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Case Report

Yolk sac tumor of endometrium: A case report and literature review

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ABSTRACT

Objective: To report a rare case of endometrial yolk sac tumor (YST) and review published cases of YST of the endometrium.**Case report:** A 68-year-old female presented with intermittent vaginal spotting for nine months. An endometrial biopsy showed adenocarcinoma. Complete surgical staging operation was performed and the final pathology revealed stage II endometrial yolk sac tumor. The post-operative α -fetoprotein (AFP) level was 133.4 ng/mL. Post-operative adjuvant chemotherapy with bleomycin, etoposide, and cisplatin (BEP) regimen was prescribed for 6 cycles. AFP levels were normal before the fourth cycle of chemotherapy. She is disease free 6 months after completion of therapy.**Conclusion:** Primary YSTs arising in the endometrium is an extremely rare disease especially in post-menopausal women. Complete surgical staging operation with adjuvant chemotherapy will lead to good outcome in this disease.© 2019 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Yolk sac tumor (YST), also known as endodermal sinus tumor, is the second most common ovarian germ cell tumor [1]. Of all the genital tumors, YSTs are relatively uncommon and they mostly developed in infants and adolescents (median age, 19 years) [2]. Ovary is the most common site of involvement [1]. However, it was occasional arising from midline extragonadal regions, such as sacrococcygeal region, mediastinum, retroperitoneum and the female reproductive tract [3]. Primary yolk sac tumor arising from the endometrium is an extremely rare condition, to our best knowledge, only 16 cases have been reported in the English literature (Table 1) [4–18]. Here we present a 68-year-old woman with the diagnosis of YST of the endometrium. We also reviewed the literature discussing YST of the endometrium.

Case report

A 68-year-old female, para 3, was admitted with abnormal vaginal bleeding that had been ongoing for 9 months. She received transvaginal ultrasound which showed a hyperechoic endometrial mass, 33×22 mm in size, highly vascularized, with hydrometra (Fig. 1A). Resistive index (RI) was 0.51. Thereafter, the diagnostic D&C was performed and the pathology revealed adenocarcinoma. A chest X ray revealed no apparent abnormalities. Laboratory testing was unremarkable, with a normal CA-125 (24.1 U/ml [reference level, <35 U/ml]). Abdominal and pelvic CT scan (Fig. 1B) disclosed a uterine mass with no obvious enlarged lymph nodes. Under the impression of endometrial cancer, surgical intervention was suggested. The patient was informed of the recommended treatment, and she gave her consent.

We performed a laparotomy with total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic lymphadenectomy, para-aortic lymphadenectomy, and omentectomy. Grossly, the tumor was yellowish-white with a central hemorrhagic area (Fig. 1C). It arose from the endometrium with involvement of more than one half of the myometrium, and had infiltrated to the cervical stroma. Microscopically, the tumor had the typical features of a yolk

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Table 1

Clinical characteristics of reported cases of yolk sac tumor of the endometrium.

CASE	Age, years	AFP level	Surgery	Chemotherapy	Recurrence	Total survival time, months
#1 [4]	28	380 ng/mL before surgery	TAH, BSO	VCR, CTX, ADM, MTX, 5-FU	Liver metastases 2 months after surgery	8
#2 [5]	24	3600 ng/mL before surgery	TSH, BSO	VAC	Yes (details unavailable)	24
#3 [6]	17	34,118 ng/mL before surgery	TAH, omentectomy, and debulking of the peritoneal tumor	BP	Did not recur	>72
#4 [7]	27	1580 ng/mL before surgery	TAH, BSO, omentectomy	VAC	Did not recur	>14
#5 [8]	42	18,530 ng/mL before surgery	TAH, BSO	BVP	Did not recur	>24
#6 [9]	49	No data before surgery	TAH, BSO, iliac lymphadenectomy	None	Did not recur	>28
#7 [10]	59	27,570 IU/mL during the second surgery	TAH, BSO, bilateral pelvic and common iliac lymphadenectomy, omentectomy	BEP, EP	Liver, diaphragm, para-aortic lymph nodes	>30
#8 [11]	65	2306 ng/mL before surgery	MRAH, BSO, pelvic lymphadenectomy	None	Did not recur	No data
#9 [12]	29	3593 ng/mL before surgery	MRAH, left adnexa resection, pelvic and para-aortic lymphadenectomy	BEP	Did not recur	No data
#10 [13]	38	37.4 ng/mL after surgery	TAH, BSO, pelvic and para-aortic lymphadenectomy, omentectomy	BEP	Did not recur	No data
#11 [14]	28	1522 ng/mL before surgery	TAH, BSO, pelvic and para-aortic lymphadenectomy, omentectomy	PT	Elevated AFP	No data
#12 [15]	31	242.3 IU/mL before surgery	TAH, BSO, pelvic and para-aortic lymphadenectomy, omentectomy	BEP	Did not recur	>24
#13 [16]	30	1762 ng/mL before surgery	TAH	BEP	Did not recur	>72
#14 [17]	63	244.6 IU/mL before surgery	TAH, LSO, omentectomy, appendectomy	BEP	Liver, lung, Intra-abdomen	No data
#15 [18]	57	31,833 IU/mL before surgery	TAH, BSO, pelvic and para-aortic lymphadenectomy, omentectomy	BEP	Expire due to septic shock	<1
#16 [18]	44	30,000 IU/mL before surgery	TAH, BSO, pelvic and para-aortic lymphadenectomy, omentectomy	BEP	Did not recur	>6
[Present case]	68	133.4 ng/mL after surgery	TAH, BSO, pelvic and para-aortic lymphadenectomy, omentectomy	BEP	Did not recur	>6

