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Case Report

Ovarian mucinous cystic tumor with sarcoma-like mural nodules and multifocal anaplastic carcinoma: a case report

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Abstract: A 48-year-old woman presented with left abdominal pain and fullness. Computed tomography scan revealed a multicystic mass with multifocal mural nodules. Histologic examination showed a mucinous cystic tumor with cystadenoma, borderline malignant cystadenoma and cystadenocarcinoma, which were associated with sarcoma-like mural nodules (SLMNs) and multifocal anaplastic carcinoma. Mural nodules showed a positive reaction for CD56 and vimentin, but were negative for cytokeratin 7 and SMA. She underwent postoperative chemotherapy and is currently under follow-up; no recurrence or metastases were found in the first year of follow-up. Ovarian mucinous cystic tumor with SLMNs and foci of anaplastic carcinoma is extremely rare. To our knowledge, this case reports the most complex neoplastic and reactive components. Our findings shed some light on the pathogenesis of this rather rare carcinoma. We think that the formation of SLMNs may be the result of the reactive proliferation of undifferentiated mesenchymal cells, while the anaplastic carcinoma may be derived from mucinous epithelium. Moreover, because of difficulties encountered in their differential diagnosis, we think that the existence of foci of anaplastic carcinoma along with SLMNs necessitates careful histologic and immunohistochemical analysis of mural nodules for the determination of treatment and prognosis.

Keywords: Mucinous cystic tumor, sarcoma-like mural nodule, anaplastic carcinoma, cystadenoma, cystadenocarcinoma

Introduction

Mucinous cystic tumors of the ovary, whether benign, borderline or malignant, may be associated with mural nodules of various types, including sarcomas, sarcoma-like mural nodules (SLMNs), foci of anaplastic carcinoma, carcinosarcoma, mixed nodules, and leiomyomas [1, 2]. However, cases of ovarian mucinous tumor associated with mural nodules are rare. Here, we report a case of ovarian mucinous cystic tumor with SLMNs, some of which coexisted with multifocal anaplastic carcinoma. To our knowledge, there are only five reports of mucinous ovarian tumors associated with both SLMNs and foci of anaplastic carcinoma [2-6], and their features are not as complex as the ones in our case.

Case report

A 48-year-old woman, gravida 2, para 2, presented with a two-week history of lower left abdominal pain and abdominal fullness. She had undergone total abdominal hysterectomy because of a uterine myoma five years ago. Physical examination revealed a palpable mass (25 × 20 cm) in the left lower abdomen. The level of cancer antigen (CA) 125 was 37.26 U/ml (normal range <35 U/ml), while carcinoembryonic antigen and CA 19-9 levels were within normal limits. Ultrasonography demonstrated a 28.7 × 19.0 × 10.0 cm multicystic mass with internal echogenicity and septation. 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; the findings indicated a cystic papillary adenocarcinoma. Laparotomy revealed a large cystic left ovarian mass. Bilateral salpingo-oophorectomy, appendectomy and omentectomy were performed. Three regimens of combined chemotherapy treatment with taxol and carboplatin were administered. The postoperative period was unevent-

