Case Report
Ovarian malignant mixed germ cell tumor with clear cell carcinoma in a postmenopausal woman

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Received September 14, 2014; Accepted November 1, 2014; Epub December 1, 2014; Published December 15, 2014

Abstract: Malignant germ cell tumors of the ovary are very rare and account for about 2-5% of all ovarian tumors of germ origin. Most patients are adolescent and young women, approximately two-thirds of them are under 20 years of age, occasionally in postmenopausal women. But clear cell carcinoma usually occurs in older patients (median age: 57-year old), and closely related with endometriosis. Here we report a case of a 55-year old woman with right ovarian mass that discovered by B ultrasonic. Her serum levels of human chorionic gonadotropin (hCG) and α-fetoprotein (AFP) were elevated. Pathological examination revealed the tumor to be a mixed germ cell tumor (yolk sac tumor, embryonal carcinoma and mature teratoma) with clear cell carcinoma in a background of endometriosis. Immunohistochemical staining showed SALL4 and PLAP were positive in germ cell tumor area, hCG, CD30 and OCT4 were positive in epithelial-like cells and giant syncytiotrophoblastic cells, AFP, AAT, CD117 and Glyp3 were positive in yolk sac component, EMA and CK7 were positive in clear cell carcinoma, CD10 was positive in endometrial cells of endometriotic area. She was treated with surgery followed by seven courses of chemotherapy. She is well and serum levels of hCG and AFP have been decreased to normal levels.

Keywords: Mixed germ cell tumor, ovary, clear cell carcinoma

Introduction

Mixed germ cell tumors of the ovary are rare malignant neoplasms containing combinations of two or more types of germ cell element [1, 2], such as dysgerminoma combined with teratoma, yolk sac tumor, choriocarcinoma, embryonal carcinoma, or polyembryoma, as well as any other possible combination of these tumor types. Like other malignant germ cell tumor, these tumors occur in the first four decades most frequently in children and adolescents and are rare thereafter. But ovarian clear cell carcinoma usually occurs in patients over 50 years old (median age: 57-year old), and can arise from endometriosis (35.9%) [3].

Herein we reported the case of a 55-year-old woman with right ovarian mixed germ tumor (composed of yolk sac tumor, embryonal carcinoma and mature teratoma) combination of clear cell carcinoma in a background of endometriosis.

Case report

The patient was a 55-year-old woman and had postmenopausal for 5 years. Recently, she presented with right lower abdomen discomfort and weakness of both lower limbs. Her past medical history was unremarkable except for dysmenorrheal and multiple uterine myomata. She had no surgery in the past. Physical examination revealed an irregular, nontender lower abdominal tumor at right rear uterus. B ultrasound examination found a solid and cystic neoplasm of right ovary (5.1 cm × 5.0 cm × 3.4 cm) and multiple myomata of uterus (the biggest measuring 2.5 cm × 2.0 cm × 1.8 cm). Her preoperative serum tumor marker levels were CA199: 14.24 U/ml, CEA: 1.39 ng/ml, CA-125: 15.45 U/ml, HE4: 1.11 pmol/L, AFP: 47.5 ng/ml, and HCG: 831.6 mIU/ml. These results strongly favored malignant ovarian germ cell tumor.

The patient then consented for surgical operation performed. The histological findings of
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Intraoperative frozen section were teratomatous component composed of microcystic and reticular structures and some epithelial-like, medium to large polygonal cells, suspicious for malignant germ cell tumor. Based on the frozen section findings, the patient eventually underwent a total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, right infundibulopelvic ligament resection and bilateral paracolic sulci peritoneum biopsies. Gross examination findings were: the right ovary with a solid and cystic tumor (Figure 1), measuring 6.0 cm × 5.0 cm × 3.5 cm. The cystic area contains chocolate-colored fluid and the inner wall partly showed dark brown tissue measuring 0.4-0.6 cm in thickness; the solid area measures 3.0 cm × 3.0 cm × 2.0 cm and shows dark brown papillary surface. The cut surface was soft and fleshy, gray to pale brown in color with some area showing cyst degeneration and hemorrhage. The left ovary and bilateral oviduct are macroscopically normal.

Postoperative histological examinations revealed that the right ovarian tumor was a malignant mixed germ cell tumor (composed of yolk sac tumor, embryonal carcinoma and mature teratoma) with clear cell carcinoma (Figure 2). There are multiple leiomyoma in uterus. The left ovary and bilateral oviduct were normal. No evidence of metastasis to omentum, right infundibulopelvic ligament and bilateral paracolic sulci peritoneum were detected. Immunohistochemical staining showed germ cell cells were positive for SALL4 and PLAP (Figure 3), hCG, CD30 and OCT4 were positive in epithelial-like cells and giant syncytiotrophoblastic cells, CK7 and EMA were positive in clear cell carcinoma, CD10 was positive in endometrials cells of endometriotic component (Figure 4). AFP was found in yolk sac cell of the embryoid bodies, AAT and CD117 was positive and Glyp3 were weakly positive in yolk sac component (Figure 5).

