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Case report

Ovarian yolk sac tumor coexisting with epithelial ovarian cancer: An aggressive rare entity

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ABSTRACT

Yolk sac tumor (YST) is the second most common subtype of ovarian germ cell tumors. It usually occurs in the second and third decades of life and is rare in postmenopausal women. In postmenopausal women, YST is commonly an aggressive tumor and can present as a pure germ cell component or as a mixed component with other germ cell or epithelial components. The recognition of this histological subtype is important not only for differential diagnosis but also for determining prognosis and treatment decisions. In this case report, we describe a 61-year-old woman with YST coexisting with epithelial carcinoma focusing on the efficacy of systemic therapies.

1. Introduction

Ovarian germ cell tumors (OGCTs) make up approximately 2% to 5% of all ovarian malignancies (Boussios et al., 2015). Yolk sac tumor (YST) is one of the most common subtypes of OGCTs and may present as a pure histologic type or mixed with other germ cell components (Boussios et al., 2015; Roth et al., 2011). YST rarely coexists with epithelial carcinoma, and this entity is rare in postmenopausal women (Koi et al., 2014). We describe a 61-year-old woman with YST coexisting with epithelial carcinoma and report on the efficacy of systemic therapies.

2. Case report

A 61-year-old postmenopausal woman presented with enlargement of the left ovary in February 2013. A routine USG revealed a left ovarian mass measuring 20.5 × 16.0 × 14.2. At that time, her CA125 level was 37.7 U/mL (upper limit, 35 U/mL).

In March 2013, the patient underwent a complete cytoreduction consisting of hysterectomy, bilateral salpingo-oophorectomy, peritoneal biopsies, and peritoneal fluid analysis. Pelvic and para-aortic lymphadenectomy was not reported. Pathology revealed a high-grade serous carcinoma arising in the left ovary with positive peritoneal cytology. Postoperative CA125 was within the normal values. Patient received adjuvant chemotherapy, consisting of six cycles of weekly intravenous (IV) paclitaxel (80 mg/m^2) plus IV carboplatin (area under the curve [AUC], 6.0) on day 1 every 3 weeks, with good tolerance and no severe adverse effects.

The patient remained free of disease for about 24 months. In September 2015, she developed abdominal discomfort and ascites. Imaging examinations, including magnetic resonance imaging and positron emission computed tomography, showed peritoneal and hepatic metastases in association with normal CA125 levels. Second- and third-line treatment with IV carboplatin (AUC, 5.0) on day 1, IV gemcitabine 1000 mg/m^2 on days 1 and 8, and IV bevacizumab 15 mg/kg on day 1 every 3 weeks and weekly paclitaxel 80 mg/m^2, respectively, were administered with no response.

At that time, an expert comprehensive pathology review sample from the initial surgery was undertaken, which excluded the first pathology diagnosis based on morphology and immunohistochemical profile. The tumor presented areas of YST (60%) coexisting with an endometrioid carcinoma (40%). The YST component present with solid, microcystic, polyvesicular, and glandular patterns with extensive tumoral necrosis, while the endometrioid component was mostly adenofibromatous with glandular structures, histologic grade 2. The immunohistochemical profile highlighted the two different patterns. Endometrioid component presented positive hormonal receptors, cytokeratin 7 and diffuse PAX-8, while the YST component was hormonal receptors and cytokeratin 7 negative, and SALL-4 positive.

The YST component showed solid, microcystic, polyvesicular, and glandular patterns. The epithelial component was an endometrioid carcinoma grade 2 (Fig. 1). β Human chorionic gonadotropin and alpha

