Immature uterine teratoma associated with uterine inversion

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Abstract

Teratomas are the most commonly diagnosed germ cell tumors and occur primarily in testes and ovaries. Platinum-based therapy followed by surgical resection of the residual lesion is generally the recommended treatment. In contrast, immature uterine teratomas are rare, with few cases reported in the literature. Moreover, there is no standard treatment for these tumors. Non-puerperal uterine inversion is also rare in women younger than 45 years of age, and neoplastic lesions are responsible for this condition. Here, we report a case of an immature uterine teratoma associated with uterine inversion. The patient underwent surgery followed by adjuvant chemotherapy and continues to be monitored.

Introduction

Teratomas are the most common type of germ cell tumor diagnosed and they primarily develop in testes and ovaries.¹ Extragonadal teratomas represent 2.3% of adult germ cell tumors, and they mainly localize in mediastinum. Teratomas rarely originate in the uterus. To date, only four cases of immature uterine teratoma have been reported.²⁻⁵

Case Report

A 23-year-old woman presented with a three-month history of vaginal bleeding and malodorous discharge. She had no known comorbidities and her gynecological history included normal menstrual cycles that started at age 11. The patient also had no history of previous sexual activity. During a gynecological consultation in January 2013, a bulky tumor was visualized at the vaginal opening and a biopsy of the lesion was performed. No adnexal masses were detected. Histopathological examination was consistent with adenocarcinoma of the cervix. Since the material was not available for confirmation of this finding, the patient was referred to a gynecological oncologist who performed a second biopsy of the tumor. The patient developed a sudden episode of intense vaginal bleeding, fatigue, and dyspepsia, resulting in hospital admittance. Her initial hemoglobin value was 5.4 g/dL (normal range, 12-16 g/dL) and blood transfusion was required. Concomitantly, the results of the second biopsy indicated necrotic tissue with inflammatory findings and an absence of neoplastic cells.

Based on the clinical findings, epidemiological profile, physical examination, and previous histopathological results, the patient was treated with a total dose of 40 mg/m² cisplatin and four fractions of 180 cGy radiotherapy. Staging exams were performed and pelvic magnetic resonance imaging revealed a uterine inversion due to a bulky lesion (110×94×82 mm³) present in the endometrium. This lesion also presented an exophytic component that extended through the vaginal canal (Figure 1A,B). No metastatic disease was detected. With evidence that the tumor originated in the endometrium, chemo-radiotherapy was suspended and a surgical approach was scheduled.

Two days after chemo-radiotherapy was discontinued, and while waiting for elective surgery, the patient experienced significant vaginal bleeding and hemodynamic instability. Emergency surgical intervention was required and a total abdominal hysterectomy with bilateral salpingo-oophorectomy and bilateral pelvic resection of suspicious lymph nodes was performed. Macroscopic analysis revealed uterine cavity inversion and a polypoid tumor mass with a lobulated surface located at the uterine fundus. The lesion measured 95×5×45 mm (Figure 1C). Microscopic analysis further revealed atypical foci of glandular epithelium combined with occasional immature tubular, cystic, and glomeruloid structures without atypia. The mesenchymal component of the tumor included mature fusocellular tissue, scarce cartilage tissue without atypia, and myxoid stroma (Figure 2A-D). The tumor had invaded 0.5 cm of a total of 2.0 cm of the myometrium thickness. In addition, no lymphovascular or perineural invasions were detected. Surgical margins, uterine cervix, fallopian tubes, ovaries, and all of the twelve lymph nodes dissected were not compromised. Immunohistochemistry analysis was performed. Epithelial components were positive for pan-cytokeratins (cytokeratin AE1/AE3) and Ki-67, while a few cells were positive for CD10. In addition, various areas exhibited focal staining for alpha-fetoprotein, hepatocyte paraffin (HepPar1), or WT1. A small area was positive for chromogranin A. In contrast, human chorionic, caldesmon, desmin, myogenin, estrogen receptor, and S100 protein were negative.

