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Ovarian borderline clear cell adenofibroma in a 42-year-old woman: a case report and a literature review

Qiongxian Long[1,2], Jiyan Liu[1], Yong Peng[3], Zhirong Tang[2], Cailiang Wu[2]

[1]Department of Abdominal Oncology, Cancer Center, West China Hospital, Sichuan University, Chengdu
[2]Department of Pathology, Nanchong Central Hospital,North Sichuan Medical University, Nanchong
[3]Department of Gynaecology and Obstetrics, Nanchong Central Hospital, North Sichuan Medical University, Nanchong (China)

Summary

Borderline clear cell adenofibroma of the ovary is rather rare since most clear cell tumors are carcinomas. Most patients with ovarian borderline clear cell adenofibroma are older than 50, with only a few cases of women younger than 50. Here, the authors report a 42-year-old woman with ovarian borderline clear cell adenofibroma. The surgical specimen was used for a pathological examination and immunohistochemistry. Macroscopically, the mass in the right ovary was relatively large, measuring 12×10×8 cm. Microscopically, the tumor showed the characteristic histologic features of borderline clear cell adenofibroma such as variation in size and shape of glands, cell atypia, and absence of stromal invasion. The patient had an uneventful recovery from the operation without any complications, recurrence, or metastasis during the two-year follow-up period. The prognosis of borderline clear cell adenofibroma is excellent, but the patient required long-term follow-up.

Key words: Carcinoma; Borderline clear cell adenofibroma; Ovary.

Introduction

Ovarian clear cell tumors are surface epithelial-stromal tumors, most of which are carcinomas, with benign and borderline tumors being quite uncommon, accounting for less than 5% of all ovarian clear cell tumors [1, 2]. Benign and borderline clear cell tumors are usually adenofibromatous, and their prognosis is favorable. However, borderline clear cell adenofibromas have been recently considered another precursor of the clear cell carcinoma other than endometrioma [3-6]. Therefore, it is important to understand the disease. In this report, the authors describe a case of borderline clear cell adenofibroma in a 42-year-old woman and discuss its clinical pathological features and differential diagnosis.

Case Report

A 42-year-old woman was admitted to the present hospital due to abdominal distension without abdominal pain, nausea, or vomiting. The abdominal color Doppler ultrasound revealed a large hypoechoic mass lesion measuring 13×10 cm in the pelvis, in which there were some linear blood flow signals and around which there were rich blood flow signals. The laboratory study showed an elevated CA-125, up to 386.3 U/mL (normal, < 35 U/mL), and other cancer-specific markers were normal, such as AFP, CEA, CA15-3, and CA19-9. The patient and patient's relatives were informed of the tumors and agreed to surgery for a complete resection. At the time of the surgery, there was a mass measuring 13×10 cm in the pelvic cavity, which derived from the right ovary and connected closely with the rectum. After the operation, the excised tissue was sent to the pathology department for pathological examination.

The mass in the right ovary was sent for pathologic examination. The size of the mass was 12×10×8 cm, and the outer surface was smooth. After bisecting the specimen, the resected surface appeared to be yellow-white, and firm without prominent hemorrhage and necrosis.

The tumor was composed of mainly solid nests of clear cells (Figure 1A) and occasionally variable-sized glands lined by a monolayer of flat, cuboidal, or hobnail cells (Figure 1B) within the fibrous stroma. The tumor cells exhibited clear or eosinophilic cytoplasms and nuclear irregularity, hyperchromatism, and occasionally prominent nucleoli, but did not present coagulative tumor necrosis or abnormal mitoses (Figure 1C). No evidence of stromal invasion was identified in the viable tumor areas, and endometriosis was not present in this case. By immunohistochemistry, the epithelial cells within the fibrous stroma were positive for EMA protein staining (Figure 1D). The pathologic diagnosis was borderline clear cell adenofibroma of the ovary.

The patient recovered well without any complications after removing the tumor. The patient was followed up for a two-year period, and no tumor recurrence or metastasis occurred during this period.

