Case Report

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Metastasis of ovarian dysgerminoma in a postmenopausal patient: a rare case report

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Abstract

Ovary dysgerminoma is one of the most good prognosis malignant tumor, which has a 5-year overall survival rate exceeding to 90%. Generally, the incidence of ovarian dysgerminoma (OD) is relatively low, accounting for ~0.6% of all ovarian tumors. Usually, it mainly occurs in very young women, about 85% of patients under 30 years old and is rare in middle-aged especially in elderly ones. This ovary dysgerminoma case report presents a 58-year-old menopausal postmenopausal woman which has a poor prognosis. Therefore, there may be differences between the elderly and young women in clinical characteristic that require separate management. This case reports a postmenopausal woman who was diagnosed with ovary dysgerminoma. After surgery, the patient was treated chemotherapy with bleomycin, etoposide, and cisplatin (BEP) according to the treatment guidelines. Unusually, the patient developed bone marrow suppression and lymph node metastasis in final. This report explored the clinical characteristic in postmenopausal woman dysgerminoma. Changes in lactate dehydrogenase (LDH) throughout the course of the disease are closely related to the progression. The patient had a disease progression when treated with the conventional treatment (BEP). The applicability of this treatment protocol to postmenopausal patients requires further research. Postmenopausal woman dysgerminoma is rare but rapid progress. Whether BEP is suitable for OD in middle-aged and elderly people remains to be further validated in the future. LDH may be a potential biomarker for monitoring the progression of OD in the elderly.

Keywords: chemotherapy, dysgerminoma, lactate dehydrogenase, menopause, ovarian cancer

Introduction

Ovarian germ cell tumors are derived from pluripotent primordial germ cells and are the second most common ovarian tumors after surface epithelial tumors. Most of the tumors (95%) in this group were benign, and malignancy is rare. The most common malignant germ cell tumor is dysgerminoma[1]. According to previous reports, dysgerminoma is more common in young women, and it is more common in 20 to 30-year-olds[2,3].

HIGHLIGHTS

- This case report describes an uncommon clinical situation where a postmenopausal woman was diagnosed with ovarian dysgerminoma.
- In terms of treatment, this patient was treated with surgery and adjuvant chemotherapy (etoposide 0.12 g, bleomycin 15 000 IU, cisplatin 30 mg) and developed metastasis.
- The changes in lactate dehydrogenase levels were closely related to the progression of the disease during the whole course of the disease.

Ovarian dysgerminoma (OD) is generally accepted to have long-term outcomes without recurrence or metastasis. It is sensitive to chemotherapy and radiotherapy. Therefore, dysgerminoma represents a group of potentially curable diseases with excellent prognosis[4]. The most common clinical symptoms include abdominal pain or related to an abdominal mass, but some patients may be asymptomatic or amenorrhea[2,3,5]. Ovarian germ cell tumor marker testing includes alpha-fetoprotein (AFP), human chorionic gonadotrophin (HCG), and lactate dehydrogenase (LDH). In this case, a rare postmenopausal dysgerminoma was reported. After surgery and adjuvant chemotherapy, bone marrow suppression and lymph node metastasis occurred, and treatment was abandoned. The changes of LDH levels in the whole course of the disease are closely related to the progression of the disease. Whether the multichemotherapy regimen of

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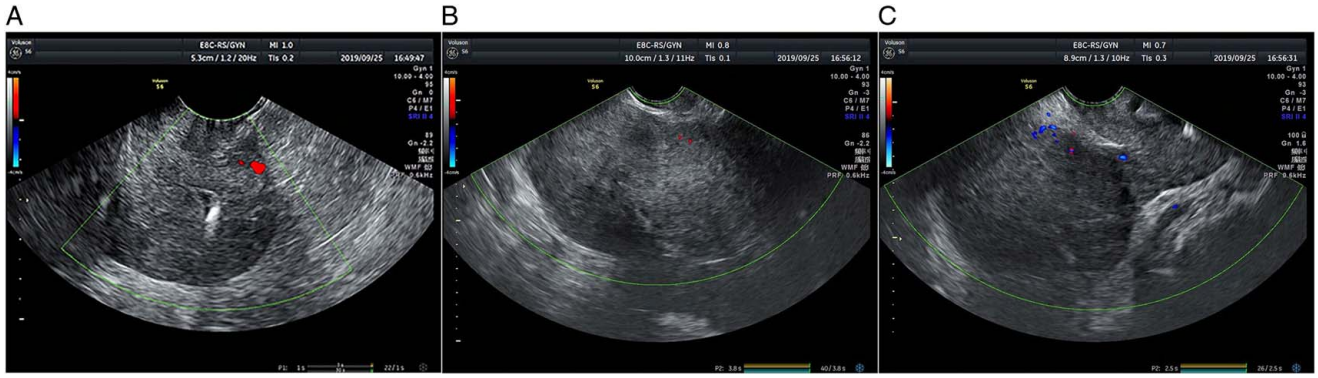