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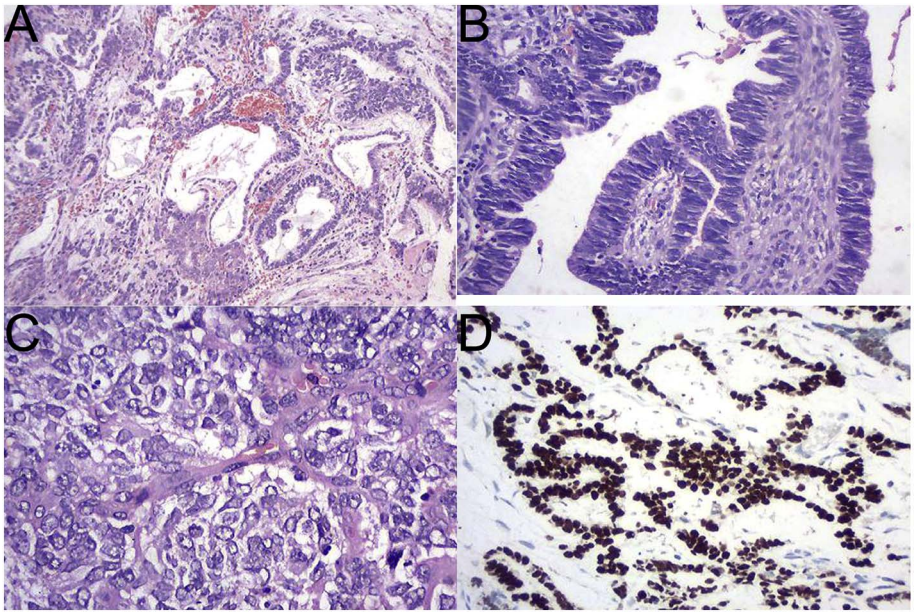

Fig. 1. Yolk-sac tumor associated with endometrioid carcinoma. A) Glandular pattern with polyvesicular structures. B) Detail of an endometrioid glandular component. C) Solid area of YST. D) SALL-4 immunostain diffusely positive in YST component.

fetoprotein levels (AFP) were normal, and lactate dehydrogenase level was two times higher than the upper limit of normal.

A planned laparoscopic procedure was done in February 2016 for staging purposes and also to obtain additional tissue for pathological evaluation. This procedure showed hemorrhagic ascites in association with extensive peritoneal disease.

The pathologic examination confirmed metastatic disease with morphologic features consistent with those of the initial pathologic findings. Immunohistochemical study showed positive staining for cytokeratin 7 (CK7) (epithelial component), cytokeratin 20 (CK20) (foci in YST component), PAX 8 (diffuse in epithelial component and focal in YST), SALL4 (YST component), GATA3, progesterone receptor (PR) (epithelial component), and estrogen receptor (ER) (epithelial component) and was negative for calretinin, Wilms tumor-1, CerbB2, and AFP.

After the new diagnosis, in March 2016, patient received four cycles of bleomycin, etoposide, and cisplatin (BEP) at the conventional doses with a partial response by image and markers. In August 2016, she initiated three salvage regimens in a sequence with no response in each of those regimens (etoposide, ifosfamide, and cisplatin; oxaliplatin and gemcitabine; and oral cyclophosphamide). She had progressive disease in the liver with hepatic failure and death few days later.

3. Discussion

YST in the postmenopausal population, either pure or associated with ovarian epithelial tumors, is a rarity and associated with a distinct biologic behavior, characterized by poor prognosis even with early-stage disease (Boussios et al., 2015; Roth et al., 2011).

YST can be pure or mixed with other germ cells or epithelial components. As was seen in our case, most postmenopausal women with YSTs present with a coexisting epithelial component; In this case, with or without an epithelial component, arise from a different molecular pathway than do germ cell-tumors in younger patients (Roth et al., 2011). Prognosis also correlates with stage of disease and the presence of elevated tumor markers (Boussios et al., 2015). Boussios et al. reported that most patients died within 8 months of diagnosis; only a few cases, particularly those with mixed YSTs, were disease-free for more than 2 years from the initial diagnosis (Boussios et al., 2015).The first case of YST coexisting with an epithelial carcinoma reported in a postmenopausal woman, similar to our patient, suggested that the epithelial component originated from a endometriotic cyst (Shaaban et al., 2014).This is in accordance with the hypothesis that endometriosis may be a risk factor for this tumor (Koi et al., 2014). Interestingly, both YST and endometrioid carcinoma components show typical features; both were separate entities (McNamee et al., 2016). McNamee et al. reported a series of 18 cases of YST of the female genital tract in women older than 40 years old and showed that most of these tumors were associated with a somatic epithelial neoplasm (McNamee et al., 2016). Due to the overlap of morphology and immunophenotype between YST and the epithelial neoplasm, they suggested the term “somatically derived YST’ for these neoplasms (McNamee et al., 2016).

