Mucinous cystic tumor with mural nodules is a rare neoplasm; only about 80 cases have been published in the past 30 years. Only two of them had carcinosarcoma in the mural nodules. In these two cases, one was a mucinous cyst adenoma and the other was a mucinous carcinoma. We report a case of a 29-year-old female with a borderline mucinous cystic tumor with mural nodules (carcinosarcoma) (FIGO stage Ia).

CASE

The patient was a 29-year-old nulliparous female and a hepatitis B carrier. She had no operative history and had a normal menstrual cycle. She was unmarried and had no family history of gynecology disease. She did not take any medication in previous years. She suffered from dysmenorrhea and constipation for years and tolerated it. Lower abdomen swelling was noted for the previous year prior to presentation. She presented with severe lower abdominal pain unrelated to menstruation. She first presented to Shuang-He Hospital and the diagnosis of ovarian tumor was made. The patient came to our (Shin-Kong Hospital) gynecology outpatient department (OPD) for a second opinion in February 2010. At that time, the physical examination was generally normal except for mild tenderness over the lower abdomen with a palpable mass. There was no rebounding pain. The laboratory investigation performed showed an abnormal cancer antigen 125 (CA125) elevated to 55.04 U/mL, CA19-9 elevated to 70.62 U/mL and CA153 elevated to 28.87 U/mL. The carcinoembryonic antigen value and other laboratory data were within normal limits.

The CT scan revealed a large cystic tumor, measuring approximately 36 cm in greatest dimension, with at least two solid foci noted and measured approximately 4.5 cm in greatest dimension, attached to the left lateral wall of the tumor (Figure 1).

The patient underwent left salpingo-oophorectomy and adhesiolysis. At the time of surgery, a large left ovarian cyst was noted with changes consistent with torsion. The cyst was found to contain a 5400 mL of reddish brown fluid on aspiration. This cystic tumor focally adhered to the peritoneum. The right adnexa were normal on gross examination. The multilocular cystic tumor was received opened in the surgical pathology laboratory. The tumor measured 28×15×3 cm in size and weighed 600 g (Figure 1).
The fallopian tube was normal on gross examination. The external surface of the cyst wall was smooth. Further examination showed two pieces of clot-like materials within the cyst wall, measuring approximately 5.5 cm in greatest dimension. The internal surface of the ovarian cyst showed multiple yellow, solid nodules measuring up to 5×4×2 cm in greatest dimension. In addition, there was also a diffuse yellow, solid area measuring approximately 25×10 cm in dimension and 0.3 cm in thickness present on the internal aspect of the cyst (Figure 2B). The septa were thickened up to 2.5 cm in diameter. A cross section of the septa showed multiple small cysts with a mucoid material (Figure 2B). Multiple sections of tumor were taken and fixed in neutral-buffered formalin and embedded in paraffin. The sections were stained with hematoxylin and eosin. Immunohistochemistry using cytokeratin (DAKO, AE1/AE3, 1:100) and vimentin (DAKO, 1:100) was done on some sections. Immunoreactivity was interpreted as positive or negative.