After surgery, serum levels of hCG and AFP decreased gradually, and they decreased to below the cutoff levels 30 days after surgery. After her gastrointestinal function got better, she received seven courses of chemotherapy with BEP (bleomycin, etoposide, and cisplatin) regimen. So far she is doing well with no complaints. Her serum levels of AFP and hCG are not elevated. The patient is receiving chemotherapy regularly and is advised to have periodic follow-up for lifetime.

Discussion

Although germ cell tumors of the ovary are much less common than epithelial ovarian neoplasms, they are the most frequent types of ovarian cancer during reproductive years [4, 5]. Malignant ovarian germ cell tumors are often classified as dysgerminoma or nondysgerminoma [6]. The latter includes neoplasms that contain teratoma, embryonal, yolk sac, and/or choriocarcinoma elements [4]. When more than one neoplastic germ cell element occurred in one neoplasm, it is called mixed germ cell tumor.

Mixed germ cell tumor are the most common ovarian malignancy in girls and young women and account for approximately two-thirds of the ovarian cancers that occur in the first two decades of life [7]. One case reported a mixed malignant germ tumor with dysgerminoma, choriocarcinoma and immature teratoma that found in one of the ovaries in a nineteen-year old patient [1]. Another papers reported a 19-year-old female with malignant mixed ovarian germ cell tumor with a large embryonal component [6], mixed germ cell tumor (immature teratoma and yolk sac tumor) with rhabdomyosarcomatous component of embryonal type in a 15-year-old girl [7], ovarian mixed germ cell tumor composed of polyembryoma and imma-
Figure 2. Histopathological found the right ovarian tumor was a malignant mixed germ cell tumor (composed of yolk sac tumor (A), embryonal carcinoma (B) and mature teratoma (C)) with clear cell carcinoma (D) by H&E staining. Original magnifications are all × 100.
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Figure 3. Immunohistochemical staining showed PLAP (A, B) and SALL4 (C, D) were positive in germ cell tumor area. Original magnifications are all × 100.

Figure 4. Immunohistochemical stains of the right ovarian tumor for embryonal carcinoma, clear cell carcinoma and endometriotic component (× 100). hCG was positive in giant syncytiotrophoblastic cells (A), CD30 (C) and OCT4 (E) were positive in epithelial-like cells of embryonal component, CD10 was positive in endometrial cells of endometriotic component (B), CK7 (D) and EMA (F) were positive in clear cell carcinoma.

ture teratoma in a 41 year old woman [8]. These cases are all occurred in reproductive age female; here we reported the rarely malignant mixed germ cell tumor of ovarian in a post-menopausal woman. The tumor co-exists with clear cell carcinoma in a background of endometriosis. Mixed epithelial and germ cell tumors had been reported in ovarian yolk sac tumor,
most cases are mixed with endometrioid carcinoma [9-12], others are serous carcinoma [12] or mucinous cystadenofibroma [13] et al. The age of the patients ranges from 35 to 82. But malignant mixed germ cell tumor of ovary mixed with clear cell carcinoma in a background of endometriosis had not been seen before.

Immunohistochemistry is important in making diagnosis of mixed germ cell tumor. AFP and hCG are the characteristic tumor markers for germ cell tumors. AFP has proved to be positive in most embryonal carcinomas and in virtually all endodermal sinus (yolk sac) tumors, whereas hCG has proved to be a useful marker in choriocarcinoma and in some embryonal carcinomas [8]. Most embryonal carcinomas stain for CD30, and OCT4 has been found to consistently positive in embryonal carcinoma. SALL4 is a novel sensitive and special marker of ovarian primitive germ cell tumors [14, 15]. It is strongly positive in more than 90% tumor cells in all yolk sac tumors, dysgerminomas, gonadoblastomas, and embryonal carcinomas and variable in immature teratomas [14], SALL4 is a more sensitive marker than PLAP [15], glypican-3 [16]. And CD117 can be used as a diagnostic marker for yolk sac tumor [16]. EMA and CK7 are makers of epithelial cells; here they are important in differential diagnosis between clear cell carcinoma and yolk sac tumor. And CD10 is positive in stromal cells of endometriosis. These markers are positive in corresponding component in this case.

Chemotherapy with the BEP is effectively to this patient. BEP regimen has dramatically improved the prognosis for patients with ovarian germ cell tumors [8]. Williams et al. reported that three courses of BEP nearly always prevented recurrence in well-staged patients with completely resected germ cell tumors and should be given to all such patients [17]. In this case, this postmenopausal woman has a malignant mixed germ cell tumor of ovary combination with clear cell carcinoma in a background of endometriosis, it is unknown epithelial and germ cell tumor which occurred first, and the relationship between them worthy of further study.

Figure 5. Immunohistochemical stains of the right ovarian tumor for yolk sac tumor component (× 100). AFP was found in yolk sac cell of the embryoid bodies (A), AAT (B) and CD117 (C) was positive and Glyp3 (D) was weakly positive in microcystic or reticular structure.
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Disclosure of conflict of interest

None.

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