Clinical Case Report

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Ultrasonic and pathological characteristics of ovarian mucinous cystic tumors with malignant mural nodules

Two cases report

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Abstract

Rationale: Sarcomatous or anaplastic carcinoma mural nodules presenting in ovarian mucinous cystic tumors are very rare. Here, we reported the ultrasonic and pathological features of 2 such cases.

Patient concerns: A 60-year-old woman presented with a complaint of lower abdominal pain. Physical examination revealed a hard, palpable mass in her right lower abdomen with mild tenderness. In addition, a 48-year-old woman presented with left abdominal pain and abdominal fullness. Physical examination revealed a palpable mass in her left lower abdomen.

Diagnoses: The diagnosis of ovarian mucinous cystic tumor (including mucinous cystadenoma, mucinous cystadenoma of borderline malignancy, and intraepithelial carcinoma) associated with the sarcomatous mural nodule was made for the first patient. The mass of the second patient was mucinous cystic tumor (including mucinous cystadenoma, borderline malignant mucinous cystadenoma, and mucinous cystadenocarcinoma) associated with sarcoma-like mural nodules and multifocal anaplastic carcinoma.

Interventions: Both patients underwent bilateral salpingo-oophorectomy and omentectomy. In addition, appendectomy was also performed for the younger patient.

Outcomes: Ultrasonic imaging showed huge pelvic cavity mixed masses with reticular or petaloid fluid sonolucent areas, uneven thickness separation, and multiple various mural nodules. The internal echo of the masses was complex and varied. The ultrasonic features of mural nodules were characteristic, including irregular shape, rough surface, wide basement, and nonuniform internal echogenicity. Pathological examination revealed multiple nodules with obvious atypia and mucinous cystic tumors with different malignancy. Sarcomatous or anaplastic carcinoma mural nodules showed irregular structure, significant cell atypia, and noticeable mitoses. The discovery of vascular invasion has an important role in the diagnosis of sarcomatous mural nodules. Immunohistochemical features of positive cytokeratin and negative vimentin can identify the anaplastic carcinoma component from the bizarre stromal components of the nodule.

Lessons: Ultrasonography was helpful to evaluate the preoperative diagnosis and determining the surgical approach, and pathology was indispensable to the diagnosis of these diseases.

Abbreviations: AFP = alpha-fetoprotein, CA = cancer antigen, CDFI = color Doppler flow imaging, CEA = carcinoembryonic antigen, HPF = high-power field, SLMN = sarcoma-like mural nodule.

Keywords: anaplastic carcinoma, mucinous cystic tumor, ovarian carcinoma, sarcoma-like mural nodule, sarcomatous mural nodule

1. Introduction

Mucinous cystic tumors of the ovary may be associated with mural nodules of various types, which are divided into benign (sarcoma-like and carcinosarcoma-like) and malignant (anaplastic carcinoma, sarcoma, carcinosarcoma).[1] Sarcoma-like mural nodule (SLMN) is the most common mural nodule, but malignant nodule had been rarely reported previously. It is very important to distinguish between benign and malignant mural nodule since the prognoses of these lesions are different.[2,3] Insufficient understanding of their clinicopathological features often lead to misdiagnosis and unreasonable treatment. To our knowledge, although some ultrasonic findings have been described in a few case studies,[4] the summary of ultrasonic features and ultrasonic differential diagnosis have not been reported previously on the ovarian mucinous cystic tumor associated with malignant mural nodule. Herein, we reported the ultrasonic and pathological features of 2 such cases, and discussed the differential diagnosis.

Editor: Farid Azmoudeh-Ardalan.

The authors have no funding and conflicts of interest to disclose.

