Ovarian adenosarcoma with elevated CA125 antigen. Case report and literature review


Abstract

**Background:** Adenosarcomas are rare tumors usually derived from the endometrium. About 50 cases of adenosarcomas of the ovary have been reported. The relationship between adenosarcoma and CA125 has not been described. The authors present a case of adenosarcoma with elevated CA125 because of the unusual presentation of this pathology and also because elevation of the CA125 antigen has not been reported in the literature.

**Clinical case:** A 42-year-old woman presented for incidental right ovarian tumor and CA125 of 1100 U/mL. Histology revealed a homologous Müllerian adenosarcoma of the right ovary with sarcomatous overgrowth. CA125 decreased to 16 U/mL after surgery. Sixteen months post-surgery, the patient is disease free and with normal CA125.

**Discussion:** Ovarian adenosarcomas are more aggressive than adenosarcomas of the uterus. Because of the embryological origin, ovarian adenosarcomas are able to produce CA125 antigen, especially in the presence of sarcomatous overgrowth. With these facts, CA125 antigen may be useful as a prognostic factor because it may represent an indirect marker of sarcomatous overgrowth.

**Conclusions:** CA125 may be useful for follow-up of ovarian adenosarcomas. Elevated CA125 antigen in adenosarcomas of the ovary may be indicative of sarcomatous overgrowth and poor prognosis.

**Key words:** adenosarcoma, CA125, ovary.

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Resumen

**Introducción:** Los adenosarcomas Müllerianos son tumores raros, que usualmente se desarrollan a partir del endometrio. Se han reportado 50 casos de adenosarcomas de ovario. La relación de estos tumores ováricos y el antígeno sérico CA125 no se encuentra bien definida en la literatura. Presentamos el caso de una paciente con adenosarcoma Mülleriano del ovario derecho con elevación del antígeno CA125 con el objetivo de documentar este caso tan inusual de patología como por su presentación con el antígeno CA125 elevado que no se ha descrito en la literatura.

**Caso clínico:** Una mujer de 42 años consulta por el hallazgo incidental de un tumor en el ovario derecho asociado a un antígeno sérico CA125 de 1100 U/mL. El reporte de patología fue un adenosarcoma Mülleriano homólogo del ovario derecho, con sobre crecimiento sarcomatoso. El nivel de CA125 descendió a 16 U/mL luego de la cirugía. La paciente está libre de enfermedad y con niveles séricos de CA125 normales, luego de 16 meses de seguimiento.

**Discusión:** Los adenosarcomas de ovario tienen un comportamiento más agresivo en comparación a los de origen uterino. Se ha propuesto que por su origen embriológico, los adenosarcomas extrauterinos podrían tener la capacidad de producir antígeno CA125, en especial en los casos con sobre crecimiento sarcomatoso. En base a lo anterior, se podría utilizar la medición del antígeno CA125 sérico como un factor de mal pronóstico al indicarnos indirectamente el sobre crecimiento sarcomatoso en el tumor.

**Conclusión:** El antígeno sérico CA125 puede ser útil en el seguimiento de los adenosarcomas de ovario. La elevación del CA125 en adenosarcomas del ovario puede ser indicativa de sobre crecimiento sarcomatoso y de mal pronóstico.

**Palabras clave:** adenosarcoma, CA125, ovario.

Introduction

Müllerian adenosarcomas are a rare type of tumors.¹ According to the description by Clement and Scully in 1974,² 50 cases of ovarian origin have been described.¹⁻¹¹

The antigen associated with cancer (CA125) is a high molecular weight glycoprotein produced from normal cells of different tissues originating in the coelomic epithelium. Its increase has been found to be associated with different pathologies, and clinical usefulness has been demonstrated in epithelial cancer of the ovary.¹²⁻¹⁴
Of the series found in the literature about Müllerian adenosarcomas, the relationship of these tumors with increased CA125 has been described in only eight cases of different origins.7,9,11,15-17

A case of ovarian adenosarcoma associated with elevated serum CA125 level is presented along with a review of the literature.

Clinical case

The patient was a 42-year-old Hispanic nulliparous woman. She presented for consultation in September 2005 with the incidental finding of ovarian tumor.

Upon physical examination, the patient was obese and upon abdominal palpation a movable, painless abdominal pelvic tumor of ~20 cm with undefined borders was identified. On vaginal palpation, a tumor was found at the fundus of the sac, which did not allow delimitation of the uterus or ovaries.

Pelvic ultrasound demonstrated a 12-cm heterogeneous tumor without determination from which ovary it originated. The uterus demonstrated normal endometrium, and there was presence of scarce free fluid in the abdominal cavity.

