other hand, normal CEA and CA 19-9 levels decrease the likelihood of gastrointestinal or pancreatic origins [15,16]. Furthermore, CK7+/CK20− and negative CDX2 immunophenotypes nearly completely exclude the possibility of colorectal carcinoma [17]. These results suggest that ovary would be the most probable origin. It has been supposed that an early blood-borne micrometastasis within the spleen may grow into an imaging-detectable metastasis after several years [18]. Solitary splenic metastasis from ovarian serous adenocarcinoma has been reported [19–24]. Those cases experienced a

disease-free period, ranging from 2 to 10 years, from the first diagnosis of ovarian cancer to the detection of splenic metastasis. Most cases had an elevated serum CA 125 level before or at the moment of imaging detection. In contrast, our patient has not been found to have any gynecologic malignancy before. It may be argued that occult cancer cells might be released from the normally appearing ovaries during surgery. However, this possibility would be never ascertained.

From the morphologic point of view, the tumor in the present case was a predominantly cystic tumor with relatively smooth wall and internal solid components (Figs. 1 and 2). Thus, the differential diagnoses may exclude most solid tumors and limited to cystic ones [25,26]. Primary benign cystic tumors, including posttraumatic, postinflammatory, or postinfectious pseudocysts; congenital cysts; lymphangioma; and littoral cell angioma, usually do not have internal solid components. Clinical information is also useful in excluding irregular-marginated cystic lesions, such as immature abscess. Primary malignant tumors with necrosis usually have irregular peripheral margin in contrast to the current case, which still possessed relatively smooth wall. Then, cystic metastasis should be the remaining consideration. The majority of splenic metastasis is originated from breast, lung, colorectum, ovary, stomach, and skin [27]. In our case, all these sites, with the exception of ovary, have been examined by physical inspection, mammography, radiography, endoscopy, and nuclear medicine study. Even so, no malignancy was found.

In conclusion, we have reported a serous cystadenocarcinoma of the spleen. The serum levels of various tumor markers, gross tumor appearance, and immunohistochemical expressions and histomorphological findings of microscopic specimens favored serous cystadenocarcinoma originated from ovary. In the absence of any evidence of other primary malignancy after serial endoscopic, radiologic, and nuclear medical imaging surveys, the clinical history elicits a possibility that minute dropped nonmalignant tissue from an intra-abdominal organ such as ovary, colon, stomach, pancreas, or others was implanted to the splenic surface during the process of hysterectomy and salpingooophorectomy and developed into serous cystadenocarcinoma 9 and half years later. Based on the above described biochemical data, that is, elevated CA 125/CA 15-3 and normal CEA/CA 19-9 levels, and immunochemical findings, that is, CK7+/CK20−/CDX2−, ovary would be the most likely origin of the splenic serous cystadenocarcinoma of the current case.

REFERENCES

[1] Kaza RK, Azar S, Al-Hawary MM, Francis IR. Primary and secondary neoplasms of the spleen. Cancer Imaging 2010;10(1):173–82.

[2] Ohe C, Sakaida N, Yanagimoto Y, Toyokawa H, Satoi S, Kown A, et al. A case of splenic low-grade mucinous cystadenocarcinoma resulting in pseudomyxoma peritonei. Med Mol Morphol 2010;43:235–40.

[3] Kriplani D, Patel MM. Immunohistochemistry: a diagnostic aid in differentiating primary epithelial ovarian tumors and tumors metastatic to the ovary. South Asian J Cancer 2013;2(4):254–8.

[4] Shuman RL, Bouterie RL. Cystadenocarcinoma of the pancreas presenting as a splenic cyst. Surgery 1976;80:652–4.

[5] Matsumoto M, Kawamura Y, Ishiguro M, Nagai T. Cystadenocarcinoma of the pancreas manifested as a splenic cyst. Acta Pathol Jpn 1981;31:1089–96.

[6] Morinaga S, Ohyama R, Koizumi J. Low-grade mucinous cystadenocarcinoma in the spleen. Am J Surg Pathol 1992;16:903–90.

[7] Zanetti G, Riccioni L, Gallo C, Salfi N, Martinelli GN. Splenic mucinous cystadenocarcinoma arising in heterotopic pancreatic tissue. Tumori 1998;84:606–10.

[8] Hirota M, Hayashi N, Tomioka T, Murakami S, Ohshima H, Yamasaki K, et al. Mucinous cystadenocarcinoma of the spleen presenting a point mutation of the Kirsten-ras oncogene at codon 12. Dig Dis Sci 1999;44:768–74.

