Case Report

Primary Appendiceal Adenocarcinoma Presenting as Advanced Ovarian Cancer: A Case Report

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Key Words
Krukenberg's tumor;
Ovarian metastasis;
Primary appendiceal cancer

Background. Account for less than 1% of all gastrointestinal tumors, primary appendiceal malignancies are rare and their diagnoses are usually made after exploratory laparotomy. Most of them present with nonspecific symptoms, such as abdominal pain, abdominal fullness and huge pelvic mass, mimicking advanced stage ovarian cancer.
Case Presentation. We described a menopausal women who was referred to our institution under the impression of advanced stage of primary ovarian cancer. However, the patient was eventually found to have primary appendiceal adenocarcinoma with ovarian metastasis at laparotomy. Initial symptoms, intraoperative finding, pathology finding, and postoperative clinical courses were recorded.
Conclusions. Comparing with primary ovarian tumor, ovarian metastasis is relatively rare. The clinical picture can be misleading and the differential diagnoses of primary appendiceal cancer should be considered when preoperative workup is planned.
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The ovarian metastatic tumor, also known as Krukenberg tumor (KT), is a rare variety of metastatic cancer which accounts for less than 2% of all ovarian tumor,[1] and although primary adenocarcinoma of the appendix only accounts for approximately 1% of all neoplasms of gastrointestinal origin, the incidence of ovarian metastasis in appendiceal adenocarcinoma is encountered in 16.7 to 37% of cases.[2,3]

Usually, these tumors are diagnosed postoperatively because of unspecific presentation or detection as an incidental finding during exploration for other surgical pathology. Even though abdominal ultrasound and computed tomography might be used, it is difficult to differentiate KT from other abdominal malignancies, including ovarian carcinoma. Here a patient with KT from an occult primary appendiceal adenocarcinoma are described that could only be identified at exploratory laparotomy. Clinical and pathological features of appendiceal tumors with ovarian metastasis are reviewed as well.

Case Presentation

A 56-year-old female patient (gravida 7, para 4, abortion 3) presented with abdominal fullness. A pelvic ultrasound showed a complex mass of 18 × 20 cm on left side of the uterus with no free fluid in the ab-

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dominal cavity. The results of preoperative examinations, including chest X-ray, colonoscopy (Fig. 1), and panendoscopy were all within normal range as were her hematology profile, serum chemistries, urinalysis and CA-125 values. However, her serum carcinoembryonic antigen (CEA) level was 17.1 ng/mL. Abdominal computed tomography (CT) scan showed a 21.4 × 14.4 cm heterogeneous mass in the right lower abdomen and pelvis with a small amount of ascites in the pelvis (Fig. 2). Ovarian cancer was then suspected. At explorative laparotomy, a right ovarian tumor measuring 21 × 15 cm (Fig. 3) and a left ovarian tumor measuring 3 × 2 cm were found. Further exploration of the abdomen revealed a mucinous content tumor of about 2 × 2 cm in the tip of the appendix with mild lumen narrowing (Fig. 4). Appendectomy was performed for frozen section pathology, and the result was adenocarcinoma of the appendix; therefore, bilateral salpingo-oophorectomy, infracolic omentectomy and radical right hemicolectomy and D2 lymph node dissection were performed. The definitive pathological findings were as follows: left ovarian tumor was solid 18.5 × 15.5 × 14.0 cm and right ovarian tumor was 5.8 × 3.3 × 3.2 cm in size, histologically composed of multiple cystic tumors lined by neoplastic mucin-producing columnar epithelial cells bearing low-grade nuclei. The appendix was 8 cm with a diameter of 1.5

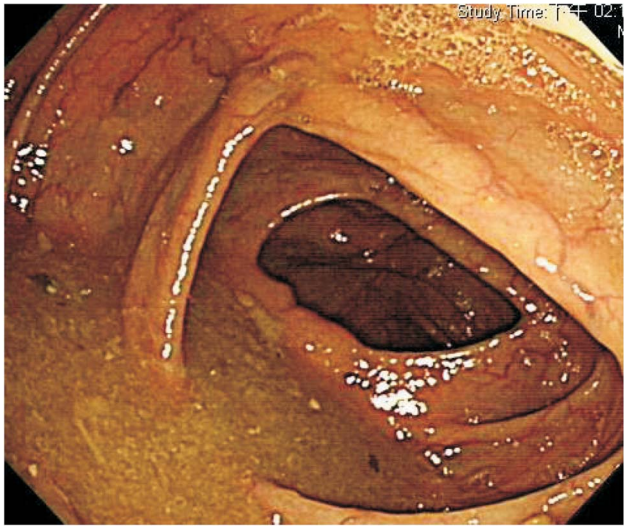

Fig. 1. The colonoscopy showed negative finding.