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Medicine (2017) 96:45(e8636)

Received: 24 November 2016 / Received in final form: 21 October 2017 / Accepted: 24 October 2017

http://dx.doi.org/10.1097/MD.0000000000008636

2. Case presentations

2.1. Case 1

A 60-year-old postmenopausal woman, gravida 4, para 1, presented with a 1-month history of lower abdominal pain. Physical examination revealed a hard, palpable mass in her right lower abdomen with mild tenderness. Preoperative serum cancer antigen 125 (CA-125), CA19-9, carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), and CA72-4 were all in the normal range. Ultrasonography displayed a huge pelvic cavity mixed mass measuring 9.74×7.62 cm with a reticular fluid sonolucent area, uneven separation, and a heterogeneous echoic nodule in the center. The mass had a clear margin and showed poor penetration in the cystic part. The mural nodule had an irregular shape, rough surface, wide basement, and nonuniform internal echo with a miniscule fluid area (Fig. 1A). Color Doppler flow imaging (CDFI) showed no blood flow in the nodule basement. Ultrasound diagnosis was ovarian (potentially mucinous) cystic tumor associated with mural nodule (prone to malignancy). Computed tomography scan of the abdomen revealed a large oval cystic and solid mass with irregular septations, and showed heterogeneous enhancement on enhanced scan. Surgical exploration revealed a mass measuring $12 \times 10 \times 7$ cm with an old surface rupture (1 cm) and proliferation of granulation tissue. Bilateral salpingo-oophorectomy and omentectomy were performed.

Macroscopic findings showed that the cysts of right ovary were filled with brownish viscid fluid or clear mucinous material. A huge brown solid mass measuring $9 \times 8 \times 6.5$ cm was observed in the largest locule, with visible hemorrhage and necrosis.

Microscopic observation showed that the tumor was composed of epithelial and stromal elements. The cysts were lined by mucinous epithelium showing benign and borderline changes focally with intraepithelial carcinoma (Fig. 2A). The mural nodule located just below the mucinous epithelium was consisted of ovoid-shaped mononucleated cells and numerous multinucleated osteoclast-like or epulis-like giant cells (Fig. 2B). The mononucleated cells showed marked nuclear pleomorphism and atypia with vesicular nuclei and evident nucleoli. Mitoses were sometimes atypical, and approximately 25 mitoses per 10 high-power field (HPF) were recorded (Fig. 2C). Extensive or focal necrosis and vascular invasion were identified (Fig. 2D). The mononucleated and multinucleated cells were positive for vimentin and CD68, but negative for cytokeratin, desmin, α-smooth muscle actin, and calretinin. The diagnosis of ovarian mucinous cystic tumor (including mucinous cystadenoma, mucinous cystadenoma of borderline malignancy, and intraepithelial carcinoma) associated with the sarcomatous mural nodule was made. Malignant cells were not found on cytologic examination of peritoneal washing.

2.2. Case 2

A 48-year-old woman presented with a 2-week history of left lower abdominal pain and abdominal fullness. Physical examination revealed a palpable mass (25×20 cm) in her left lower abdomen. CA-125, CEA, and CA 19-9 levels were all within normal limits. Ultrasonography demonstrated a $28.7 \times 19.0 \times 10.0$ cm multilocular mass with internal echogenicity and septation in pelvic cavity (Fig. 1B). The boundary of the mass was clear with lateral shadows at the margins. Irregular fluid sonolucent areas were observed in the mural nodules. Most nodules were round and the walls of the masses were continuous. CDFI showed minor flow in the nodules basements, and the resistance index[5] was 0.67. Ultrasound diagnosis was ovarian (potentially mucinous) cystic adenocarcinoma associated with mural nodules (prone to malignancy). Computed tomography scan of the abdomen revealed a huge multicystic mass originating from the left ovary with several nodules protruding into the largest cystic space. Laparotomy revealed a large cystic left ovarian mass measuring $28 \times 20 \times 15$ cm. Bilateral salpingo-oophorectomy, appendectomy, and omentectomy were performed.