Figure 1. B-ultrasound examination revealed solid hypoechoic mass in the pelvic cavity. The uterus was regular in shape with moderate parenchymal echo. There were several round dark areas in the myometrium of the cervix. A solid hypoechoic focus was found in the pelvic cavity, the boundary was visible and the shape was irregular. Beside it, a liquid mass was seen, the boundary was visible and the shape was regular, and the left and right ovaries were not detected. (A-C)

bleomycin, etoposide, and cisplatin (BEP) is suitable for the treatment of such diseases in the elderly needs to be further verified in the future.

Case presentation

The patient was a 58-year-old postmenopausal female in her usual good health. In August 2019, the patient developed left lower abdominal pain with abdominal distension without obvious cause, which was persistent and without metastasis to other places. After anti-inflammatory symptomatic treatment, the abdominal pain symptoms were slightly relieved, but the symptoms were repeated. On September 25, she came back to the hospital and underwent a B-ultrasound examination. The result showed that a solid hypoechoic focus was found in the pelvic cavity, with a size of $11.1 \times 7.8 \times 9.8$ cm, the boundary was visible and the shape was irregular. Beside it, a liquid mass of $62 \times 33 \times 73$ mm was seen, the boundary was visible and the shape was regular, and the left and right ovaries were not detected (Fig. 1). The patient denied that there was similar medical history in her family members. For further diagnosis and treatment, the patient was admitted to the hospital for the 'nature of pelvic mass unknown'. On admission, the blood routine examination showed no abnormality, tumor markers such as CA125, AFP, and CEA were normal, and the detection value of LDH is 1112 U/l (normal value: 120–250 U/l).

Surgery is the preferred treatment. The patient's abdomen was thoroughly explored, and the procedure was performed under general anesthesia with endotracheal intubation by an associate chief physician in the Department of Surgery at our hospital. During exploratory laparotomy, a tumor originating from the left adnexa was found, about $12 \times 10 \times 10$ cm in size, with an irregular shape, gray-white surface, basically complete capsule, and no rupture. After resection, a section of the tumor showed that the tumor was solid with a white necrotic area of about $6 \times 4 \times 4$ cm in size, which did not exclude the possibility of a tumor. The patient underwent abdominal hysterectomy, bilateral adnexectomy, partial resection of rectum and sigmoid colon, pelvic adhesion lysis, and intestinal adhesion lysis. The patient recovered well after surgery. Postoperative pathological results showed an ovarian malignant tumor in the left adnexa. Immunohistochemical results were CD117(+), CK (a few cells +), KI-67 (about 50%), SALL-4(+), CD30(-), OCT3/4(+). Based on these results, a clinical diagnosis of dysgerminoma of the left ovary was made.

The next step in treatment is chemotherapy. The patient was treated with three courses of chemotherapy, which consisted of etoposide 0.12 g, bleomycin 15 000 IU, and cisplatin 30 mg. LDH was 291 U/l before the first chemotherapy, which was significantly lower than that before the operation. The white blood cell (WBC) was $7.47 \times 10^{\wedge}9$. The patient received the first chemotherapy on November 6. One week after the first chemotherapy, WBC decreased (WBC:$3.10 \times 10^{\wedge}9$), and the WBC increased after treatment with recombinant human granulocyte stimulating factor (rhG-CSF). Before the second chemotherapy, LDH was 242 U/l and returned to the normal level. On December 4, the patient received the second chemotherapy. After 1 week of chemotherapy, the WBC decreased significantly (WBC: $2.25 \times 10^{\wedge}9$), and the WBC increased significantly after treatment. Before the third chemotherapy, the LDH was 258 U/l, which was higher than before (Fig. 2). On December 30, the patient received the third chemotherapy. On January 12, the WBC decreased significantly (WBC: $0.63 \times 10^{\wedge}9$, and the patient developed severe bone marrow suppression. Subsequently, the

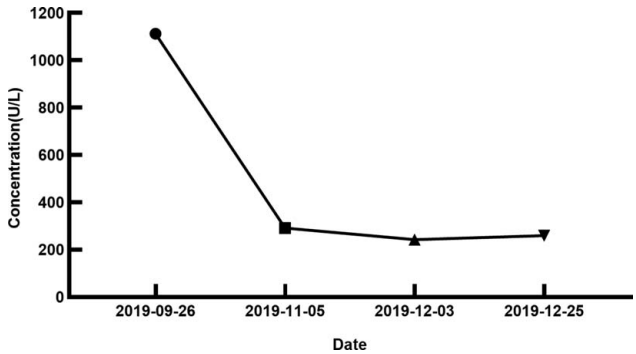

Figure 2. LDH changes during treatment LDH decreased significantly (1112-291 U/l) after surgery (September 27), decreased to normal level (242 U/l) after the first chemotherapy (November 5) until the second chemotherapy (December 02), and increased again (258 U/l) when measured before the third chemotherapy (December 25).