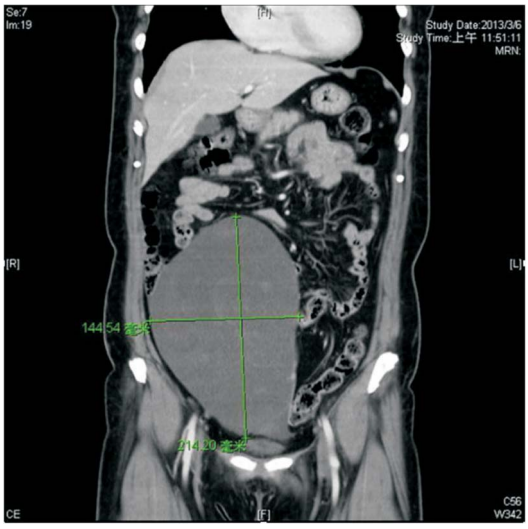

Fig. 2. Contrast-enhanced computed tomography scan reveals a 21.4 × 14.4 cm heterogeneous mass, which evidences a metastatic ovarian tumor.

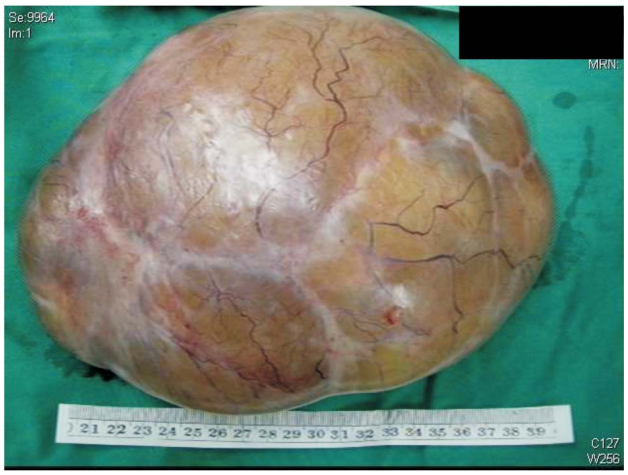

Fig. 3. A huge right ovarian cystic lesion measuring 21 × 15 cm was found.

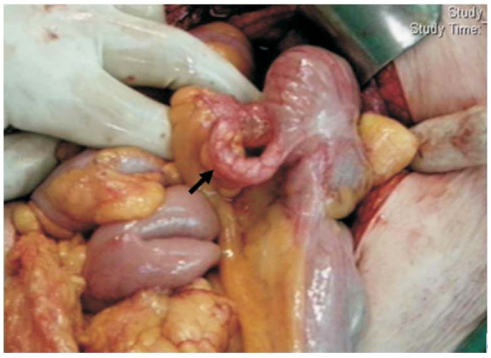

Fig. 4. A black arrowhead indicates a swollen appendix with mucinous content tumor of about 2 × 2 cm in the tip of appendix.

cm. The tumor had grown through the submucosa and muscular layers. Immunohistochemical (IHC) staining with cytokeratin (CK) 7 and CK20 were performed for ovarian specimens and the results were positive for CK20 and negative for CK7 (Fig. 5 and Fig. 6). The results were consistent with an adenocarcinoma of the appendix. The final pathological staging was pT4aN0M1b, stage IVB. Postoperatively, the patient received chemotherapy with oxaliplatin 85 mg/m^2 as a 2-hour infusion on day 1, leucovorin 400 mg/m^2 as a 2-hour infusion on day 1, followed by a loading dose of fluorouracil (5-FU, 400 mg/m^2) IV bolus on day 1, then 5-FU (2,400 mg/m^2) administered via ambulatory pump for a period of 46 hours every 2 weeks. The treatment course was 6 months. The CEA levels were then followed up and CT scan showed no evidence of recurrence 14 months after the surgery.

Discussion and Conclusion

Primary appendiceal cancer with ovarian metastasis often presents with vague and nonspecific abdominal symptoms, and usually mimic advanced-stage ovarian primary malignancy. Because of the rarity of this disease and limited information provided by preoperative imaging, it is difficult to confirm the diagnosis before the operation; therefore, the case is often mistaken as primary gynecological tumors rather than primary ovarian cancer rather than KT.[4]

Reported factors that account for misdiagnosis include lack of history of gastrointestinal symptoms, abdominal distention, elevated serum tumor marker such as CA 125 levels, and outside pathology reports in support of ovarian primary.[5] Oncological surgeons should keep in mind that primary appendiceal cancer is a possible origin source when the diagnosis of ovarian tumor cancer is confirmed.

