Introduction

Ovarian cancer, particularly endometrioid adenocarcinoma and clear cell adenocarcinoma, often presents with concurrent chocolate cysts. Consequently, recent research has investigated the possibility that endometriosis may cause ovarian cancer.1 Although endometriosis is generally limited to the uterus, ovaries, and pelvic peritoneum, extragonadal endometriarial lesions are also found. Approximately 80% of endometriosis cases originate in the ovary, and malignant transformation (MT) of endometriosis occurs in only 1–2.5% of endometriosis cases. Therefore, MT of endometriosis of extra ovarian origin is extremely rare, and late diagnosis may result in a poor prognosis.

There are very few reported cases of extragonadal endometrioid adenocarcinoma, either de novo or arising from MT of endometriosis. Herein, we present the case of an unmarried nulligravida woman with no history of endometriosis and who developed endometrioid adenocarcinoma originating from the serous surface of the small intestine.

Case Report

A 25-year-old woman consulted her local physician for symptoms of lower abdominal bloating and frequent urination. She was gravida 0, para 0, with no symptoms of hypermenorrhea or dysmenorrhea and no notable medical or family history. An internal examination and ultrasound revealed a tumor-like mass approximately 80 mm in diameter in the region of the right ovary. She was referred to our hospital for further investigation. On vaginal examination, a soft rubbery mass with good mobility was palpated in the left pelvis, and slight pressure-induced pain was observed in the lower abdomen. Transvaginal ultrasoundography showed normal ovaries but a somewhat hypoechoic mass 82 mm in diameter was observed near the right ovary. Therefore, an ovarian tumor was suspected.

Laboratory tests revealed a normal white cell blood count of 10,000 cells/µL but an elevated C-reactive protein of 2.9 mg/dL (normal <0.8). Among the tumor markers carcinoembryonic antigen (0.4 ng/mL (normal <5)), cancer antigen (CA)125 [469 IU/mL (normal <40)], and CA19-9 [10.0 IU/mL (normal <37)], only CA125 was above the normal range. Uterine cervical cytology was negative for intraepithelial lesions and malignancy. Uterine endometrial cytology and endometrial biopsy (curettage) were negative for carcinoma.

T1-weighted magnetic resonance imaging (MRI) of the pelvis revealed an 80×50 mm lobulated mass isointense to skeletal muscle on the ventral side of the uterus. On T2-weighted MRI, the mass was slightly hyperintense with multiple hyperintense foci (Figure 1A). On diffusion-weighted images, the mass showed hyperintensity with low apparent diffusion coefficient (ADC) value. Contrast-enhanced imaging showed irregular enhancement of the tumor (Figure 1B). There was no evidence of left ovarian enlargement, and the right ovary could not be clearly identified. Because the organ of tumor origin could not be identified and malignancy could not be ruled out, laparotomy was performed 1 week after the initial examination. Bloody ascites was observed on incision of the abdomen. Within the abdominal cavity, a soft, rubbery 90-mm tumor was observed covering the greater omentum, with adhesions to the left side of the bladder fundus and the sigmoid colon. However, no abnormalities of the uterus or bilateral adnexa were observed. The mass was identified as a tumor of the small intestine 40 cm from the ileocecal junction on the oral side. It originated from the ileal mesentery, and there were severe adhesions between the tumor and the bladder and sigmoid colon. Therefore, 10 cm of the ileum, including the tumor, was resected, and the stump was reconstructed using functional end-to-end anastomosis. The local lymph nodes did not appear to be enlarged.

The resected tumor was 95×55×50 mm in size with accumulations of a reddish-brown fluid and a yellowish-white solid center that was soft and rubbery. Histopathology showed that the tumor was an adenocarcinoma limited to the subserosa of the small intestine, with adhesion and proliferation of highly columnar tumor cells forming an irregular gland along with some solid components. A high degree of dyskaryosis and nuclear fission was observed. The tumor cells were positive for cytokeratin (CK)7 (Figure 2B) and estrogen receptor α.
receptor (ER) and negative for CK20 (Figure 2C) and progesterone receptor (PgR); this confirmed a diagnosis of endometrioid adenocarcinoma. The tumor was grade 1 because of the presence of some solid components and dyskaryosis. There were no findings suggestive of endometriosis in the small intestine wall, and ascites cytology was negative for carcinoma. Based on the above findings, the tumor was not diagnosed as originating in the small intestine but as endometrioid adenocarcinoma originating from the serous surface of the small intestine with some adhesion to the bladder fundus. This adhesion was easily detached. Postoperative 18 F-fluoro-2-deoxy-D-glucose positron emission tomography and fiberscopic examination of the large intestine showed no findings of residual or metastatic lesions. The final diagnosis was endometrioid adenocarcinoma of unknown origin and TNM/FIGO stage 3C. We recommended adjuvant chemotherapy; however, the patient and her family refused further treatment.