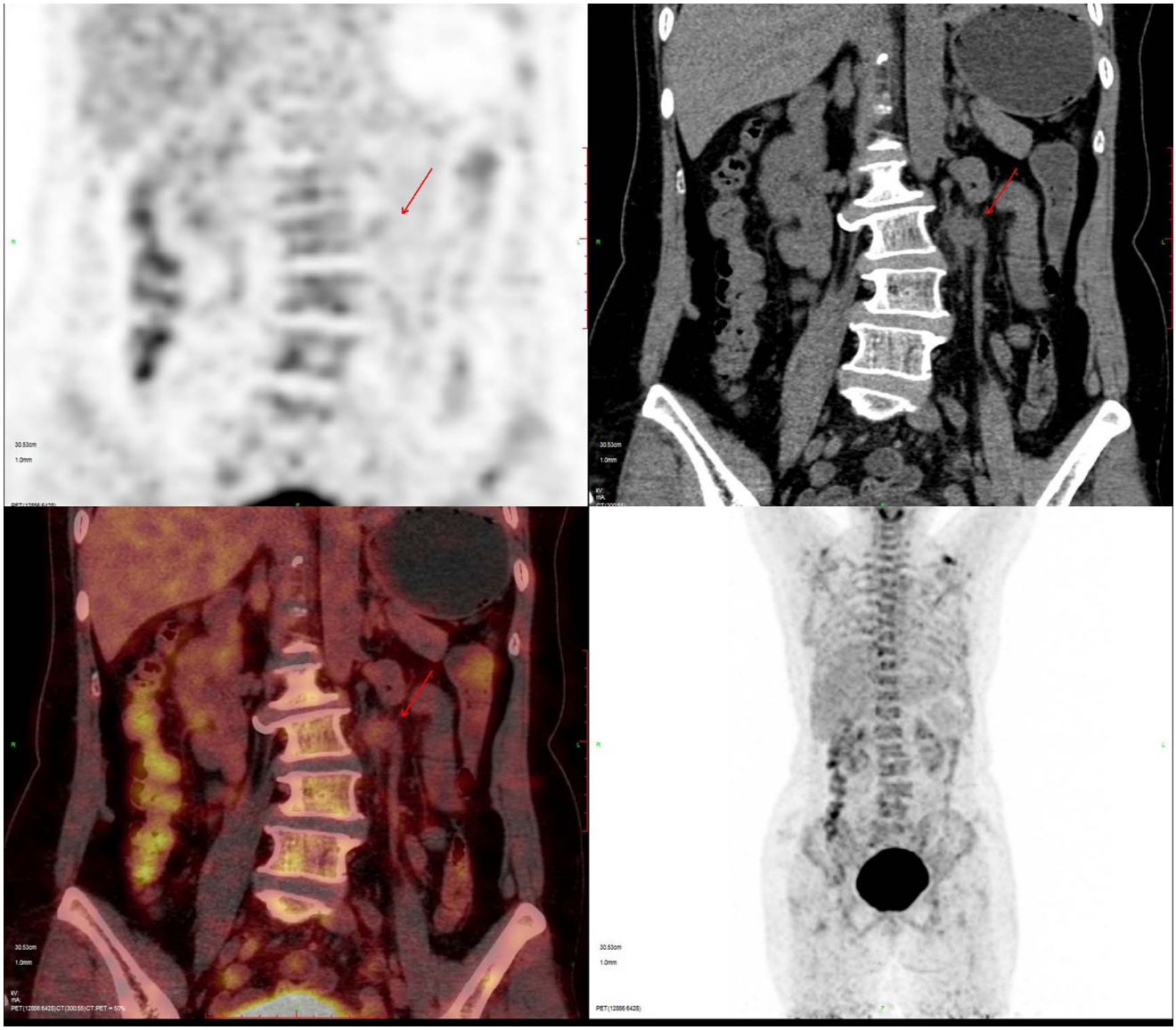

Figure 3. PET CT showed enlarged lymph nodes at the left renal hilum, increased glucose metabolism, slightly thickened intestinal anastomotic wall, and abnormal glucose metabolism.

patient underwent an abdominal PET-CT examination, which showed the postoperative changes of OD (Fig. 3). The wall of intestinal anastomosis was slightly thickened and the glucose metabolism was abnormally increased. Enlarged lymph nodes in the left renal hilum and slightly increased glucose metabolism were observed. The possibility of metastasis was considered. Due to severe bone marrow transplantation, the patient abandoned treatment.