Abbreviations: ADM, adriamycin; AFP, α -fetoprotein; BEP, bleomycin, etoposide, cisplatin; BP, bleomycin, cisplatin; BSO, bilateral salpingo-oophorectomy; BVP, bleomycin, vinblastine, cisplatin; CTX, cyclophosphamide; EP, etoposide, cisplatin; FU, fluorouracil; MRAH, modified radical hysterectomy; MTX, methotrexate; TAH, transabdominal hysterectomy; TSH, transabdominal supracervical hysterectomy; VCR, vincristine; VAC, vincristine, actinomycin, cyclophosphamide; PT: paclitaxel, carboplatin.

sac tumor in that it had reticular and solid growth patterns, and Schiller-Duval bodies were present (Fig. 1D). The neoplastic cells stained positively for AFP. The morphologic and immunohistochemical pattern was consistent with a primary yolk sac tumor (YST) of the endometrium. The final pathologic stage was pT2N0M0 based FIGO staging [19].

Six days after the operation, the patient was discharged. The postoperative levels of AFP were 133.4 ng/mL. Adjuvant chemotherapy with bleomycin, etoposide, and cisplatin (BEP) regimen was prescribed for 6 cycles. AFP levels were normal before the fourth cycle of chemotherapy. She is still alive and has remained disease free 6 months after completion of chemotherapy.

Discussion

YSTs, also known as endodermal sinus tumors, are malignant germ cell tumors that occur usually in the ovary and rarely in the endometrium. Such cases principally occur in children and young adults, and it has been assumed that they arise from germ cell precursors that have become arrested and misplaced during embryological migration. By this theory, yolk sac tumor can occur in endometrium [4]. The most frequent symptom of endometrial YST was abnormal vaginal bleeding and elevated serum alfa-fetoprotein levels before or immediately after surgery. Primary yolk sac tumors of the endometrium are extremely rare. To our knowledge, only 16 cases have been reported in the literature including our case (Table 1). In the literature, ovarian YST components have been in association with other tumors, usually ovarian endometrioid carcinoma in older women, and these tumors may be less responsive to chemotherapy [20]. Among these 16 cases, 14 cases were pure yolk sac tumors and only 2 cases were in coexistence with endometrial carcinoma. In a reported case with

endometrial YST in coexistence with endometrial carcinoma, the histopathologic examination of the uterine tumor revealed well to moderately differentiated endometrial adenocarcinoma with yolk sac tumor-like differentiation intra-endometrium, with a close transition between the two components. It may support that the YST component was originated from aberrant differentiation of somatic cells.

Yolk sac tumors can show variable presentation under a microscope, and pathologists may have difficulty in differentiating microcystic or endodermal sinus-like structures from clear-cell carcinoma [6]. Indeed, the diagnosis of YST was not made by initial D&C specimen in our patient. In addition to morphologic differences, immunohistochemical staining is helpful in diagnosis of YST [7]. Yolk sac tumors are strongly positive for alfa-fetoprotein/CDX2/Hep-par-1 and focally positive to CK20 [8]. In addition, serum alfa-fetoprotein determinations are important in the diagnosis of yolk sac tumors and monitoring metastasis or recurrence after therapy.