**Microscopic features**
The cyst was lined by mucinous epithelium showing a benign and borderline change focally with intestinal differentiation (Figure 3A). The multicystic cavity contained mucus materials inside. The external aspect of the cyst showed no reactive response and no evidence of rupture. The mural nodules were composed of spindle-shaped to ovoid-shaped cells with marked nuclear pleo-
morphism (Figure 3B). They had large clear nuclei with prominent nucleoli. These cells were located just below the mucinous epithelium that appeared circumscribed but devoid of a capsule. The mitotic activity was increased, and approximately 8 mitoses per 10 high-power field were recorded. Focally, there was osteoid metaplasia (Figure 3C). There was no evidence of vascular invasion. These spindle-shaped cells were seen to invade into the stroma of the cyst. The diffuse yellow patch seen on gross examination also contained pleomorphic spindle-shaped cells that were similar in appearance to those seen in the mural nodules (Figure 3D). Some large mural nodules extended toward the lumen of the cyst and showed hemorrhage, acute and chronic inflammation, and necrosis (Figure 3E). Immunohistochemistry performed showed the atypical spindle-shape cells to exhibit strong vimentin positivity. Cytokeratin was negative. This reaction pattern was consistent with a nonepithelial component (sarcoma). Some areas were reported with several large cells that contained eosinophilic cytoplasm, and enlarged hyperchromatic and pleomorphic nuclei with large eosinophilic nucleoli. A higher magnification view of these components is shown in Figure 3F. Some of these cells were dispersed within the sarcoma stroma (Figure 4A) and some formed glandular structures (Figure 4B). The immunostaining performed using cytokeratin demonstrated a strong positive reaction and a negative reaction to vimentin (Figure 4C), confirming that they were epithelial in nature. These cells were not similar in appearance to the mucinous epithelium lining the main cyst. No transitional area was seen. The sarcoma cells were clearly distinguished from the carcinoma cells by vimentin positivity (Figure 4D).

The microscopic examination of the left tube showed no evidence of tumor. The abdominal washing cytology performed was negative. Based on the above findings, a borderline mucinous cystic tumor with mural nodules (carcinosarcoma), pathologic FIGO stage Ia, was diagnosed. No further biopsy or operation done after the left salpingo-oophorectomy.

After the operation, CA125 decreased to 21 U/mL in April. The patient had adjuvant chemotherapy taxotere (75 mg/m²) and carboplatin (5AUC) every 3 weeks for 6 cycles after the operation, but had to stop because of hepatitis B exacerbation after 4 cycles of chemotherapy. After chemotherapy, CA125 decreased to 13 U/mL in December. She was followed at National Taiwan University Hospital OPD for 10 months and is free of the disease.

**DISCUSSION**

Cystic ovarian epithelial tumors with mural nodules
outcome of cystic ovarian epithelial tumors with mural nodules depends on the histology of nodules (carcinoma or sarcoma) and the stage of the disease. Thus, it is very important to determine the exact components of the mural nodules since the prognosis of these tumors is related to the histology.

As the number of these cases increased, it became easier to determine the different components within the mural nodules. The main difficulty with mural nodules arises when there is more than one component within nodules, especially sarcoma and sarcoma-like components. It is not easy to distinguish between sarcoma and sarcoma-like components within nodules since both of them contain pleomorphic cells with bizarre nuclei and many mitotic figures. The sarcoma nodules typically are seen in older patients and are large in size. They contain a monotonous cell population, showing poor circumscription, with vascular or stromal invasion and lack of inflammatory cells. On the other hand, sarcoma-like nodules show a polymorphous population of cells composed of inflammatory cells and giant cells, with no evidence of vascular or stromal invasion.

Immunohistochemistry is useful to separate the

are rare neoplasms and were first described by Prat in 1979. The epithelium of the cyst may be lined by benign, borderline, or malignant cells. Several kinds of mural nodules have been reported. They are further classified into sarcoma-like, sarcoma, and anaplastic carcinoma. Baergen et al classified mural nodules into reactive (sarcoma-like), benign, carcinoma (with a variant of combined carcinoma and reactive elements), sarcoma, and combined carcinoma and sarcoma (carniosarcoma) in 1995. The WHO Classification divided the mural nodules of ovarian mucinous cystic tumors into malignant (anaplastic carcinoma, sarcoma, or carcinosarcoma) and benign (sarcoma-like) in 2003. On review of the published studies of the serous borderline ovarian tumor with mural nodules, Gungor et al found that they were extremely rare and only five cases have been published.