The morphology associated with the immunohistochemical panel was compatible with a grade 2 immature teratoma and a polyvesicular vitelline neoplasia. These findings suggest that a yolk sac tumor associated with an immature teratoma. A region (1.7 mm) that exhibited neuroendocrine differentiation was also observed, and this was compatible with the presence of a carcinoid tumor in the midst of the teratoma. Tumor markers were subsequently assayed, and the following results were obtained: 874 U/L lactate dehydrogenase (normal range, 240-480 U/L), 1.29 mU/mL human chorionic gonadotropin (positive >25 mU/mL), and 5.7 ng/mL alpha-fetoprotein (normal range, <10 ng/mL). No tumor marker measurements were made preoperatively.

According to guidelines of the International...
Federation of Gynecology and Obstetrics, the current patient had a stage IA immature uterine teratoma. However, the patient had poor prognostic characteristics due to the carcinoid component detected. For this reason, adjuvant chemotherapy was performed with three cycles of bleomycin, etoposide, and cisplatin (BEP). Since August 2013, the patient has continued to be monitored and is disease-free twelve months later.

Discussion and Conclusions

Non-puerperal uterine inversion is rare in women younger than 45 years of age, and neoplastic lesions are often its cause. Few carcinomas and sarcomas of the endometrium have been found to be associated with uterine inversion, and there is only one report of an immature teratoma of the uterus causing this complication. Since immature uterine teratomas are rare, there is no standard treatment for this condition. Therefore, most of the evidence for stage I disease after surgical treatment is obtained from case reports. In these case reports, clinical observations were used to determine various treatment methods, and these included two cycles of chemotherapy vincristine, actinomycin-D, and cyclophosphamide (VAC), an undescribed treatment regimen, and radiotherapy (Table 1). In addition, not all of the reports described patient follow-up and outcomes, thereby preventing a comparison of treatment decisions. Iwanaga et al. reported a patient that received adjuvant treatment with VAC, and subsequently presented no evidence of tumor recurrence five years post-treatment. However, Newsom-Davis et al. described a para-aortic lymph node recurrence that occurred six months after surgery in a patient that was submitted to clinical follow-up alone. Therefore, rescue treatment was needed and involved an initial dose of cisplatin (20 mg/m²) and etoposide (100 mg/m²) in week 1, followed by a two-week alternating regimen of paclitaxel (135 mg/m²) and etoposide (150 mg/m²), and paclitaxel (135 mg/m²) and cisplatin (60 mg/m²). This rescue regimen led to a partial lymphadenopathy reduction and an increase in the cystic component of the lesion. Therefore, the patient underwent retroperitoneal lymphadenectomy.

Table 1. Previous uterine teratoma case reports with their management and outcomes.

<table>
<thead>
<tr>
<th>Study</th>
<th>Management</th>
<th>Recurrence</th>
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<tbody>
<tr>
<td>Newsom-Davis et al.</td>
<td>Surgery + clinical observation</td>
<td>Para-aortic lymphadenopathy</td>
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<tr>
<td>Gomez-Lobo et al.</td>
<td>Surgery + adjuvant chemotherapy (not described)</td>
<td>Not described</td>
</tr>
<tr>
<td>Iwanaga et al.</td>
<td>Surgery + adjuvant VAC ×2</td>
<td>No</td>
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<tr>
<td>Ansah-Boateng et al.</td>
<td>Surgery + adjuvant radiotherapy</td>
<td>No</td>
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VAC: vincristine, actinomycin-D, and cyclophosphamide.

![Figure 1. Radiological (A, B) and surgical images of uterine inversion (C) associated with an immature uterine teratoma. Arrows point to uterine fundus.](image1)

![Figure 2. Microscopy images (200× magnification) of immature glandular tissue (A); squamous epithelium (B); glandular, muscular, and cartilaginous components (C), and smooth muscle and glandular tissue (D).](image2)
node dissection, which confirmed a metastatic teratoma recurrence by histopathological analysis. The patient died one month after surgery due to postoperative complications.

In the current report, both previous publications regarding the treatment of ovarian germ cell tumors and the presence of a carcinoïd tumor as a factor for poor prognosis were considered in the decision to select an adjuvant BEP treatment.11-15

In summary, this case report describes a rare puerperal uterine inversion due to an immature uterine teratoma, for which there is no established therapeutic management. According to the available case reports, surgical treatment is the only standardized treatment previously described, while indications for adjuvant therapy remain uncertain. For the current patient, a treatment of a germ cell tumor and a neuroendocrine tumor included three cycles of BEP in order to reduce the potential for relapse.

References