YSTs metastasize early and invade surrounding structures. Metastases often occur via the blood and the lymphatic system. Because of their rarity, there has been no systematic study on the proper management of endometrial YSTs with a large number of cases. Chemotherapy with a regimen of bleomycin, etoposide, and cisplatin (BEP) is recommended for germ cell tumors of ovary and hence is used in yolk sac tumor of endometrium and seems to be effective [10]. Among these 16 reported cases, only 4 cases had tumor recurrence (case #1, #2, #7, and #14). Because lack of detail clinical information of case #2 and #14, we could only compare case #1 and case #7. Case #1 recurred within 2 months after treatment and had short overall survival (8 months). This case did not receive comprehensive staging surgery. The adjuvant chemotherapy was VAC (vincristine, actinomycin, and cyclophosphamide)

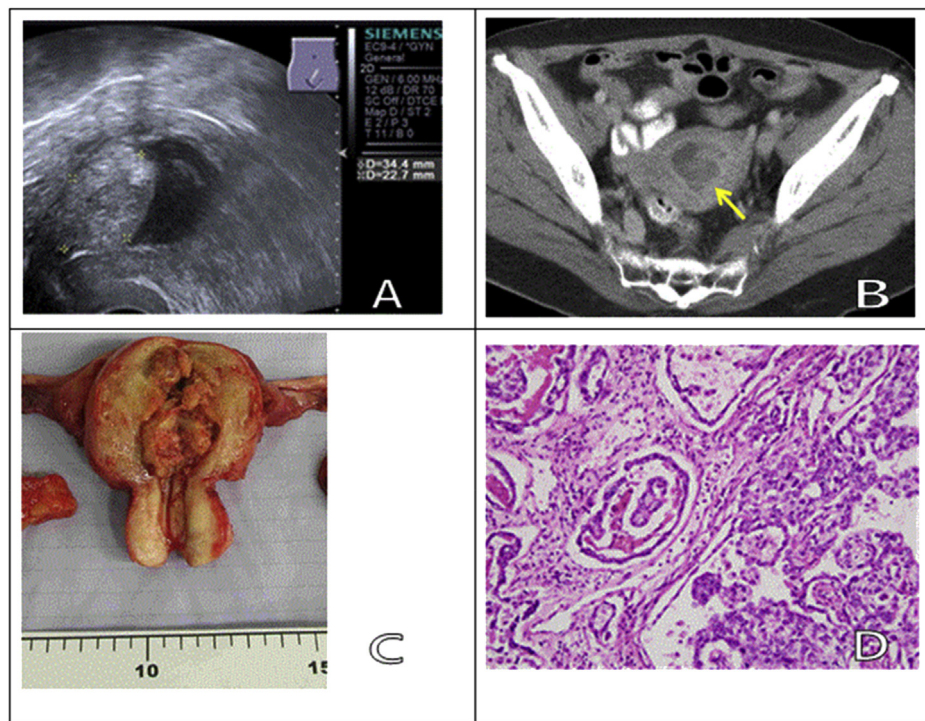


Fig. 1. (A) Transvaginal ultrasound revealed an endometrial mass with hydrometra. (B) Computed tomography showed a uterine mass (arrow) with no regional lymph node enlargement. (C) Yellowish-white tumor with central hemorrhagic area in endometrial cavity. (D) Papillary elements with structure of Schiller-Duval body (H&E, 100X).

regimen, not BEP regimen. In contrast, case #7 had better overall survival (30 months). This patient received comprehensive staging surgery and secondary cytoreductive surgery, and the adjuvant chemotherapy was BEP regimen. Although no consensus guidelines exist for treating endometrial yolk sac tumors, most patients in the literature underwent cytoreductive surgery, followed by BEP regimen as first-line adjuvant treatment. A combination of comprehensive surgery and chemotherapy seems to have a better outcome.

In conclusion, YST arising in the endometrium is a rare malignant neoplasm. It should be differentially diagnosed from other uterine malignancies. Serum AFP and immunohistochemical stain may help the diagnosis of this disease. Complete surgical staging combined with chemotherapy may have a better survival impact on endometrial YST. A greater number of cases are needed to determine the most adequate and appropriate treatment.

Conflict of interest

There is no conflict of interest.

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