The prognosis of these cystic ovarian epithelial tumors with mural nodules is uncertain. Sarcoma-like nodules are considered to be reactive and do not affect the prognosis. Sarcoma and anaplastic carcinoma are considered to have a poor prognosis except in cases staged as FIGO stage Ia with no tumor rupture. The

### Table 1. The summary of previous classification and analysis of different variants of mural nodules.

| Feature                | Sarcoma   | SLMN   | Anaplastic carcinoma | Carcinosarcoma-like | Carcinosarcoma |
|------------------------|-----------|--------|----------------------|---------------------|----------------|
| Patient age            | Older     | Younger| Older                | Younger             | Young         |
| FIGO stage             | I-IV      | Ia     | I-IV                 | I                   | I-?           |
| Prognosis              | Poor      | Not effective | Poor | ? | ? |
| No. of nodules         | -         | One to several | Usually single | One | Several |
| Size (cm)              | Large     | Small (0.6-6) | Large (1-10) | Small (1.2-5) | 1.5-5.5 |
| Circumscription        | Good (grossly) | Good, sharp | Poor               | Poor               | Variable |
| Vascular or stromal invasion | Present | Absent | Present | Present | Present |
| Cell composition       | Monotonous | Heterogeneous | Homogenous | Heterogeneous | Homogenous |
| Inflammatory cells      | Sparse    | Numerous | Few, variable | Numerous | Few, variable |
| Giant cells            | Common    | Common  | Uncommon             | Common             | Few           |
| Spindle cells          | Common    | Common  | Occasional           | Common             | Common |
| Large eosinophilic cells | -     | Occasional | Common | Common | Common |
| Cytokeratin            | -         | Scattered, negative | Diffuse positive | Positive of carcinoma cells | Positive of carcinoma cells |
| Vimentin               | Positive  | Positive | Sometimes positive  | Carcinoma: + Stroma: + | Carcinoma: + Stroma: + |
| Necrosis               | Common    | Often   |                      |                     |                |

SLMN: Sarcoma-like mural nodules ? unknown.
components within the mural nodules. Before the advent of immunohistochemistry, some carcinoma nodules were misdiagnosed as sarcoma-like (reactive). When using cytokeratin, the positive epithelial cells are identified within the bizarre stromal components of the nodules. On the other hand, immunohistochemistry is not useful to distinguish sarcoma and sarcoma-like nodules since vimentin is positive and cytokeratin is negative in both malignant and reactive components of the nodules.

The age of the patient, prognosis, histologic features, and immunohistochemistry reaction for various mural nodules are summarized in Table 1.5,8,9 The summary here is useful for making the differential diagnosis of the components within the nodules, but exceptions do occur. Within the last 30 years, the terminology used to describe carcinoma and carcinosarcoma components of mural nodules has been somewhat confusing. We reviewed the published studies, and in particular looked at the histology and immunohistochemistry of tumors with mural nodules where the diagnoses of sarcomatoid carcinoma6,12,13 and carcinosarcoma-like14,15 were made. After analysis of the histology and immunohistochemistry, sarcomatoid carcinoma and carcinosarcoma-like

Table 2. Summary of the cases of ovarian mural nodule tumors, with new terminology and carcinosarcoma.

