Clear cell carcinoma arising from abdominal wall endometriosis with lymph node metastasis – a rare case report and review of the literature

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Summary
Abdominal wall endometriosis represents 1-2% of all endometriotic lesions. The malignant transformation of abdominal wall endometriosis is rare, though it can occur. Herein the authors report a rare case of clear cell adenocarcinoma arising from abdominal wall endometriosis with extensive lymph node metastasis. In this case, a 51-year-old woman presented with a growing mass in the right periumbilical area. Computed tomography scan revealed a 5-cm solid mass located on the right rectus muscle. A punch biopsy of the abdominal lesion was performed and histology showed metastatic adenocarcinoma of unknown origin. She had a surgical history of laparoscopic subtotal hysterectomy with right salpingo-oophorectomy. The patient underwent radical excision of the mass, trachelectomy, left salpingo-oophorectomy, and lymph node dissection. The abdominal wall mass showed clear cell adenocarcinoma arising from endometriosis on histology. There were extensive lymph node metastases. The patient underwent adjuvant chemotherapy. Both lymphatic and local invasion are key routes of clear cell adenocarcinoma arising from abdominal wall endometriosis. Extensive lymph node metastasis could be associated with poor prognosis.

Key words: Clear cell carcinoma; Endometriosis; Lymph node; Metastasis.

Introduction
Endometriosis is known as an inflammatory condition characterized by the proliferation of endometrial-like tissue outside the uterus that is associated with pelvic pain and infertility [1]. Although the main site of endometriosis is inside the pelvic cavity, it can also occur outside the pelvis. Abdominal wall endometriosis represents 1% to 2% of all endometriotic lesions [2] and a prior history of surgery is typically mentioned in such cases. The malignant transformation of abdominal wall endometriosis is rare, although it can occur [3]. While most previously reported cases in the literature showed local surgical scar invasion, herein the authors report a rare case of clear cell carcinoma arising from abdominal wall endometriosis with lymph node metastasis, without surgical scar invasion.

Case Report
A 51-year-old female, gravida 3 para 1, presented with a growing mass in the right periumbilical area. She had no special medical history, but had a gynecological surgical history of subtotal hysterectomy and right salpingo-oophorectomy ten years prior due to menorrhagia. She did not have any family history of gynecological malignancies.

This patient had noticed a slow enlargement of a periumbilical mass and abdominal swelling. She first visited the gastroenterological clinic in our hospital and a CT scan was recommended for evaluation of the lesion. On CT scan, a 5 cm-sized solid mass was located on the right rectus muscle showing a heterogeneously enhancing lesion, with a hypodense cystic component with irregular septa visible inside the mass (Figure 1). The location of the mass was totally separated from the low midline scar of the previous surgery. There was no specific finding on the uterus, but a 4-cm unilocular hypodense cystic lesion was observed on the left adnexa without any enhancing solid portion. Several lymph node enlargements were detected in the bilateral inguinal, left external iliac, left common iliac, left para-aortic, and aortocaval areas. CA125 and CA19-9 were 12 and 15.8, respectively, on laboratory findings at the first visit.

A punch biopsy of the abdominal lesion was performed, which revealed metastatic adenocarcinoma of unknown origin on histology. PET-CT was performed to identify the primary origin of malignancy, but no additional lesion was found except for hyper-

Figure 1. — Images from CT scan on the initial work-up revealing a 5-cm solid mass on the right lower abdominal wall.
metabolism in the gallbladder fundus, which was considered an inflammatory change due to chronic cholecystitis.

The patient was referred to the gynecologic department for further evaluation and an explorative laparotomy was promptly performed. A midline incision extending from the xiphoid to 2 cm above the symphysis pubis was made. The patient underwent trachelectomy with left salpingo-oophorectomy, bilateral pelvic lymph node dissection, para-aortic and aortocaval lymph node dissection, inguinal lymph node dissection, omentectomy, and pelvic washings along with complete excision of the mass and free margins of 1 cm. A mesh was applied to the fascia for the prevention of hernia.

Final pathology showed the uterine cervix and left ovary to be without abnormality, and a paratubal cyst on the left salpinx was reported. The abdominal wall mass showed clear cell adenocarcinoma arising from endometriosis on histology, without lymphovascular or perineural invasion. There was metastasis in 29 out of 36 regional lymph nodes (Figure 2). The omentum showed no malignant lesion.

The postoperative period was uneventful, and the patient underwent adjuvant chemotherapy with paclitaxel, carboplatin, and bevacizumab. After two cycles of chemotherapy, the patient visited the emergency room complaining of abdominal pain, which was due to a ventral hernia. An abdominal support aided in pain relief and chemotherapy proceeded as scheduled. She underwent laparoscopic ventral herniorrhaphy and small bowel adhesiolysis after six cycles of chemotherapy, after which three more cycles of chemotherapy were administered.

The follow up CT and PET-CT scans showed a 2-cm newly developed soft tissue lesion in the small bowel mesentery and multiple enlarged lymph nodes in the aortocaval, retrocaval, and left para-aortic spaces, and the bilateral inguinal chain. Second-line chemotherapy with belotecan was started and the patient is still alive.

