Conservative Surgery for a Young Nulligravid with Ovarian Yolk Sac Tumor and Concurrent Contralateral Mature Teratoma

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Ovarian cancer is the second most common gynecologic cancer worldwide and the sixth most common cancer among females. Germ cell tumors are the most common ovarian neoplasm in the first two decades of life constituting approximately two-thirds of all ovarian tumors. Malignant germ cell tumors constitute one-third of germ cell origin tumors and two-thirds of all ovarian malignancy in this age-group. This paper presents a case of a 19 year-old nulligravid who presented at the emergency room with abdominal pain, and was intraoperatively diagnosed with yolk sac tumor of the right ovary, stage 1A with mature cystic teratoma of the left ovary. She subsequently underwent unilateral salpingooophorectomy and contralateral oophorocystectomy, left. Patient is advised chemotherapy postoperatively, with Bleomycin, Etoposide and Paclitaxel. This paper discusses the incidence, risk factors, prognosis and management of yolk sac tumor in a young nulligravid.

Keywords: yolk sac tumor, germ cell tumor, mature teratoma, conservative surgery

Introduction

Ovarian cancer is the second most common gynecologic cancer worldwide and the sixth most common cancer among females.[1] Based from the crude incidence rate last 2013 in United Kingdom, it shows that there are 22 new ovarian cancer cases for every 100,000 females.[2] Most common gynecologic neoplasms found in young women is ovarian in origin, constituting one percent of all childhood-malignancies.

It is known that germ cell tumors are the most common ovarian neoplasm in the first two decades of life constituting approximately two-thirds of all ovarian tumors. Malignant germ cell tumors constitute one-third of germ cell origin tumors and two-thirds of all ovarian malignancy in this age-group.

Yolk sac tumor, also known as Endodermal sinus tumor, form a separate entity within the group of germ cell tumors based from the World Health Organization (WHO) classification of ovarian tumors. It is a rare type of tumor that usually affects children and young women and it occurs as the second most common malignant germ cell tumors of the ovary. However, it is quite rare to encounter a germ cell tumor case with concomitant mature teratoma in the contralateral ovary.

The choice of treatment for a woman with ovarian cancer should take into consideration the following factors: 1) Age of the patient, 2) desire for future reproduction, and 3) stage and nodal spread of the disease. The objective of this case report is to discuss the contemporary management of ovarian yolk sac tumor in a nulligravid woman

The Case

This is a case of C.R., 19 years old, nulligravid, who consulted at the emergency room due to abdominal pain. History of present illness started at four months prior to consultation when patient complained of intermittent episodes of constipation,

with no other associated signs and symptoms. No medication was taken nor any consultation done. Approximately one month prior to consultation, patient noted weight loss, gradual enlargement of abdomen with associated non-radiating right flank pain (6-9/10 in severity). No associated vomiting, abnormal vaginal bleeding, nor change in bowel movement. No consultation was done.

Two days prior to consultation, she complained of increased severity of abdominal pain 10/10, this time crampy in character, with associated weight loss, loss of appetite, and high fever (Tmax 39°C). She self-medicated with Paracetamol 500mg/tab every 4 hours which provided temporary relief. But due to persistence of hypogastric pain, she opted to consult at the emergency room of our institution.

Patient has no known co-morbidities. Past medical and family history are non-contributory. Patient claimed that she has been irregularly menstruating since 13 years old, with menstrual interval of two months, lasting for four days, using up three pads per day, fully soaked with associated dysmenorrhea. Sexual and personal histories are unremarkable.

At the emergency room, she came in conscious, coherent and ambulatory with stable vital signs and body mass index of 19.3 kg/m^2 (from 23.4kg/m^2). Patient has pink palpebral conjuctivae. There was no supraclavicular lymphadenopathy noted. Abdomen was soft and flabby, with no abdominal guarding, but with direct tenderness at the right lower quadrant. There was a large, palpable, non-moveable, doughy abdominal mass approximately measuring 15cm x 10cm. Speculum examination was unremarkable. Internal examination revealed a closed and firm cervix, with no cervical motion tenderness, and the uterus cannot be assessed due to the enlarged pelvoabdominal mass. She had full and equal pulses. Complete blood count, urinalysis and chest x-ray findings were all normal. Pregnancy test was negative. Pelvic ultrasound revealed a complex mass at the right lower quadrant that measured 14.0cm x 8.6cm x 11.9cm, located posterior to the urinary bladder, with doppler interrogation which showed no significant intralesional vascular flow. Ultrasound interpretation was complex pelvic mass at the right (Figure 1). There was also a 5cm dermoid cyst at the left ovary.