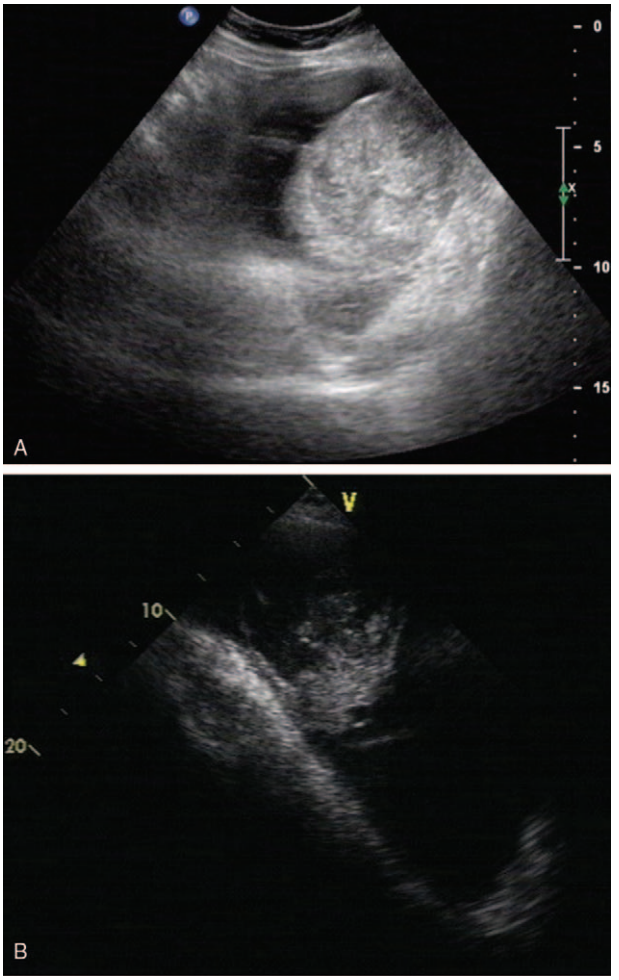

Figure 1. Ultrasonic imaging of ovarian tumor. (A) Ovarian mucinous cystic tumor associated with sarcomatous mural nodule; the nodule had a rough surface, wide basement, poor penetration, and uneven thickness separation in the cystic area. (B) Mucinous cystic tumor associated with SLMNs and multifocal anaplastic carcinomas showed irregular fluid sonolucent areas in the largest nodule. SLMN = sarcoma-like mural nodule.

The final pathological analysis showed a mucinous cystic tumor (including mucinous cystadenoma, borderline malignant mucinous cystadenoma, and mucinous cystadenocarcinoma) associated with SLMNs and multifocal anaplastic carcinoma. The pathological characteristics of this tumor have been described.[6]

2.3. Ethical statement

The study was approved by the Ethical Committee of the General Hospital of Jinan Military Command. Written informed consent was obtained from the patients involved in the study.