The histopathogenesis of this rare entity is still unknown (Rutgers et al., 1987). Pathologic differential diagnoses include clear cell carcinoma, serous carcinoma, müllerian mixed tumor, and the intestinal variant of YST (Roth et al., 2011). Accurate diagnosis is based on morphologic features and immunohistochemical profile.

CK7 and EMA are important stains for differentiating ovarian YST from endometrioid adenocarcinoma (McNamee et al., 2016) Usually, CK7 and EMA are negative in YST and positive in endometrioid adenocarcinoma, while AFP is positive in YST but negative in endometrioid adenocarcinoma. However, in other series most part of the immunohistochemical findings showed positive for EMA and CK7 in the YST component (McNamee et al., 2016).

Newer markers for YST, including glypican-3 and SALL-like protein 4 (SALL4), may be useful in the identification of the YST component (Roth et al., 2011). Glypican-3, an oncofetal protein expressed in fetal liver and malignant tumors of hepatocytic lineage, is more sensitive than AFP but not as specific (Nogales et al., 1996). SALL4 is a specific and sensitive marker for germ cell tumors (Nogales et al., 1996). Our patient's tumor sample was positive for SALL4, but glypican-3 was not tested.

Plasma AFP roughly correlates with the YST component (Roth et al., 2011). In postmenopausal women with an ovarian mass and an elevated serum AFP level, this rare neoplasm should be included in the differential diagnosis (Roth et al., 2011). Of note, advanced stage and elevated tumor markers have been shown to be independent poor prognostic indicators (Boussios et al., 2015).

Although YST associated with endometrioid adenocarcinoma is extremely rare, the recognition of this histologic subtype is important not only in differential diagnosis but also prognosis (Koi et al., 2014). This tumor is greatly different from pure YST in terms of the response to chemotherapy or the postoperative clinical course (Roth et al., 2011). As previously postulated, YST arising from epithelial tumors by transformation may be less sensitive to chemotherapy than *de novo* YST

because of the mixed epithelial component (Roth et al., 2011). Because of its rarity, no systemic treatment guidelines are available, BEP chemotherapy is a potential choice for first-line treatment and may be effective not only in the germ cell but also in the epithelial component because of the platinum component (Boussios et al., 2015). In contrast to the current data, our patient achieved a long-term response with carboplatin and paclitaxel, both agents active against the germ cell and epithelial components; at the time of progression, a second response was obtained with platinum re-challenge and bevacizumab. The role of antiangiogenic agents in this setting is unknown but worthy of further study. A BEP regimen was also administered as third-line therapy when the pathologic features were reviewed, and a partial response of short duration occurred.

4. Conclusion

Mixed YST–epithelial carcinoma is a rare entity and must be recognized as an aggressive tumor. Because of its prognosis, complete surgical staging and aggressive systemic therapy must be considered in an attempt to improve disease outcome. Future studies that include more patients will help to delineate the optimal systemic approach in the first-line and salvage settings.

Conflict of interest

No conflict of interest to disclose.

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References

Boussios, S., et al., 2015. Malignant ovarian germ cell tumors in postmenopausal patients: the royal marsden experience and literature review. Anticancer Res. 2015 (35), 6713–6722.

Koi, C., et al., 2014. A case of ovarian yolk sac tumor associated with endometrioid adenocarcinoma. Gynecol. Oncol. Case Rep. 9, 11–14.

McNamee, T., et al., 2016. Yolk sac tumours of the female genital tract in older adults derive commonly from somatic epithelial neoplasms: somatically derived yolk sac tumours. For. Hist. 69, 739–751.

Nogales, F.F., et al., 1996. Ovarian endometrioid tumors with yolk sac tumor component, an unusual form of ovarian neoplasm. Analysis of six cases. Am. J. Surg. Pathol. 20, 1056–1066.

Roth, L.M., et al., 2011. Ovarian yolk sac tumors in older women arising from epithelial ovarian tumors or with no detectable epithelial component. Int. J. Gynecol. Pathol. 30, 442–451.

Rutgers, J.L., et al., 1987. Ovarian yolk sac tumor arising from an endometrioid carcinoma. Hum. Pathol. 18, 1296–1299.

Shaaban, A.M., et al., 2014. Ovarian malignant germ cell tumors: cellular classification and clinical and imaging features. Radiographics 34, 777–801.