The results of permanent IHC staining for CK are different for primary appendiceal cancer and primary ovarian cancer. In primary adenocarcinomas of the large intestine and appendix, it is uniformly stained positively for CK20 and presents typically in a diffuse pattern. Although CK20 is also positive for 75% of primary ovarian mucinous carcinomas, the staining is commonly patchy. In contrast, primary ovarian epithelial tumors of all cell types are stained for more than 96% of cases and the cytoplasm are typically strongly marked.[6,7] However, permanent result of IHC staining is usually confirmed after surgery. If the diagnosis of primary appendiceal cancer can be established intraoperatively, it would not only lead to a correct diagnosis and optimal surgery but also avoid any subsequent operation; otherwise, occult appendiceal metastases might occur in patients with primary epithelial ovarian cancer (5-10% in early stage) and are diagnosed only after microscopic examination of the appendix.[8,9] Appendectomy should be part of staging surgery in patients with presumed ovarian cancer. Especially in cases without definite primary lesion, routine appendectomy should be recommended, because the appendix might appear macroscopically normal.

Adnexal tumors are common among women of all ages and malignant ovarian tumors need to be recognized in order to expedite appropriate treatment. Survival from primary appendiceal cancer depends on extent of tumor, tumor location, and cell type. Because of the rarity of primary appendiceal cancer, issues regarding diagnosis, surgical management, and adjuvant chemotherapy are not well established, although

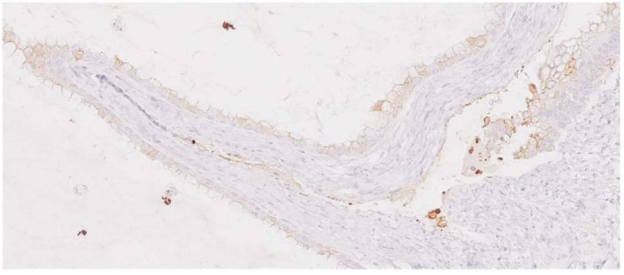

Fig. 5. CK7 in ovary metastatic tumor (IHC stain) showed negative.

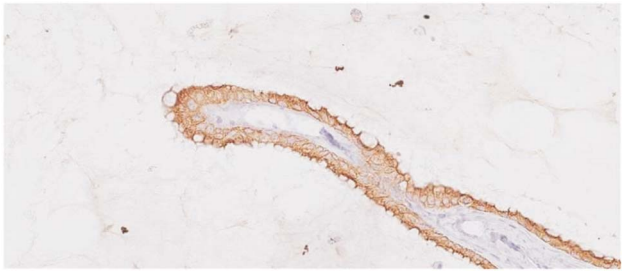

Fig. 6. CK20 in ovarian metastatic tumor (IHC stain) showed positive.

aggressive resection and treatment should be offered to young patients with ovarian metastasis, as this generally confers a 5-year survival advantage of 20-30%.[8]

Managing a pelvic mass is one of the common problems for gynecologists; unfortunately, there is no reliable method to distinguish between benign and malignant ovarian tumors. Gynecologists as well as radiologists should consider carcinoma of the appendix in the differential diagnosis of pelvic mass. Though the colonoscopy of our case was normal, this patient did have elevated CEA level. This might be a clue for us to make the diagnosis of metastatic ovarian tumor from GI tract. Abnormal elevation of CEA level is less common in early stages of primary ovarian cancer. On the other hand, in patients with colorectal cancer, it is associated with all stages of the disease. Some reports suggest that ovarian metastasis from colorectal origin should be consider in any patient whose CA-125/CEA ration is less than 25.[10]

Recent studies reveal human epididymis protein 4 (HE4) is superior to distinguish benign ovarian tumors from primary ovarian malignancies.[11] Whether HE4 can be used to identify the primary ovarian cancer from metastatic tumors might need further evaluation. We suggest that the CEA and HE4 tests be offered to women patients with suspected ovarian tumors to assist in making preliminary diagnosis before surgery, especially those with primary sites that are difficult to determine.

Since primary appendiceal adenocarcinoma is rare, these cases remind gynecological surgeons to be familiar with primary appendiceal tumors and to inspect the appendix when the initial exploration surgery is to be performed. The clinical picture can be misleading and the differential diagnoses of primary appendiceal cancer should be considered when preoperative work-up is planned.

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病歷報告

以晚期卵巢癌表現之原發闌尾惡性腫瘤：個案報告

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背景 原發闌尾惡性腫瘤僅佔所有腸胃道惡性腫瘤的百分之一以下，且常於剖腹探查時術中診斷。病人常表現出非特異性症狀，如腹痛、腹脹、或相似於晚期卵巢癌的巨大骨盆腔腫瘤。

個案報告 我們描述了一位經診斷為晚期原發性卵巢癌並轉診至本院的停經後婦女。然而，此患者在術中診斷為闌尾惡性腫瘤併卵巢轉移。術前表現、術中發現、病理報告及術後臨床病程皆被記錄。

結論 相較於原發性卵巢癌，卵巢之轉移性惡性腫瘤相對少見。臨床表徵常誤導診斷者，而在術前評估時，闌尾原發惡性腫瘤須列入鑑別診斷。

關鍵詞 克魯根勃氏瘤、轉移性卵巢腫瘤、原發性闌尾惡性腫瘤。