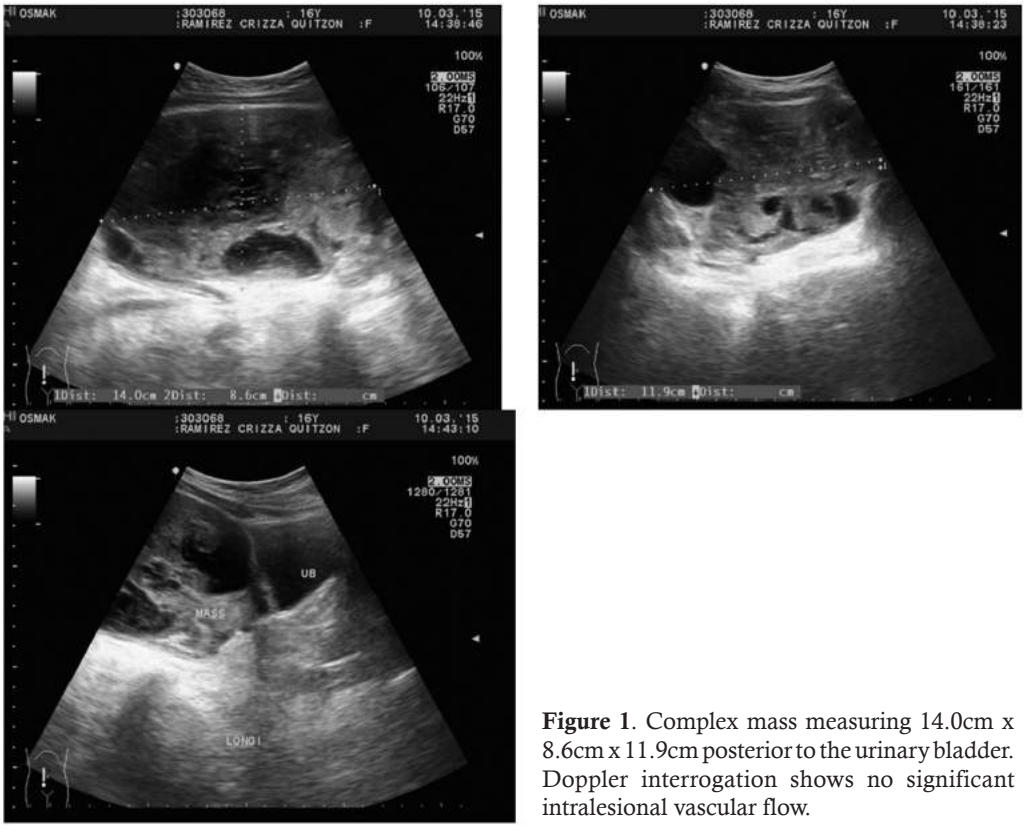

Figure 1. Complex mass measuring 14.0cm x 8.6cm x 11.9cm posterior to the urinary bladder. Doppler interrogation shows no significant intralesional vascular flow.

Patient was admitted with initial impression of complex ovarian new growth, right, in complication; dermoid cyst, left. The plan was to do an emergency exploratory laparotomy with peritoneal fluid cytology, right salpingooophorectomy, left oophorocystectomy.

On exploratory laparotomy, there was minimal ascites. The uterus and bilateral fallopian tubes were grossly normal. Peritoneal and liver surfaces were smooth. The right ovary was enlarged to 18cm x 16cm x 8cm. The left ovary was enlarged to 5cm x 4.5cm x 2.5cm. The omentum was caked and densely adherent to the right ovary. There were no palpable paraaortic lymph nodes noted. Peritoneal fluid cytology, right salpingooophorectomy, left oophorocystectomy, and infracolic ometectomy were done. On cut section, the right ovarian mass was mostly solid with multiple cystic spaces filled with mucin; the left ovarian mass was filled with hair and sebum. (Figures 2,3 & 4)

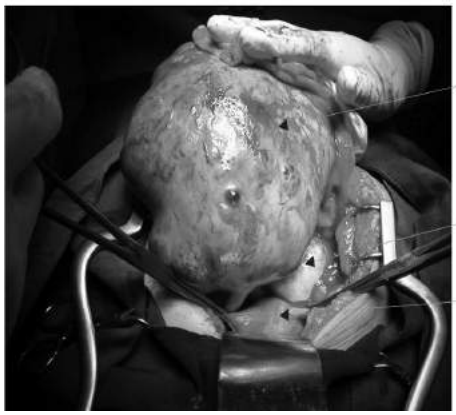

Figure 2. Intraoperative findings: The right ovary was enlarged to 18cm x 16cm x 8cm. On cut section, the right ovarian mass was mostly solid with multiple cystic spaces filled with mucin. The left ovary was enlarged to 5cm x 4.5cm x 2.5cm. On cut section, the left ovarian mass was filled with hair and sebum.