Discussion

Endometriosis has been considered a precursor of clear cell adenocarcinoma of the ovary [4]. However, the malignant transformation of endometriosis is very rare, affecting 1% of women suffering from endometriosis, and the most common sites are the ovaries. Approximately 20% of cases occur in extragonadal sites, including the rectovaginal septum, colon, and vagina [5]. Of the three subtypes of extragonadal malignant endometriatal transformations, endometrioid subtypes represent 69%, sarcoma subtypes represent 25%, and clear cell subtypes represent 4.5%, although clear cell carcinoma is the most common malignancy of the abdominal wall arising from endometriosis [6].
This case is distinct from other cases in two aspects. In this case, the authors reported a malignancy in the abdominal wall arising from endometriosis, following laparoscopic subtotal hysterectomy and unilateral salpingo-oophorectomy. The seeding of the endometriosis into the abdominal wall affects 1% of women who undergo intrapelvic surgery, indicating iatrogenic causation [7]. Most of the previous cases reported that the malignancy occurred at the site of a previous scar lesion; however, in this patient, the abdominal wall mass was located apart from the umbilical and other small scars from the previous laparoscopic surgery, which is a distinguishing feature of this case.

Secondly, the malignant transformation of endometriosis in the abdominal wall usually invades locally, but it rarely spreads through lymphatic drainage. Only four other cases with lymph node metastasis have been reported in the literature (Table 1). The average latency was 15.4 years in all five cases and the tumor had a wide range of local invasion to all layers of the abdomen with a size of more than 5 cm. While one case showed mixed endometriotic and serous carcinoma, the others had a histology of clear cell adenocarcinoma [6, 8-10]. In two cases, preoperative evaluation had missed the lymphadenopathy; however, in the other two cases and also in the present case, multiple lymphatic metastases were found before the operation via imaging scans and subsequently confirmed by histology. In three cases including the present case, inguinal and pelvic lymph nodes showed metastases. Only one recent case and the present case showed para-aortic lymph node invasion. Given these lymphatic invasions, it can be assumed that the lymphatic metastasis pathway of abdominal wall malignancy arising from endometriosis proceeds from the inguinal lymph node to the para-aortic lymph nodes via the pelvic lymph node. This path corresponds to the route of lymphatic fluid reflux in the lower abdomen.

Sampson originally suggested three criteria for the diagnosis of malignant transformation of endometriosis: demonstration of concomitant benign and neoplastic tissue in the tumor, and the compatibility of the pathology with endometrial origin without any other primary site. Therefore, Scott proposed a fourth criterion of transition between benign endometriosis and carcinoma on histology, defined as atypical endometriosis with cytological atypia in the endometriotic glands [11]. These criteria were based on the characteristics of the malignant transformation of endometriotic ovarian lesions. Only a few cases of malignant abdominal wall endometriosis have satisfied all of those criteria [6]. In the present case, they were all confirmed on histology.

Treatment options introduced in the literature range from only surgery [12] and surgery combined with adjuvant chemotherapy [8, 13, 14] or with radiation [15], to neoadjuvant chemotherapy followed by surgery [6, 16]. However, the optimal treatment strategies must be further elucidated due to the rarity of the disease. The authors conducted surgery with adjuvant chemotherapy and the patient is currently receiving second-line chemotherapy due to the progression of the disease after nine cycles of first-line chemotherapy. The multiple lymph node metastases might be a factor of poor prognosis in this case.

### Conclusion

Clear cell adenocarcinoma of the abdominal wall arising from endometriosis is a very rare complication and a poorly understood disease entity. Gynecological surgical history such as hysterectomy or cesarean section could be a causal factor in this condition, but occasionally it would not be relevant. Both lymphatic and local invasion are important routes of tumor metastasis and extensive lymph node

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### Table 1. — Five cases of malignant transformation of endometriosis in the abdominal wall with lymph node metastasis.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Time to onset</th>
<th>Tumor size</th>
<th>Histology</th>
<th>Lymph node metastasis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bats, et al. [6]</td>
<td>38</td>
<td>13</td>
<td>10</td>
<td>CCC</td>
<td>Right iliac (1/28)</td>
<td>TAH + BSO, radical resection, omentectomy, LND, adjuvant chemotherapy</td>
</tr>
<tr>
<td>Williams, et al. [8]</td>
<td>53</td>
<td>21</td>
<td>5</td>
<td>CCC</td>
<td>Inguinal (17/17) Pelvic (10/14)</td>
<td>TAH + BS, radical resection, omentectomy, LND</td>
</tr>
<tr>
<td>Du Ines, et al. [9]</td>
<td>48</td>
<td>16</td>
<td>6</td>
<td>Mixed endometriotic and serous carcinoma</td>
<td>Left iliac (2/?)</td>
<td>TLH + BSO, radical resection, curettage, LND, adjuvant chemotherapy</td>
</tr>
<tr>
<td>This case</td>
<td>51</td>
<td>10</td>
<td>5</td>
<td>CCC</td>
<td>Inguinal (12/17) Pelvic (7/9) Para-aortic (21/26) Aortocaval (1/1)</td>
<td>Trachelectomy + LSO, radical resection, omentectomy, LND, adjuvant chemotherapy</td>
</tr>
</tbody>
</table>

metastasis could be associated with poor prognosis.

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References

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