Hematic biometry, blood chemistry, and hepatic function tests were found to be within normal limits. Serum CA125 antigen level was 1100 U/mL. Chest x-ray was normal.

Exploratory laparotomy was performed and a soft, whitish-gray right ovarian tumor was identified, being 12 cm at its greatest diameter and associated with foci of endometriosis. The left ovary appeared normal, and the uterus demonstrated a 5-cm myoma at the fundus, which was also found to be adhered to the tumor. Peritoneal lavage was performed along with extrafascial hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic lymph nodes, partial omentectomy and parietal peritoneal biopsies.

Pathology

The right ovary weighed 350 g and measured $11 \times 5 \times 5$ cm. The external surface was demonstrated to be smooth and pearly white. On cutting, a single cystic cavity was appreciated and partially occupied by a $9 \times 5 \times 5$ cm solid polypoid lesion, reddish-brown in color and chalky, brittle and with areas of necrosis and hemorrhage. Sections demonstrated a pattern of nodular zones of light brown and white color, semi-firm, and with cysts up to 0.7 cm. Residual ovary of $2 \times 1.4$ cm is observed (Figure 1). The left ovary measured $5 \times 4 \times 2.5$ cm externally as well as cut with cystic aspect, with internally smooth wall and “chocolate” content.

Ovarian neoplasia histologically demonstrated a polypoid nodular mass with biphasic pattern characterized centrally by medium or small glands and covered by endometrial epithelium that was not atypical and that externally covered the papillary formations. Atypical fusocellular stroma, generally low grade, proliferated around the glands, focally of intermediate grade with anisonucleosis and multinucleated cells of histiocytic aspect (Figure 2).

In the zones of greater mitotic activity not more than five mitoses per 10 fields with ‘40 magnification were counted. This stromal component represented 25% of the tumor. Areas of hemorrhage and necrosis were confirmed. On multiple cuts, no heterogeneous components were observed (Figure 3). Contralateral ovary demonstrated a siderophagic cyst, compatible with an endometriotic cyst.

The rest of the material to be examined (peritoneal washing, uterine horns, uterus, biopsy of the peritoneum, and iliac lymph nodes) did not present with relevant alterations.

Tumor diagnosis was homologous adenocarcinoma of the right ovary.

Figure 1. Approach of the neoplasia, the nodular pattern of the right side and presence of cysts is prominent.

Figure 2. Glands with benign epithelium and presence of atypical stroma (magnification ×112).
Follow-up

The tumor was classified as clinical stage IA with sarcomatous overgrowth. CA125 antigen returned to normal serum level immediately after surgery.

It was decided to continue treatment with hormonal therapy using medroxyprogesterone. There was no other type of adjuvant therapy administered.

The patient is presently disease free with normal serum CA125 levels after 16 months of follow-up.

Discussion

The World Health Organization (WHO) classification of ovarian tumors includes among the epithelial-stromal surface tumors those classified as endometrioid tumors. In these tumors, epithelial or stromal elements or both are demonstrated, and they resemble those neoplasias found with greater frequency in the endometrium. As with other neoplasias of the superficial epithelium of the ovary, they can be benign, borderline or malignant.18

Included among the malignant neoplasias are adenosarcoma, mixed mesodermic tumor (Müllerian) or carcinosarcoma and stromal endometroid sarcoma. The first two could be homologous or heterogeneous. With regard to homologous tumors, the mesenchymatous structures are normal for the organ, whereas heterogeneous refers to the presence of mesodermal structures not usual for the organ (cartilage, bone, fat, striated muscle, etc.).18

WHO defines adenosarcoma as a biphasic tumor characterized by the proliferation of Müllerian epithelium of benign appearance or occasionally labeled atypical when absorbed in or covering a predominant sarcomatous stroma.18

From the description by Clement and Scully in 1978,10 multiple sites of origin for these tumors have been described1,11,15,17,19-21 with the ovary being second in frequency (up to 18% of the cases).3 However, to our knowledge, this only represents 51 cases reported, including the present one.