This case has been reported in line with the Surgical CAse REport (SCARE) criteria[6].

Discussion

Dysgerminoma is the most common malignant germ cell tumor, affecting mainly young women[2,3]. The age of onset was broadly distributed, ranging from 4 to 56 years, with a median age of 20 or 22 years[3,5,7]. The most common clinical symptoms include abdominal pain or related to an abdominal mass, but some patients may be asymptomatic or amenorrhea. Serum tumor markers tested in postmenopausal women are frequently elevated including LDH, CA125, HCG, and placental alkaline phosphatase (PLAP)[8].

The cause of OD is unknown, which may be related to the malformation of the reproductive system[7]. Metastasis of simple ovarian asexual tumors is rare, most of them are direct invasion or lymphatic metastasis. Due to the discovery of an effective chemotherapy regimen, some scholars have proposed contralateral ovary dissection to explore how normal patients can retain the contralateral annex and uterus. It can be seen that the prognosis is effective[3,5].

The National Comprehensive Cancer Network (NCCN) recommends adjuvant BEP chemotherapy[9]. In this study, surgery and BEP combined chemotherapy were used. Although a

temporary decrease in LDH was observed, bone marrow suppression was significant. Lymph node and intestinal metastases were found during the third chemotherapy. The major irreversible side effect of the BEP regimen is bleomycin-induced pulmonary fibrosis, which is due to the minimal content of protective hydrolase in lung tissue[10]. Studies have shown that bleomycin lung injury is more common in older patients and patients with renal insufficiency[11]. A case has been reported in which postmenopausal dysgerminoma patients have been successfully treated with a regimen of surgery and adjuvant bleomycin and cisplatin-free etoposide[12]. OD is rare in postmenopausal patients, more data on this population are needed to determine the optimal treatment strategy and outcome, and further studies are needed to verify the efficacy of this regimen in such patients.

The source of serum LDH of patients with ovarian germinoma is likely germinoma cells. Histological examination of dysgerminoma cells revealed large amounts of intracellular glycogen, indicating higher glycolytic activity than normal tissue[13]. Since LDH is a glycolytic enzyme, it is likely to be abundant in dysgerminoma cells. Alterations of tumor cell membrane permeability or necrosis of tumor cells may release enzymes into the circulation. It has a variety of molecular forms, and this heterogeneity allows its electrophoretic separation into at least five isoenzymes. In 1964, Zondag first reported that the distribution of serum LDH isoenzymes in patients with testicular germinomas and OD was different[14]. He found the fractions of LDH-1 and 2 to be increased and similar findings have been documented in OD by Sheiko and Hart and in a few other cases of testicular and extragonadal germinomas[15,16]. LDH is secreted by dysgerminoma, which is helpful for the preoperative diagnosis of occult cell tumors. It has been reported in the literature that a young female patient with dysgerminoma had a highly elevated LDH level before treatment, which decreased to normal levels after treatment[17]. In this case, LDH was increased to 1112 U/l before surgery, which was significantly higher than the reported asexual tumor in young women[18,19]. LDH decreased significantly after surgery. LDH decreased to normal levels after the first and before the second chemotherapy. LDH elevation was detected again before the third chemotherapy, at which time the patient was considered to have lymph node metastasis and severe bone marrow suppression, and finally, the patient discontinued treatment. This case illustrates the possible role of LDH as a tumor marker for recurrent dysgerminoma. Therefore, LDH may be a potential indicator for the observation of curative effect and the judgment of prognosis of OD.

Conclusion

Factors such as metabolism and hormone tolerance to chemotherapy drugs may differ between middle-aged and elderly patients and adolescents. The treatment regimen of OD in middle-aged and elderly patients needs to be further verified. The changes of LDH levels in the whole course of the disease are closely related to the progression of the disease. LDH may be a potential indicator for the observation of curative effects and the judgment of the prognosis of OD.

Ethical approval

This study was approved by the Ethics Committee of Affiliated Qingyuan Hospital, Guangzhou Medical University, Qingyuan People's Hospital.

Consent

The patient has died, and the corresponding author is acting as a guarantor of the case report.

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Author contribution

Z.F., X.Z., and P.W.: drafted the manuscript; Q.H. and J.L.: revised and approved the manuscript; P.W.: provided guidance and technical support; X.Z. and Q.H.: surgical team evaluated the patient and participated in the whole treatment of the patient. All of the authors have contributed to this article, and have approved the submitted version

Conflicts of interest disclosure

The authors have no conflicts of interest to declare.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

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Data availability statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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