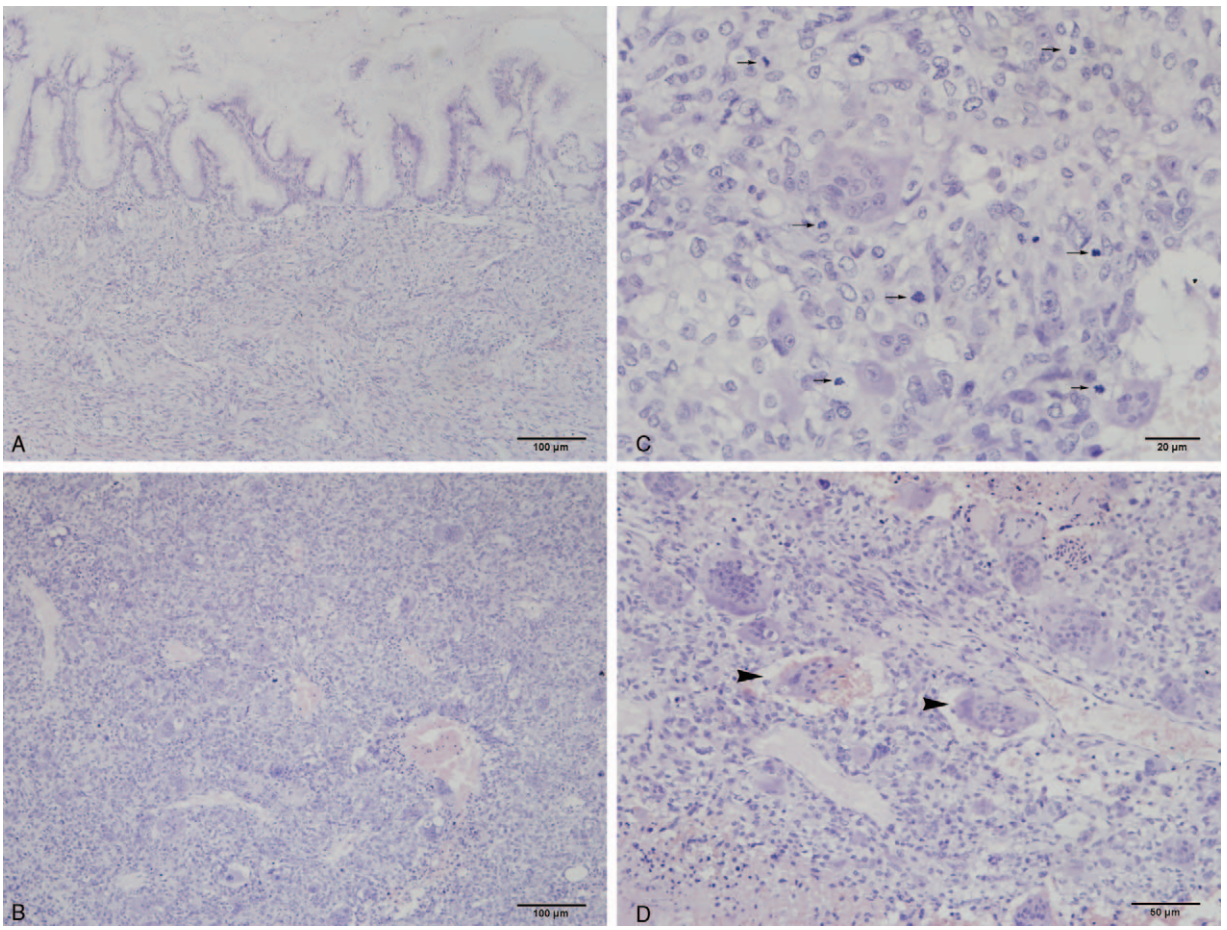

Figure 2. Microscopic findings of ovarian mucinous cystic tumor associated with sarcomatous mural nodule (hematoxylin-eosin staining). (A) Mucinous cystadenoma was the main part of epithelial elements (×100). (B) The mural nodule was consisted of ovoid-shaped mononucleated cells and numerous multinucleated osteoclast-like giant cells (×100). (C) Seven mitotic figures (long arrows) per HPF were observed in sarcomatous nodule (×400). (D) Vascular invasion (short arrows) was observed (×200). HPF = high-power field.

3. Discussion

Mucinous cystic tumor with malignant mural nodules is a rare neoplasm. To our knowledge, only about 43 cases have been reported in English literature in the past 40 years. Anaplastic carcinomas (28/43) were the most common malignant nodules, and only 9 cases had sarcomatous mural nodules.[7,8] The patients with malignant mural nodule had a wide age range from 17 to 77 years, with the median age of 37 years. They usually presented with abdominal pain or discomfort, but lacked the characteristic symptoms. In our study, 2 cases of mucinous cystic tumor with malignant mural nodule were described in middle-age and old women with the history of lower abdominal pain.

Mural nodule of sarcoma or anaplastic carcinoma within SLMN should be separated from pure SLMN because of the poor prognosis of the 2former. However, it is not easy to distinguish between sarcoma and sarcoma-like components within nodule since both of them contain pleomorphic cells with bizarre nuclei, extensive or focal necrosis, and many mitotic figures. Immunohistochemistry is not useful to distinguish sarcomatous nodule from sarcoma-like nodule, because vimentin is positive and cytokeratin is negative in both malignant and reactive components of the nodule. Sarcomatous nodule contains a monotonous cell population, showing poor circumscription, and lack of inflammatory cells. It is generally believed that they have more mitoses than SLMN, and the mitoses of latter are usually not more than 10 per 10 HPF. Vascular or stromal invasion is the most effective evidence for the diagnosis of sarcomatous mural nodule. On the contrary, sarcoma-like nodule shows a polymorphous population composed of inflammatory cells and giant cells, without vascular or stromal invasion. The identification of anaplastic carcinoma within SLMNs is relatively easy, because immunohistochemistry is useful to distinguish the epithelial components from the bizarre stromal components of the nodule. Nonetheless, because of the morphological similarity between anaplastic carcinoma and SLMN, pathologists should observe the histological images of tumor carefully to avoid missed diagnosis, even more tissue samples are needed.