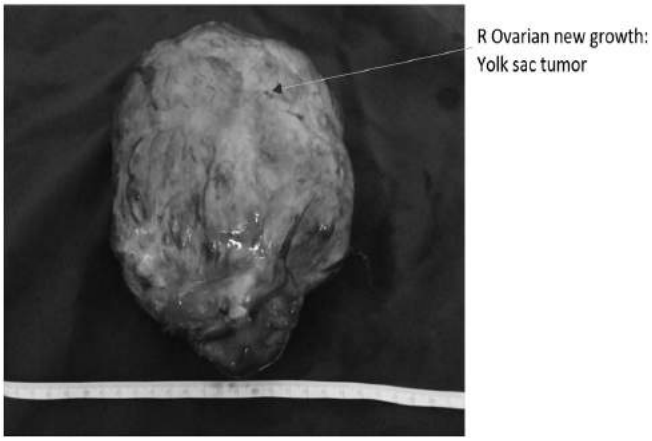

Figure 3. Yolk sac tumor of the right ovary enlarged to 18cm x 16cm x 8cm.

Figure 4. Omentum consists of a yellow tan fibrofatty tissue with areas of hemorrhage. No solid area is noted.

Postoperative course was unremarkable. Additional ancillary laboratory tests done included the following: serum CEA 1.78ng/mL (reference range <5.0ng/mL), serum alpha-fetoprotein 1558.85ng/mL (reference range 0-10.9ng/mL), serum CA 12-5 299.6U/mL (reference range <35U/mL) and serum CA 19-9 90.16U/mL (reference range <37U/mL). She was discharged from the hospital on day 4 post-surgery.

Histopathology result revealed yolk sac tumor of the right ovary, congestion of right fallopian tube, mature cystic teratoma of left ovary, acute omentitis, peritoneal fluid was negative for malignant cells,

Final diagnosis is Yolk Sac tumor, right ovary, Stage 1A, Mature cystic teratoma, left ovary, s/p peritoneal fluid cytology, right salpingooophorectomy, left oophorocystectomy, infracolic omentectomy. Patient was then advised to undergo chemotherapy with Bleomycin, Etoposide and Paclitaxel.

Discussion

Ovarian cancer is the second most common gynecologic cancer worldwide and the sixth most

common cancer among females. In 2010, ovarian cancer ranks 5th (5%) among the leading cancer site in women with 2,165 new cases and 1,016 deaths per year.[3] The incidence rate starts steeply at age 40. In 2008, the estimated age-standardized national incidence rate was 5.7 per 100,000 and the estimated national standardized mortality rate was 2.8 per 100,000.

Mature cystic teratomas are the most common ovarian tumors seen in children and adolescents.[4] Ovarian teratomas are the most common germ cell neoplasms and, in many series, the most common excised ovarian neoplasms.[5] The most common of these tumors are the benign mature cystic teratomas (also known as dermoid cysts), representing 12-15% of the ovarian neoplasias.[6] Mature cystic teratomas are bilateral in about 10% of cases.[7]

Some risks factors for ovarian malignancy include nulligravidity, menstrual irregularities and history of breast cancer or endometrial cancer. Hereditary predisposition in some women is also a risk factor. Pregnancy and oral contraceptives, on the other hand, could be protective. Ovarian cancer is usually detected late due to a later onset of symptoms.

There are three categories of ovarian tumors: Benign tumors which are the most common, seen in about 80% of affected women, and usually involve young women ages 20 to 45. Borderline and malignant tumors usually occur in women of older ages, usually between the ages of 45 and 65 years.[8]

Germ cell tumors constitute 15% to 20% of all ovarian tumors. Most are benign cystic teratomas, but the remainder, which are found principally in children and young adults, have a higher incidence of malignant behavior and pose problems in histologic diagnosis and in therapy. They are derived from primitive germ cells of the embryonic gonad. Depending on the origin of differentiation, malignant ovarian germ cell tumors are classified as dysgerminomas and non-dysgerminomas. The most frequently encountered subtype is dysgerminoma. The majority of non-dysgerminomatous tumors, consist of yolk sac tumor, immature teratomas and mixed germ cell tumors. Embryonal carcinoma, choriocarcinoma and polyembryoma type account for only 5%–10% of patients and rarely exist in pure form. These tumors can occur in women at any age, but peak incidence is seen during early 20's.[2]