[9] Nisar PJ, Zaitoun AM, Lobo DN, Rowlands BJ. Heterotopic pancreas in the spleen: malignant degeneration to mucinous cystadenocarcinoma. Eur J Gastroenterol Hepatol 2002;14:793–6.

[10] Berezowski K, Stastny JF, Komstein MJ. Cytokeratins 7 and 20 and carcinoembryonic antigen in ovarian and colonic carcinoma. Mod Pathol 1996;9(4):426–9.

[11] Loy TS, Calaluce RD, Keeney GL. Cytokeratin immunostaining in differentiating primary ovarian carcinoma from metastatic colonic adenocarcinoma. Mod Pathol 1996;9(11):1040–4.

[12] Vang R, Gown AM, Wu LSF, Barry TS, Wheeler DT, Yemelyanova A, et al. Immunohistochemical expression of CDX2 in primary ovarian mucinous tumors and metastatic mucinous carcinomas involving the ovary: comparison with CK20 and correlation with coordinate expression of CK7. Mod Pathol 2006;19:1421–8.

[13] Wang B, Li D, Ou X, Yi Q, Feng Y. Diagnostic accuracy of Ber-EP4 for metastatic adenocarcinoma in serous effusions: a meta-analysis. PLoS One 2014;9(9):e107741.

[14] Yedema C, Massuger L, Hilgers J, Servaas J, Poels L, Thomas C, et al. Pre-operative discrimination between benign and malignant ovarian tumors using a combination of CA125 and CA15.3 serum assays. Int J Cancer 1988;41:61–7.

[15] Bagaria B, Sood S, Sharma R, Lalwani S. Comparative study of CEA and CA19-9 in esophageal, gastric and colon cancers individually and in combination (ROC curve analysis). Cancer Biol Med 2013;10:148–57.

[16] Poruk KE, Gay DZ, Brown K, Mulvihill JD, Boucher KM, Scaife CL, et al. The clinical utility of CA 19-9 in pancreatic adenocarcinoma: diagnostic and prognostic updates. Curr Mod Med 2013;13(3):340–51.

[17] Bayrak R, Haltas H, Yenidunya S. The value of CDX2 and cytokeratins 7 and 20 expression in differentiating colorectal adenocarcinomas from extraintestinal gastrointestinal adenocarcinomas: cytokeratin 7-/20+ phenotype is more specific than CDX2 antibody. Diagn Pathol 2012;7:9.

[18] Compérat E, Bardier-Dupas A, Camparo P, Capron F, Charlotte F. Splenic metastases: clinicopathologic presentation, differential diagnosis, and pathogenesis. Arch Pathol Lab Med 2007;131(6):965–9.

[19] Minaqawa Y, Kanamori Y, Ishihara H, Morishita K, Kiqawa J, Ito T, et al. Solitary metastatic ovarian carcinoma of the spleen: a case report. Asia Oceania J Obstet Gynaecol 1991;17(1):45–8.

[20] Farias-Eisner R, Braly P, Berek JS. Solitary recurrent metastasis of epithelial ovarian cancer in the spleen. Gynecol Oncol 1993;48(3):338–41.

[21] Ushijima K, Nishida T, Okura N, Sugiyama T, Komai K, Tanaka H, et al. Solitary splenic recurrence of ovarian cancer: case report and review of the literature. Arch Gynecol Obstet 1999;263(1-2):79–81.
[22] Yang CQ, Zhang ZC, Yu Q, Pan JX. Clinicopathologic characteristics of metastatic carcinoma to spleen. Zhonghua Bing Li Xue Za Zhi 2006;35(5):281–4.
[23] Otrock ZK, Seoud MA, Khalifeh MJ, Makarem JA, Shamseddine AI. Laparoscopic splenectomy for isolated parenchymal splenic metastasis of ovarian cancer. Int J Gynecol Cancer 2006;16(5):1933–5.
[24] Dawoud E, Jansen M, Shurbagy DA. Solitary splenic metastasis from ovarian serous adenocarcinoma: a case report. Austral Asian J Cancer 2013;12(3):175–80.
[25] Urrutia M, Mergo PJ, Ros LH, Torres GM, Ros PR. Cystic masses of the spleen: radiologic-pathologic correlation. Radiographics 1996;16:107–29.
[26] Warshauer DM, Hall HL. Solitary splenic lesions. Semin Ultrasound CT MR 2006;27(5):370–88.
[27] Lam KY, Tang V. Metastatic tumors to the spleen: a 25-year clinicopathologic study. Arch Pathol Lab Med 2000;124(4):526–30.