| Reference (year) | Case | Epithelial ovarian tumor | Mural nodule | Age | FIGO stage | Therapy | Follow-up |
|------------------|------|--------------------------|--------------|-----|------------|---------|----------|
| Andrews et al (2008) | 1    | Serous, borderline       | Sarcomatoid carcinoma | 49  | I          | TAH + BSO + Omen + appen | DOD, 32 months (liver metastasis) |
| Chang et al (2005) | 1    | Mucinous borderline      | Carcinosarcoma-like | 35  | I          | TAH + BSO + Omen + appen | NED, 14 months |
| Bagué et al (2002) | 2    | Mucinous borderline      | Sarcoma-like + anaplastic carcinoma | 75  | Ia         | Surgery + ChT | NED, 15 years |
| Suurmeijer (1991) | 1    | Mucinous carcinoma       | Carcinosarcoma-like | 30  | I, Rupture | TAH + BSO + Omen + ChT | NED, 5 years |
| Søndergaard and Kaspersen (1991) | 1 (Case 2) | Mucinous cystadenocarcinoma | Sarcoma-like + anaplastic carcinoma | 37  | I          | RH + BSO + Omen + appen | NED, 18 months |
| Rosa et al (1991) | 1    | Serous, borderline       | Sarcomatoid carcinoma | ?   | ?          | ?        | DOD, 6 months (pulmonary, bone metastasis) |
| McCullough et al (1988) | 1    | Serous, cystadenocarcinoma | Sarcomatoid carcinoma | 44  | III        | TAH + BSO + ChT | DOD, 6 months (liver metastasis) |
| Fuji et al (1985) | 1    | Mucinous borderline      | Sarcoma-like + anaplastic carcinoma | 29  | I          | TAH + BSO | NED, 22 months |
| Present case (2010) | 1    | Mucious borderline       | Carcinosarcoma | 29  | Ia         | USO + ChT | NED, 10 months |
| Søndergaard and Kaspersen (1991) | 1 (Case 3) | Mucinous cystadenoma | Carcinosarcoma | 29  | I          | RH | NED, 24 months |
| Bruijn et al (1987) | 1    | Mucinous carcinoma       | Carcinosarcoma | 27  | Ia         | USO + Omen | ? |

RH=radical hysterectomy; TAH=total abdominal hysterectomy; BSO=bilateral salpingo-oophorectomy; USO=unilateral salpingo-oophorectomy; appen=appendectomy; Omen=omentumectomy; ChT=chemotherapy; DOD=died of disease; NED=no evidence of disease; ?=unknown
case report

tumors were found to be epithelial in nature and represent carcinoma. The cases of sarcomatoid carcinoma have epithelial cells that are often spindle shaped. These epithelial spindle cells and the transition zone between glandular epithelial cells and the stroma cells are cytokeratin positive. The transition zone was not present in our case. Two cases were described in 1991 and 2005 using the term carcinomasarcoma-like, and they described features of carcinoma and sarcoma-like (reactive) elements. In our case, there were malignant stroma cells (sarcoma). Only two real carcinosarcoma cases have been previously published. The mural nodule tumors used new terminology that we reclassified as carcinoma and carcinosarcoma. They are summarized in Table 2.

Mucinous cystic ovarian tumor with mural nodules should be distinguished from malignant mixed mesodermal tumor (MMMT). MMMT is usually a solid neoplasm composed of epithelial and stromal elements. These elements usually do not merge with each other. It is also unusual to find mucinous epithelium in an MMMT. Moreover, MMMT occurs almost exclusively in older patients. In our case, there were several mural nodules. The cyst was lined by mucinous epithelium with subepithelial sarcoma. Some mural nodules had a patch-like appearance. The sarcoma invaded the stroma of the cyst. The sarcoma stroma contained pleomorphic spindle cells with no inflammatory cells. Foci of osteoid metaplasia were present. No evidence of vascular invasion was reported. The eosinophilic large cells dispersed within sarcoma stroma were cytokeratin positive, confirming their epithelial nature (carcinoma).

Reports of carcinosarcoma elements inside mural nodules are rare. A review of the published studies reveals that the mural nodules with anaplastic carcinoma usually had a poor prognosis and were seen in older patients. The two cases shown in Table 2 reveal that carcinosarcoma occurred in young patients (27 and 29 years old). One was alive well after 24 months of follow-up and the other one was lost to follow-up. Thus, follow-up was only available for two patients including our case. The follow-up periods were also not long enough (24 and 10 months) to ascertain prognosis.

Mural nodules are rarely identified in ovarian cystic tumors, and thus the prognosis is not well defined. It is surprising that even the carcinosarcoma cases also had anaplastic carcinoma components inside. They occur in patients of younger age (below 30 years), and the patients have a relatively better clinical outcome. Because of the above reasons, the existence of sarcoma combined with carcinoma components in mural nodules necessitates careful examination, as the outcome of the tumor depends on the histology.

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