Primary retroperitoneal mullerian adenocarcinoma

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Abstract

Mullerian tumors are extremely rare malignancies in the retroperitoneum. We report a case of a 46-year-old woman who presented with an eight-year history of lower abdominal mass. Ultrasonography (US) and computed tomography (CT) demonstrated a 15x10 cm cystic mass in the left lower retroperitoneum. As serial percutaneous needle aspiration cytology was negative for malignancy, she was observed for seven years. Eleven months ago, the mass was excised. The histopathology was reported as mucinous adenocarcinoma of the retroperitoneum. Six cycles of intraperitoneal (IP) chemotherapy was administered during the last six months after diagnosis of recurrence by aspiration cytology and high serum tumor markers (CEA, CA19-9). A few days ago, positron emission tomographic (PET) scanning showed evidence of local recurrence and single vertebral metastasis, so she was admitted again for systemic chemotherapy. Meticulous revision of additional sections of the tumor revealed papillary, serous, mucinous, and endometrioid subtypes of the mullerian adenocarcinoma. To our knowledge, there has been no similar case described in the literature.

Introduction

Malignant mullerian tumors usually arise in the uterine corpus,1 but cases in other sites of the genital tract, such as vagina,2 uterine cervix,3 fallopian tube,4 and ovary,5 have occasionally been reported. Extranodal malignant mullerian tumors arising from the peritoneum, the pelvic wall, or omentum have been documented.6–8 Among the extragenital sites, the retroperitoneum is one of the rarest sites, and, to the best of our knowledge, primary retroperitoneal adenocarcinoma of mullerian origin has been documented in only 3 case reports.9–11 We report here the first case of retroperitoneal primary mullerian cystadenocarcinoma with serous papillary, mucinous, and endometrioid components.

Case Report

A premenopausal 46-year-old woman had noticed a painless slowly enlarging mass in the left lower abdomen eight years ago. There was no history of endometriosis, pelvic irradiation, or exogenous estrogen administration. Physical examination revealed a slightly tender, ill-defined mass about 15 cm in size over the left lower abdomen. The remaining systemic examination did not reveal any coexistent lesions. The laboratory tests, including the complete blood count, the chemistry profile, urinalysis and chest X-ray, were all within normal limits. Abdominopelvic computed tomography (CT) scanning revealed a large unilocular cystic mass with an enhancing solid portion, and this was probably located in the retroperitoneal space (Figure 1A). There was no evidence of extracystic extension or distant metastasis. Serial percutaneous aspiration cytology was negative for malignancy. Eleven months ago, the patient was referred to our center where a repeat CT scanning demonstrated cystic mass of the same previous size with a thick wall and homogenous fluid content. Percutaneous aspiration by 14G needle yielded brownish red thick fluid, but the cytology was also negative for malignancy. Laparotomy revealed a grossly normal uterus, 2 ovaries, 2 fallopian tubes and an appendix. There were no abnormal findings in the liver, stomach, small bowel, large bowel and spleen. A large, encapsulated cystic mass about 15 cm in diameter was found in the left retroperitoneum. It was not connected to the bowels or other organs. The descending colon was displaced medially to the mass, and no ascites was found. Excision of the cystic mass with a part of the left fallopian tube was carried out. However, the capsule was ruptured accidentally during resection releasing necrotic and brown mucoid viscous material. Hysterectomy, salpingoophorectomy, appendectomy and lymphadenectomy were not performed. The serum tumor markers were not checked before tumor excision.

The gross pathological findings showed a 15x12 cm sized, unilocular cystic mass covered by a thick fibrous capsule and focally by peritoneum. The inner surface of the cyst showed cobblestone appearance with three solid mural nodules that were 1.5, 1 and 2 cm in diameter, respectively. The cystic wall measured 0.7 cm at the maximum thickness. There was evidence of capsular rupture. The mural nodules were soft and yellowish (Figure 1B and C). Microscopically, as the cyst was lined by atypical columnar cells of mucinous type, the diagnosis was mucinous cystadenocarcinoma. Two months later, a peritoneal port system was introduced into the abdominal cavity for administration of IP chemotherapy.12 After the patient was subsequently treated with 3 cycles of IP cisplatin and docetaxel (40 mg each) in 500 mL physiological saline, the aspiration cytology was negative for malignancy, but after a further two months, it showed class-V adenocarcinoma. A repeat CT did not show relevant data (Figure 2A) but PET scanning revealed an area of 8x7 cm with high standard uptake value (SUV) of 18F-FDG in the left iliac fossa, and in the 12th thoracic vertebral body, and some accumulation of 18F-FDG in the pelvis, paracolic gutters and peritoneum (Figure 2B and C). The serum CEA increased to 6.8 ng/mL, CA 19-9 was 465 U/mL (normal range: <37), and the CA125 was 19.9 U/mL (normal range: <35).