Discussion

Borderline clear cell adenofibroma is extremely rare. Approximately 30 cases of borderline clear cell adenofibroma have been reported, and most of them were in women older than 50 [7]. Borderline clear cell adenofibroma has no char-

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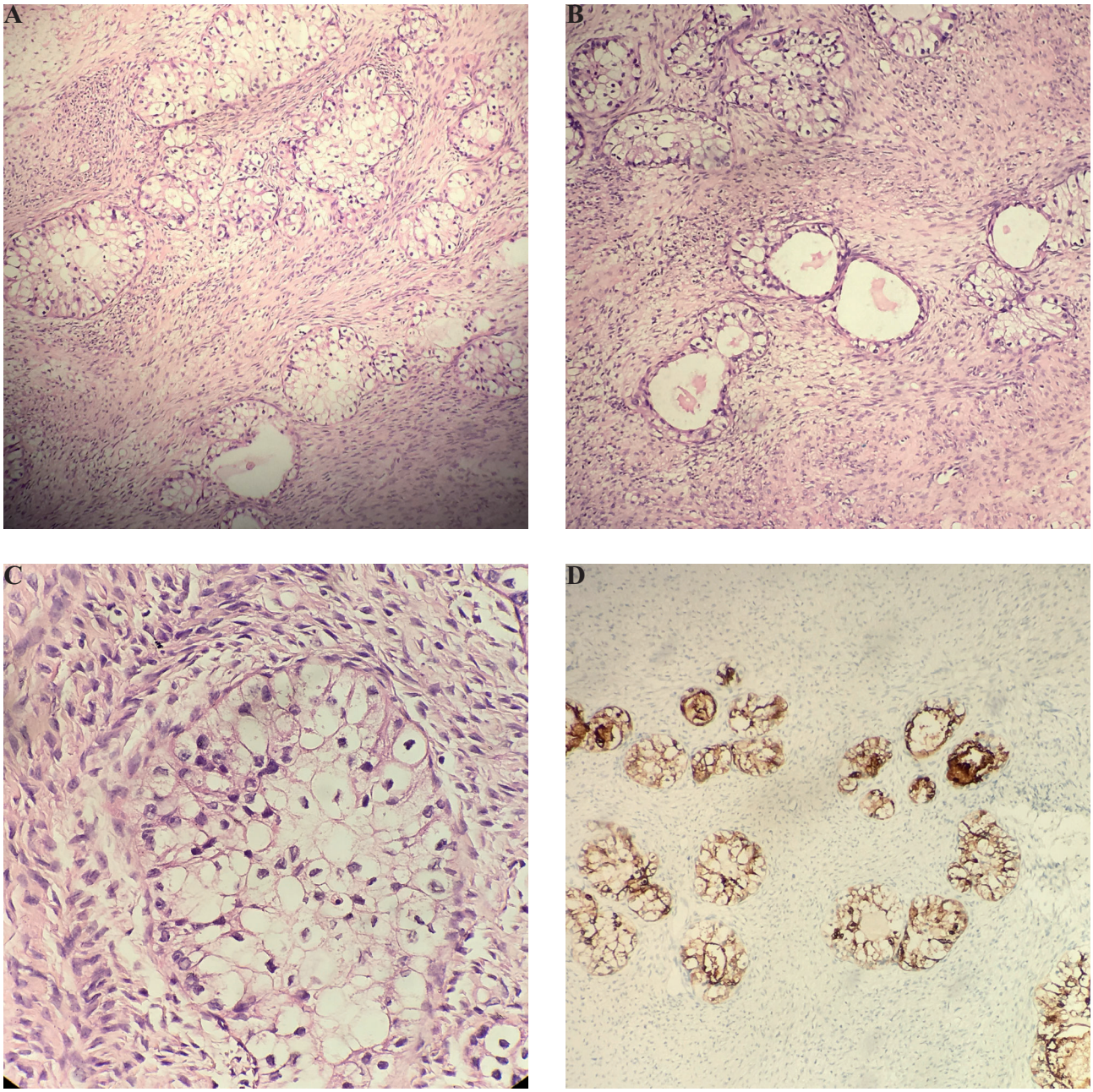