Macroscopically these tumors measure ~10 cm in average in diameter, some with smooth external surface. Others show, as their uterine counterpart, exophytic polypoid masses and wide papillary projections. On cutting, they are medium brown in color with zones of necrosis and hemorrhage and with the presence of small cysts. The cut surface is spongy and multicystic with clear or yellowish-colored fluid. The largest tumors could present hemorrhagic zones.1,3,22

Histologically, a leaf-form pattern similar to phylloid tumor of the breast is appreciated. There are fissures or cysts or scant cells sometimes with elongated and distorted highlights, covered with some type of benign or atypical epithelium of Müllerian origin. In general they are endometrial in origin, sometimes with pseudostratification and nuclear hyperchromasia. These glandular structures are trapped in a sarcomatous component and are abundant and predominant. They are similar in appearance to the endometrial stroma and fibromatosus, which resemble stromal neoplasias. Occasionally they can contain other heterologous elements (cartilage, bone).1,3,22

The sarcomatous component is characteristically condensed around the glands with a greater degree of atypia that is generally mild, although this finding may vary among tumors and with a greater quantity of mitoses than the rest of the stroma.1,3,22

Mitoses have been widely described from 2 to >40 per field with 40 magnification.23

The differential diagnosis of adenosarcoma should be established with adenofibromas, polypoid endometriosis, stromal sex-cord tumors, and sarcoma of endometrial stroma.24

A common embryological origin has been proposed for the coelomic epithelium and for peritoneal epithelium as well as for Müllerian tissue of the genital tract, which could explain the existence of extrauterine adenosarcomas. This coelomic origin gives them the ability to produce CA125 antigen.7,20,21

Table 1 shows data of the cases of adenosarcoma in which CA125 serum antigen levels are reported, including the present case, before as well as after treatment.7-9,11,15-17

It is important to mention that in the cases reported by Inoue et al.7 and Fukunaga et al.,8 the pattern of CA125 elevation on tumor recurrence has also been described.

Ovarian adenosarcoma presents a pattern of aggressive behavior as opposed to its uterine counterparts, which present more indolent behavior and less frequency of overgrowth of the sarcomatous component.2,3,8,15 This is defined as the presence of sarcomatous component in >25% of the sample and represents one factor for poor prognosis in these types of tumors.3,17,25,26

With regard to the case reported here, co-existence of siderophagic cyst compatible with cystic endometriosis on the
contralateral ovary is brought to our attention. It is unknown if the ovary with adenosarcoma had pre-existence of endometrial cells. Recently, a common origin for endometrial stromal cell lesions located in the endometrium has been postulated due to the low-grade malignant transformation of the originating stroma. Sarcomas of the endometrial stroma are associated with benign epithelium, and in the case of high-grade transformation would be considered a sarcoma. In cases of co-existence of benign epithelium, these would be classified as adenosarcomas with sarcomatous overgrowth.27

Our case fulfilled the criteria required for histological diagnosis of adenosarcoma, also presenting a pattern of sarcomatous overgrowth,1-3,26 which according to what has been previously described has been associated with a poor prognosis.

Another important factor found with this case is that it was diagnosed as a clinically early stage, as opposed to all other cases previously reported where the stages have been advanced. This makes clinical treatment decisions more difficult, especially in the field of adjuvant therapy. The few reports in the literature do not demonstrate benefit using adjuvant chemo- or radiation therapy. The only case in which adjuvant therapy was used was reported by Hines et al.16 where medroxyprogesterone was used, and there was a significant partial response of the tumor. For this reason we decided to use it on our patient who, despite being in an early clinical stage, demonstrated sarcomatoid overgrowth posing a probable poor prognosis.

The relationship between the increase of serum CA125 and the presence of sarcomatous overgrowth,27 has been described as associated with a poor prognosis.

In conclusion, on the basis of the literature review, we suggest that determination of the CA125 serum antigen level be performed in patients with Müllerian adenosarcomas of the ovary because this may indirectly represent the presence of sarcomatous overgrowth as a factor of poor prognosis and also be used in the follow-up for detection of tumor recurrence.

Table 1. Cases of adenocarcinoma associated with an elevation of serum levels of CA125 reported in the literature

<table>
<thead>
<tr>
<th>Author</th>
<th>Origin</th>
<th>Serum CA125 (U/ml)</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
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<tbody>
<tr>
<td>Inoue</td>
<td>Ovary</td>
<td>354</td>
<td>17</td>
<td></td>
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<tr>
<td></td>
<td>Vagina</td>
<td>130</td>
<td>60</td>
<td></td>
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<td>Fukunaga</td>
<td>Ovary</td>
<td>1100</td>
<td>NR*</td>
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<td>Hirakawa</td>
<td>Ovary</td>
<td>930</td>
<td>7.4</td>
<td></td>
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<tr>
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<td>Peritoneal</td>
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<td>0</td>
<td></td>
</tr>
<tr>
<td>Östör</td>
<td>Sac of Douglas</td>
<td>425</td>
<td>NR</td>
<td></td>
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<tr>
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<tr>
<td>Recinos</td>
<td>Ovary</td>
<td>1100</td>
<td>16</td>
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*NR = not reported

References

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