Meticulous revision of additional sections, however, revealed mixed adenocarcinomatous components containing many subtypes; papillae and tubules of serous adenocarcinomas subtype that have complex branching papillae with prominent epithelial stratification yielding epithelial tufts and an apparently detached epithelial cell cluster (Figure 3A and B). Mucinous adenocarcinoma subtype is composed of cells similar to those present in adenocarcinomas of the large intestine with many goblet cells. There is also pseudostratification, and only small amounts of intracellular mucin present (Figure 3C and D). Scattered areas of endometrioid adenocarcinoma subtype was also evident with the characteristic histology of tubular glands. The cells tend to be stratified and have oval nuclei that were arranged with their long axis perpendicular to the basement membrane of the gland. The cells do not contain mucin and have less cytoplasm (Figure 3E and F). The predominant cell
type was mucinous adenocarcinoma. Each component of the other cell type was about 15%. In carcinoma cells, immunohistochemical staining was strongly positive for cytokeratin 7 (monoclonal, DAKO, 1:50) but was negative for CK20 (monoclonal, DAKO, 1:50). The stromal cells which were focally found in the cyst wall were positive for CD10 (monoclonal, DAKO, 1:50) (Figure 3G and H). However, no immunoreactivity was found to estrogen and progesterone receptors (ER/PR).

The excised segment of the left fallopian tube was associated with a surrounding dense fibrosis but the tube itself did not show mucosal abnormalities. There was no lymph vascular invasion and the peritoneal biopsies were negative for metastasis. The patient is currently receiving repeat chemotherapy with 6 courses of cisplatin and docetaxel.\(^{11}\)
Case Report

Discussion

Although extragenital malignant Mullerian tumors occur infrequently, their clinical feature and diverse spectrum of histopathological pattern has been a subject of interest. Approximately half the cases reported in the literature were located in the pelvic peritoneum, followed in decreasing frequency from the serosal surface of colon, retroperitoneum, anterolateral abdominal peritoneum and omentum.1–4 Our case of Mullerian adenocarcinoma appears to have originated in the retroperitoneum in view of its location and gross appearance. Although a part of this tumor was attached to the peritoneum and had ruptured into the pelvic cavity, an origin in the peritoneal surface can be excluded, judging from the clinical history and findings at surgical exploration.

Most extragenital malignant Mullerian tumors occur in elderly postmenopausal women. The relation between their occurrence and previous irradiation or chemotherapy for other gynecological malignancies has been reported in the literature.5–7 We believe this case to be of importance because the patient in this report was a premenopausal woman who had neither carcinomas in the genital tract nor had a history of irradiation or chemotherapy. However, its occurrence in the reproductive age may suggest a possible hormonal influence on the etiology.

One of the features of female genital carcinomas is the presence of steroid receptors in tumor cells, including ER/PR. In our case, immunohistochemical studies showed the tumor cells were negative for ER/PR suggesting that they are hormone-independent tumors.

Mullerian-type neoplasms have been reported infrequently in the retroperitoneum, including benign Mullerian cyst, mucinous cystadenoma, carcinoma arising in Mullerian cyst, serous and mucinous(cyst)adenocarcinomas, clear cell carcinoma, and endometrial stromal sarcoma.8–10 The present case showed unifocal tumor that consisted of an admixture of malignant epithelial components. These epithelial components represent a variety of different histological subtypes; papillary, serous, mucinous, and endometrioid features. To the best of our knowledge, this is the first reported case of primary retroperitoneal Mullerian tumor having these mixed subtypes of adenocarcinoma. Interestingly, Shinmura et al.11 documented, incidentally at autopsy, a clear cell adenocarcinoma of the remnant uterus in persistent Mullerian duct syndrome in a man who died in a traffic accident, and suggested remnant of the Mullerian duct in the retroperitoneum as a possible origin of the tumor. The histogenesis of extragenital neoplasms of Mullerian-type remains largely speculative. Two major hypotheses have been proposed. The first hypothesis assumes the presence of endometriosis as a possible origin of these neoplasms.4 Although this possibility is difficult to rule out, supporting evidence has been found in only a small number of cases.12–13 In most reported cases of extragenital Mullerian-type tumors, and also in this case, coexistence of endometriosis with the tumor has not been demonstrated. The second hypothesis is based on the existence of the “secondary Mullerian system”, which was extensively discussed by Lauchlan.14 According to this hypothesis, the coelomic epithelium covering the female peritoneal surface has the potential for Mullerian differentiation, a potential shared by the underlying “subcoelomic mesenchyme”, which may be the origin of the extragenital Mullerian-type neoplasms arising in the retroperitoneum.15–17

The present tumor was difficult to diagnose not only because it is a rare condition in the retroperitoneum but also due to microscopic findings of many subtypes of adenocarcinoma. To identify the primary malignancy of the tumor, we performed immunohistochemical analysis to achieve a differential diagnosis. The positive CK7, the negative CK20, and the presence of CD10 positive stromal cells in the present case provided immunohistochemical evidence suggesting a Mullerian origin.

The early tumor recurrence we experienced in this case may reflect the aggressive nature of the tumor with tendency toward local spread, and hematogenous metastases, or the intraperitoneal seeding due tumor rupture that occurred accidentally at the time of surgery. It is, therefore, essential to avoid tumor rupture during the operation because malignant cells may exist in the spilled fluid; this results in subsequent peritoneal tumor implantation. We recommend PET as a useful diagnostic tool in defining the recurrence of disease, in identifying metastases, and assessing treatment effectiveness.

Primary retroperitoneal adenocarcinoma is a rare tumor and in all reported cases, the duration of follow-up was not more than five years.17 Due to the rarity of this tumor, no evidence based management guidelines are available. Laparotomy and complete tumor excision should be the principal modality of treatment. Pathological examination is inevitable to make a correct diagnosis. As the role of adjuvant chemotherapy and/or radiotherapy is not well-defined, patients with metastatic disease can be treated with palliative chemotherapy. Long-term follow-up is essential to evaluate the course and prognosis of this disease.

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