Ovarian yolk sac tumors account for 20% of malignant ovarian germ-cell tumors, and are the second most frequent histological subtype, after ovarian dysgerminoma. Yolk sac tumors occur mostly in adolescent and young women. Index patient here is a 19 year old nulligravid. The incidence rate of yolk sac tumors is 0.048/100, 000 women-years in the United States.[9] These tumors were named yolk sac tumor because of the similarity with the extraembryonal yolk sac and vitelline structures. Serum alpha-fetoprotein (AFP) is a useful marker for the diagnosis and management of yolk sac tumor, because it is elevated in all patients with tumors containing an YST component.[10] The patient's serum alpha-fetoprotein level was 1558.85ng/mL, which is 142 times increased from the upper limit of normal (reference range 0-10.9ng/mL).

Clinically, a substantial majority of patients with germ cell tumors present with abdominal pain, abdominal distension or a pelvic mass. Approximately 10 percent of patients will present with acute abdominal pain, usually caused by rupture, hemorrhage or torsion of the ovarian mass.[11]

Ovarian tumors are staged and classified according to clinical and pathological information. The histology is defined according to the World Health Organization classification.[7] Tumors are staged according to the International Federation of Gynecology and Obstetrics (FIGO) staging system for ovarian cancers.[9] The patient here was assessed to have a Stage 1A ovarian malignancy (yolk sac tumor). Stage IA is defined as a tumor strictly limited to one ovary with an intact capsule and without ascites and stage IC tumors are strictly limited to one ovary but exhibit capsular rupture or ascites >100 ml.[10]

There are plenty of factors to consider in considering the type of surgery recommended for a patient with malignant germ cell tumor, and these include: 1) age of the patient, 2) desire for future reproduction, and 3)stage and nodal spread of the disease.

Prior to the availability of combination chemotherapy, patients with stage I yolk sac tumor had a poor prognosis, indicating that micrometastases is already present in most patients,

even though the tumor appeared confined to only one ovary. The surgical treatment for yolk sac tumor in young women desirous of pregnancy is unilateral salpingooophorectomy with limited debulking of extraovarian tumor. Bilateral tumors are rare, and it is not necessary to biopsy a grossly normal contralateral ovary. If they appear uninvolved, the contralateral ovary and uterus need not be removed even in patients with more advanced disease.[12] The index patient here underwent conservative surgical management in the form of right salpingooophorectomy, and left oophorocystectomy mainly due to her very young age, and her desire to preserve her reproductive potential. By FIGO guidelines, in cases of early-stage disease in young women, the recommended surgical treatment is unilateral salpingooophorectomy with peritoneal staging procedures (routine peritoneal cytology, multiple peritoneal biopsies and omentectomy). In the case of advanced-stage disease, the recommended surgical treatment is unilateral salpingooophorectomy, omentectomy and resection of macroscopic lesions on the peritoneum, with a fertility-sparing intent attempted whenever possible.[12]

At the end of the 1970s, the prognosis of yolk sac tumor dramatically improved with the introduction of novel chemotherapeutic regimens.[13] Especially following the addition of cisplatin to combination regimens, survival rates have reached excellent values, even for patients with advanced stage tumors. However, the prognosis for some patients still remains unsatisfactory. Recent reports showed that the FIGO stage and tumor-reductive surgery strongly affected the prognosis of this disease.[14]

For this case, combination chemotherapy was started soon after the surgery. During treatment, serum AFP, full blood counts, electrolytes, liver function tests, magnesium, urea and creatinine levels were measured weekly. Monitoring of the patient should be done every 1-2 years with MRI and serum alpha fetoprotein test to detect recurrence of malignancy. A recent study reported that an elevation of the serum markers β-human chorionic gonadotropin and AFP are independent poor prognostic factors in malignant ovarian germ cell tumors.[15,16]

Based from the study of Tomokazu Umezu, Hiroaki Kayajiyama[17], the 5-year overall survival and progression-free survival for this case are approximately 66.6% and 68.8%, respectively. Patients with no or minimal ascites (volume of less than 100 ml) or a residual tumor measuring less than 1 cm had, over the years, improved to a relatively good prognosis, due to its responsiveness to combination chemotherapy. Neither serum AFP level nor age had any significant correlation with the prognosis in this study.

Conclusion

Malignant ovarian germ cell tumor is a rare disease and can be seen in any age group from infants to old age. As most of the patients are young and nulligravid, fertility preservation is strongly advocated as a secondary objective in women treated for malignant ovarian germ cell tumors. These tumors are very chemosensitive, and therefore, chemotherapy should be started as soon as possible in order to improve survival rates.

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