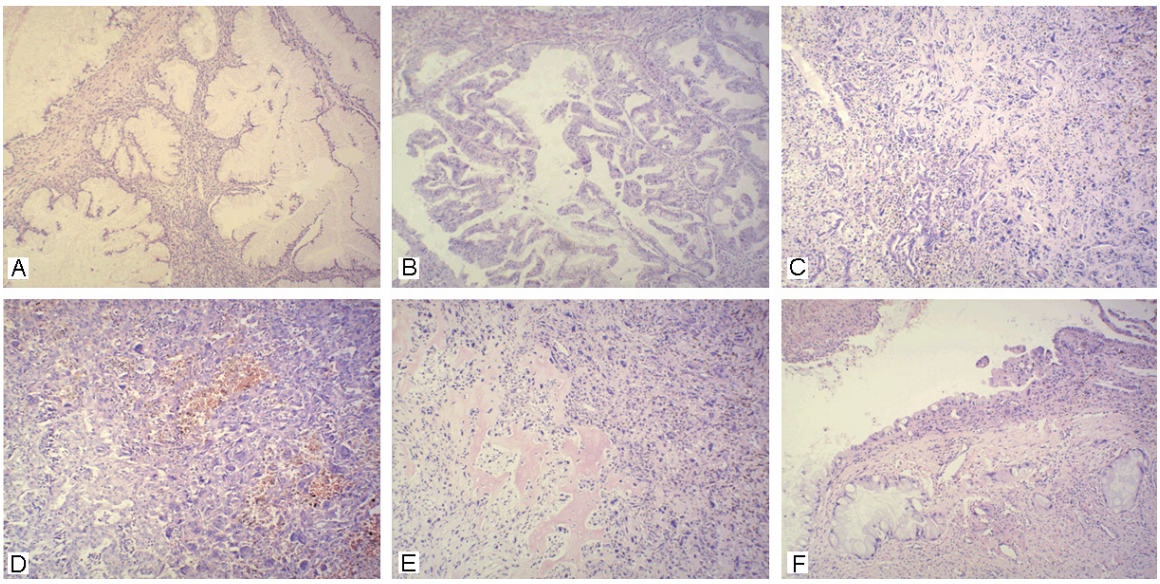

Figure 1. Histological findings (H&E, 100×). A: Ovarian mucinous cystadenoma. B: Borderline malignant mucinous cystadenoma. C: Cystadenocarcinoma (lower left) and anaplastic carcinoma. D: Anaplastic carcinoma (lower left) and sarcoma-like mural nodules. E: Osseous metaplasia within the mural nodules. F: Linear proliferation of multinucleated and mononucleated cells without formation of true nodules.

ful, without recurrence or metastasis for one year after surgery. The patient is still under follow-up.

Macroscopic findings

The specimen consisted of multilocular cysts measuring 28 × 20 × 15 cm that were gray with a smooth external surface. Section analysis showed that the cysts were filled with clear mucinous material or brownish viscid fluid. The largest locule measured up to 22.5 cm (greatest diameter). The other locules were small and aggregated at the periphery of the largest one, measuring about 8 × 7 × 6 cm. The inner surface of the largest locule was mostly smooth, with several rough grey mural nodules projecting into the cyst cavities measuring up to 1 × 1 × 0.8 cm in size. In addition, a solid mural nodule, about 4.5 cm in diameter, protruding into the largest locule was noted; it showed focal necrosis.

Histological findings

Microscopic observation showed that the cystic walls were lined mainly by single-layered tall columnar cells with abundant clear cytoplasm and small basally located nuclei (**Figure 1A**). Occasionally, the epithelium showed slightly atypical proliferation with glandular budding, tufting of the epithelium, decreased cytoplasmic mucin, and some stratification of slightly irregular nuclei (**Figure 1B**); these findings indicated borderline malignancy, particularly around the mural nodules. These atypical mucinous epithelia seemed to be associated with solid mural nodules. In the most superficial areas of the mural nodules from where the outer mucinous epithelium had already detached, there existed spindle-shaped cells with epithelium-like stratification; this could indicate epithelioid differentiation of mesenchymal cells. In addition, there were also atypical glands distributed back-to-back that exhibited a cribriform or glandular pattern with malignant nuclear features and definite stromal invasion (**Figure 1C**).

The mural nodules were well circumscribed without vascular invasion, and consisted of spindle-shaped and round mononucleated cells and numerous multinucleated osteoclast-like or epulis-like giant cells (**Figure 1D**). Focal hemorrhage, hemosiderin pigmentation and necrosis were found. The osteoclast-like giant cells were concentrated around areas of hemorrhage and contained several round to oval uniform nuclei. The diffuse infiltrate of inflammatory cells, mainly lymphocytes, was found in all nodules in variable proportions. Osteoid or