The patient’s postoperative course was uneventful, and she was discharged on postoperative day 12. There were no signs of recurrence 10 months after surgery.

Discussion

The ovaries are the most common site of endometriosis (80% of cases), and MT of endometriosis only occurs in 1-2.5% of all cases.2,3 Ulrich et al.4 reported that the site of extraovarian MT of endometriosis was the gastrointestinal tract in 40 of 139 patients (28%), the rectovaginal septum in 18 (13%), the uterus (from adenomyosis) in 12 (9%), the peritoneum in 8 (6%), and various other sites such as the bladder, vagina, and umbilicus in the remaining patients. Horiuchi et al.5 insisted that molecular studies are necessary for the differential diagnosis of MT of endometriosis. Molecular studies were not performed in our case. Though our case had almost no signs of de novo carcinoma, molecular studies should be demanded to confirm the origin.

In 1925, Sampson reported the first case of MT of endometriosis.6 He proposed the following three criteria for cancer originating from endometriosis: i) there should be coexistence of cancer and benign endometriosis within the same tissue; ii) the cancer should originate from same tissue, and there should be no metastasis or infiltration from another site; and iii) the cancer should originate within the endometrial tissue, and there should be no other primary site of malignancy.6 In 1996, Scott suggested an additional qualification to complete Sampson’s criteria:7 iv) there should be findings of benign endometriosis contiguous with the tissue of the endometrial carcinoma. Because the tumor in our case developed from the serosa of the small intestine, the differential diagnosis included MT and primary small intestine carcinoma. Immunohistochemical staining for CK7 and CK20 proved useful to confirm the diagnosis of MT of endometriosis.8 Chu et al.9 reported that 75-90% of primary adenocarcinomas of the large intestine are CK7+ and CK20+, and 80-100% of endometrioid adenocarcinomas originating from the endometrium are CK7− and CK20−.8,10 The present case only met criteria 2 and 3 of the four criteria proposed by Sampson and Scott.6,7 However, we diagnosed MT of ectopic endometriosis because it is very rare that all four criteria are met, even in patients with concurrent endometriosis and epithelial ovarian cancer.9 Moreover, the immunohistochemical findings of ER+, PgR−, CK+, and CK20+ were consistent with endometrioid adenocar-
cinoma based on the report by Chu et al. In the present case, MRI of the pelvis could not identify the organ of origin of the tumor. When a relatively large tumor is found in the pelvic cavity and it is difficult to identify the organ of origin, dynamic computed tomography (CT) may be useful to identify the organ of origin by identification of the feeding artery and draining vein.

Conclusions

We present a rare case of endometrioid adenocarcinoma that developed from the serous surface of the small intestine. Preoperative MRI revealed no clear findings indicating the organ of origin, and immunohistopathology was required to arrive at the diagnosis. When a young woman presents with a pelvic tumor of unknown origin and with no history of endometriosis, endometrioid adenocarcinoma should be considered and dynamic CT should be used as part of the investigation. Prognosis may be poor depending on the staging.

Furthermore, some previous reports including Heaps et al. described the case of a woman with a history of endometriosis and who developed MT with hyperestrogenism from estrogen replacement therapy following menopause. When evaluating intestines and/or mesenterium neoplasm in women, it is important whether the neoplasm occurred in endometriosis or not. This is particularly important when the patients have the history of endometriosis and hormone replacement therapy.

References

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Figure 2. Histology of the resected specimen. A) Hematoxylin and Eosin stain showed endometrioid adenocarcinoma (×100). B) The adenocarcinoma was immunopositive for cytokeratin7 (×100). C) The adenocarcinoma was immunonegative for cytokeratin20 (×100).
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