Figure 1. — Pathological examination. (A) The tumor is composed of mainly solid nests of clear cells within the fibrous stroma (HE ×200). (B) Cystically dilated glands are occasionally observed (HE ×200). (C) The tumor cells exhibit nuclear irregularity, hyperchromatism, and occasionally prominent nucleoli (HE ×400). (D) The epithelial cells express EMA with immunohistochemical staining (IHC ×200).

acteristic clinical manifestations. In the limited case reports, the common clinical manifestations are pelvic pain, but some patients have no obvious symptoms. The present patient was a 42-year-old woman with abdominal distension without abdominal pain. However, the laboratory study showed cancer-specific marker CA-125 that was significantly elevated compared to normal value. Meanwhile, the mass of the ovary was relatively large by the abdominal color Doppler ultrasound examination. The patient was therefore diagnosed with an ovarian malignant tumor before the operation. In order to decide the operation method, it is necessary to perform intraoperative frozen section examination for these cases. Studies on clear cell tumors show that they originated from the epithelium of the Müllerian duct and are related closely to endometriosis [1]. However, in the present case, endometriosis was not found in either the bilateral ovarian specimens or in pelvic cavity.

According to the classification of the World Health Or-

ganization, clear cell tumors are divided into benign, borderline, and malignant types. The borderline clear cell adenofibroma is diagnosed when the epithelial cells in a benign clear cell adenofibroma show some de- gree of cytologic atypia without definite stromal invasion. However, identification of the focal of stromal invasion is very difficult in clear cell adenofibromatous tumors. Bell *et al.* [1] proposed the criteria of invasion in clear cell tumors, which included the presence of glands, small solid nests of malignant cells, or single malignant cells extending irregularly into the stroma, and/or the presence of a desmoplastic, myxoid, or edematous stromal reaction. In the present case, the authors did not find any characteristics of the above criteria. If epithelium cells in the borderline tumor present obvious atypia without invasion, the term "borderline clear cell adenofibroma with intraepithelial carcinoma" is advised [7].

A study showed that ovarian clear cell adenofibroma, atypical proliferative (borderline) clear cell adenofibroma, and clear cell carcinoma represented a continuous morphologic spectrum [8]. Since clear cell carcinoma sometimes is accompanied by adenofibromatous areas, extensive sampling of any benign or borderline clear cell adenofibromas is essential to exclude areas of carcinoma. Yamamoto *et al.* [9] observed that each component in the clear cell tumors containing these three components displayed progressively higher Ki-67 proliferation indices, respectively. In another study by Yamamoto *et al.*, loss of heterozygosities on 5q, 10q, and 22q were frequently present in each of the three clear cell components. Meanwhile, the overall frequency of loss of heterozygosities in each component increased from benign clear cell adenofibromas to clear cell carcinoma, respectively [10]. Zhao *et al.* [8] speculated that there were two pathways to pathogenesis of ovarian clear cell carcinoma. In the endometriotic cyst pathway, endometriosis forms an endometriotic cyst and, through epithelial atypia (atypical endometriosis), develops into clear cell carcinoma. In the adenofibromatous pathway, they speculated that noncystic endometriosis induces a fibromatous stromal reaction resulting in the formation of clear cell adenofibromatous. With further glandular proliferation, it progresses, which subsequently develops into an invasive carcinoma, possibly through intraepithelial carcinoma.

The prognosis of patients with borderline clear cell adenofibroma is favorable. In the present patient, no tumor recurrence or metastasis occurred during the two-year follow-up period. However, borderline clear cell adenofibromas are considered as a precursor of the clear cell carcinoma. Moreover, due to its rarity, the clinicopathological features of borderline tumors are limited. Therefore, it is necessary to evaluate the exact histological features of the borderline clear cell adenofibroma and recommend long-term follow-up in all patients. The present patient was a 42-year-old, and the size of the tumor was relatively large. Therefore, the present authors will perform long-term follow-up of their patient to determine the characteristics of the tumor.

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Corresponding Author:
JIYAN LIU, M.D.
Department of Abdominal Oncology, Cancer Center
West China Hospital, Sichuan University
No. 37 of WainanGuoxue Lane, Chengdu
Sichuan Province (China)
e-mail: liujiyan1972@163.com