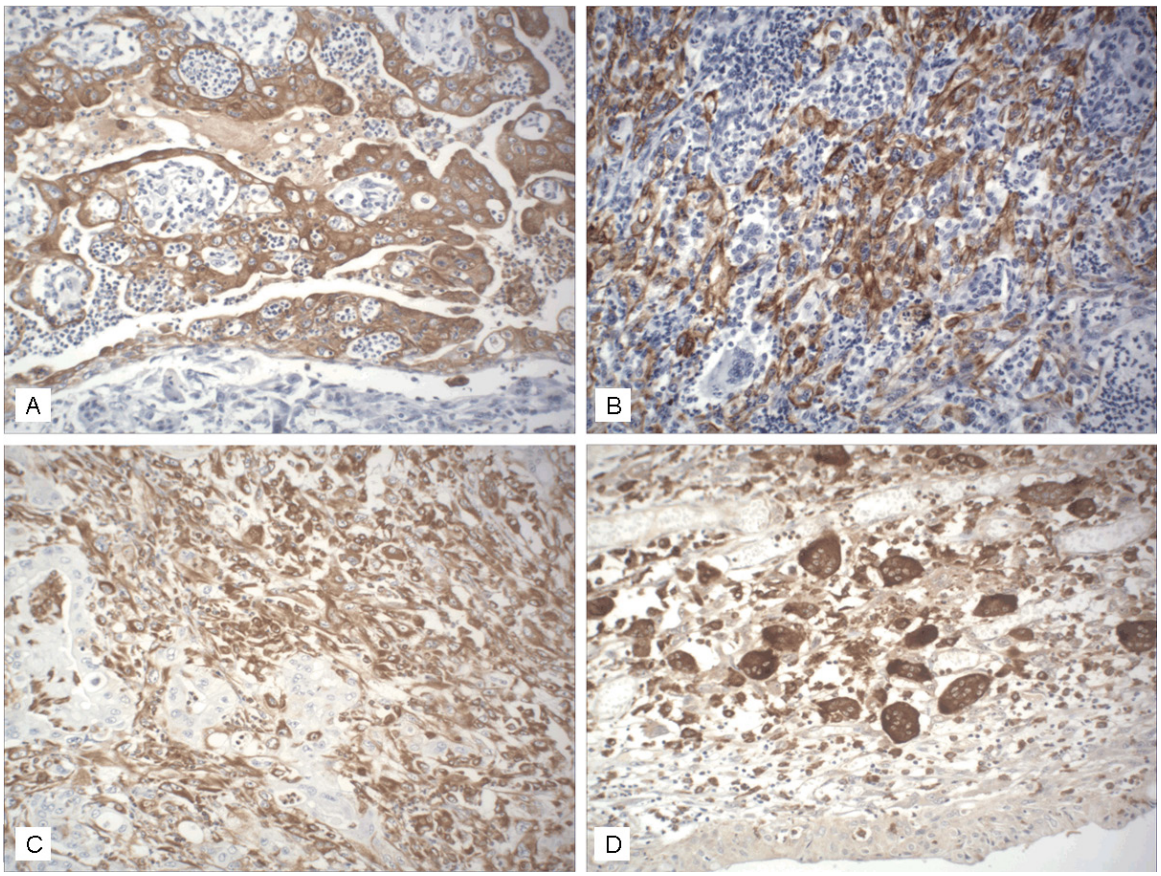

Figure 2. Immunohistochemical features (IHC, 200×). A: Cystadenocarcinoma cells were immunoreactive for CK7. Small purulent foci were noted in the center of the glands. B: Anaplastic carcinoma cells were positive for CK7. C: Vimentin was expressed in the multinucleated and mononucleated cells within the mural nodules. D: Multinucleated and mononucleated cells were positive for CD56. Epithelioid cells were present at the surface of mural nodules where the outer mucinous epithelium had detached.

osseous metaplasia was discerned (**Figure 1E**). Several minute mural nodules and linear proliferation of multinucleated giant cells without true nodule formation were observed in focal hemorrhagic areas beneath the outer mucinous epithelium (**Figure 1F**). These minute nodules may represent the earlier or initial stage of this entity.

In the inner portions of some nodules, the foci of anaplastic carcinoma merged imperceptibly with the sarcoma-like tissue, which was characterized by irregular sheets or nests and was composed of epithelioid cells and spindle cells with abundant hypochromatic cytoplasm and pale vesicular nuclei. The density of eosinophilia was lower and the size of these cells was larger compared to stromal cells (**Figure 1D**). Small purulent foci were noted in the center of the glands (**Figure 2A**). There was no evidence of endometriosis or teratomatous organoid differentiation.

Immunohistochemical findings

The specimen was fixed in 10% neutral-buffer formalin. Representative samples were routinely processed and embedded in paraffin blocks. Sections (3 μm thick) were stained with hematoxylin and eosin using parallel routine immunohistochemistry. The antigens used for IHC were cytokeratin 7, cytokeratin 20, vimentin, CD10, CD34, CD56, calretinin, desmin, and α-smooth muscle actin (SMA) (All antibodies were purchased from Dako Corp., Carpinteria, CA, USA).