Although many cases of malignant mural nodule have been reported in the English literature, few of these studies primarily focused on ultrasonic features, which was extremely important for the preoperative diagnosis of ovarian tumors. Ultrasonic imaging showed huge pelvic cavity mixed masses in both cases. Due to reticular or petaloid fluid sonolucent areas, nonuniform thickness separation, and multiple mural nodules, the internal echoes of the masses were complex and varied. The dimensions of the mural nodules also varied, and the largest one was 4.5 cm in diameter. The features of the mural nodules were characteristic, including irregular shape, rough surface, wide basement, and nonuniform internal echo. The irregular fluid sonolucent areas were observed in the mural nodules of both cases, which

indicated hemorrhage and focal necrosis. CDFI showed no or very limited dotted blood flow in the nodule base.

Diagnostic difficulties, both from clinical and imaging perspectives, results in the reduced preoperative diagnostic accuracy. These 2 cases showed many similar features that have not been described in the previous literature. Malignant mural nodule should be considered as differential diagnoses of other ovarian cystic lesions, such as pure cyst, hematoma, ovarian mucinous or serous cystic tumor, and mature/immature cystic teratomas. The main points of differential diagnosis are as follows:

1. Pure ovarian cyst: It usually presents as a round or oval clear fluid sonolucent area with a well-defined boundary, thin and smooth cyst walls, measuring 3 to 8 cm in diameter. Acoustic enhancement effect can be observed at the back wall and posterior of cyst. CDFI reveals no blood flow in the cyst wall.
2. Hematoma: The ovarian hematoma presents as a single ovary expansion ranging from 2.5 to 5.5 cm in diameter. Ultrasonography usually reveals a well-defined cyst or cyst-solid mass with thick walls. CDFI shows flow signals around the hematoma, with medium flow velocity and resistance index.
3. Ovarian mucinous cystic tumor with or without SLMN: The cyst wall and separation of mucinous cystic tumors may form multilocular structures; however, the thickness of these walls is less than 3 mm in benign and borderline mucinous cystadenomas. Signs of smaller vesicles clusters in the sidewall of the larger capsule may be helpful for making a diagnosis of mucinous cystadenoma.[9] SLMN of ovarian mucinous cystic tumor may show the characteristics including regular shape, smooth surface, and uniform internal echo. However, the characteristics of malignant mural nodule are often varied, with some even showing crab-like sign. CDFI shows low velocity and low resistance index of arterial flow in malignant nodule and separation, whereas most SLMNs show no flow signs.
4. Cystic teratomas: Most ovarian cystic teratomas have clear boundaries with complete and smooth cyst walls. Bones, teeth, cartilages, and hair can be seen on the sonogram echogram of cyst. When fat and mucus coexist in a cyst, it shows a fat-liquid level that is unlikely to appear in ovarian mucinous cystic tumors.[9] Despite the thick, uneven wall, rough separation and irregular papillary solid nodule may often present, especially in immature cystic teratomas, uneven echo signals are different from sarcomatous mural nodule.

4. Conclusions

In conclusion, for the 2 ovarian masses discussed in this report, we focused on the ultrasonic and pathological characteristics. These 2 cases showed huge pelvic cavity mixed masses with reticular or petaloid fluid sonolucent areas, uneven thickness separation, and multiple mural nodules with different size. The features of sarcomatous or anaplastic carcinoma mural nodule were characteristic, including irregular shape, rough surfaces, wide basement, nonuniform internal echo, and none or only minor dotted blood flow in nodule basements. Accordingly, we predisposed the malignant nature of the cystic tumor and mural nodules by ultrasonography. Therefore, as an important auxiliary examination for the preoperative diagnosis, ultrasonography could display the characteristics of ovarian mucinous cystic tumors and mural nodule, and was helpful to the choice of clinical treatment. Vascular invasion and much mitoses were crucial to the pathological diagnosis of sarcomatous mural nodule. Owing to the morphological similarity between anaplastic carcinoma and SLMN, the identification of anaplastic carcinoma was determined by immunohistochemical features of positive cytokeratin and negative vimentin.

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