We observed diffuse strong cytoplasmic staining for vimentin and CD56 (**Figure 2C** and **2D**), but no staining for cytokeratin, calretinin, SMA,

desmin, CD34 and CD10 in both mononucleated and multinucleated cells of SLMNs. Cytokeratin 7 and cytokeratin 20, meanwhile, highlighted the foci of anaplastic carcinoma (**Figure 2A** and **2B**).

Based on all the above observations, the final diagnosis was ovarian mucinous cystic tumor, including mucinous cystadenoma, mucinous cystadenoma of borderline malignancy, and mucinous cystadenocarcinoma, in association with SLMNs and multifocal anaplastic carcinoma (stage Ia).

Discussion

The present report describes a mucinous cystic tumor associated with SLMNs and multifocal anaplastic carcinoma. Even though five such reports have already been published [2-6], the neoplastic and reactive components were most complex in our case, making it rather unique.

SLMNs mainly exhibit a heterogeneous cell composition, and appear sharply demarcated from the adjacent mucinous epithelium. The indolent clinicopathological features of the nodules as well as the favorable outcome of several patients with prolonged follow-up suggest that SLMNs are reactive rather than neoplastic [7]. We observed proliferation of mononucleated cells between the basement membrane of the outer mucinous epithelium and hemorrhagic lesions in the cyst wall that was continuous with the mesenchymal cells, especially in minute mural nodules. Based on these findings, we think that the formation of SLMNs may be the result of differentiation of undifferentiated mesenchymal cells beneath the mucinous epithelium into epithelial cells, elicited by some stimulation, for example, intramural hemorrhage or cyst contents.

Foci of anaplastic carcinoma in mucinous ovarian tumor are extremely rare. It can occur not only in patients with cystadenocarcinoma, but it may also occur in patients with benign mucinous cystadenoma [3]. SLMNs are differentiated from sarcomas and foci of anaplastic carcinoma based on histological findings and their favorable prognosis. However, there are some difficulties in differential diagnosis because of the existence of tumors containing both SLMNs and foci of anaplastic carcinoma [4], as well as nodules exhibiting morphological features of both lesions. Immunohistochemistry can be useful in distinguishing between the different types of nodules. However, SLMNs may contain a few scattered keratin-positive cells because of which they can be confused with anaplastic carcinoma; in such cases, a strong and diffuse keratin immunoreaction favors the diagnosis of anaplastic carcinoma [2]. Small purulent foci are first observed in anaplastic carcinoma, and they always appear in the lumen; they may prompt to the present of epithelial components. However, the presence of epithelioid components may indicate not only epithelioid differentiation of undifferentiated mesenchymal cells, but also foci of anaplastic carcinoma. Therefore, careful and thorough examination of mural nodules within a mucinous cystic tumor is essential for determining their type. In the present case, we did observe epithelioid differentiation of mesenchymal cells, but the epithelial component was negative for cytokeratin, which is not the finding in the case of anaplastic carcinomas. We therefore think that the foci of anaplastic carcinoma are a different entity from SLMNs, and that the anaplastic carcinoma was derived from mucinous epithelium with concomitant loss of the ability to produce mucin rather than epithelioid differentiation of mesenchymal cells.

Bague et al. [2] stated that the prognosis of SLMNs is excellent as long as they appear sharply circumscribed and do not invade into surrounding tissues or vascular spaces; in such cases, their presence does not influence the prognosis of cystic ovarian tumor. In contrast, the foci of anaplastic carcinoma are aggressive components of cystic ovarian tumors. They were first thought to carry an invariably unfavorable prognosis [8, 9], and most patients with mural nodules of anaplastic carcinoma have a malignant, often rapid course [9]. Although most patients with nodules of anaplastic carcinoma receive postoperative adjuvant treatment, the mortality rate is high, even in the case of benign or borderline malignant ovarian tumors. However, recent data indicate that this does not necessarily apply to stage Ia tumors [2, 10]. This is in agreement with the present case, in which the patient had stage Ia and was successfully treated with three regimens of combined chemotherapy treatment with taxol and carboplatin. The patient was free of disease in her first year of follow-up, and long-term follow-up is ongoing.

In conclusion, the findings of this rare case have shed some new light on the pathogenesis of both anaplastic carcinomas and SLMNs associated with ovarian mucinous tumors.

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Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Disclosure of conflict of interest

The authors declare no conflicts of interest.

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