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Ovarian Endometrioid Adenocarcinoma with a Yolk Sac Tumor Component

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Ovarian endometrioid adenocarcinoma (EAC) with a yolk sac tumor (YST) component is extremely rare. Only twelve cases have been reported in the English literature. We report here two additional cases of this rare tumor. The YST component showed classic microscopic features, and immunohistochemically stained positive for alpha-fetoprotein (AFP), but negative for cytokeratin 7 (CK7), epithelial membrane antigen (EMA), estrogen receptor (ER) and progesterone receptor (PR). The EAC appeared to blend into the YST in several areas and immunohistochemically stained positive for CK7, EMA, ER, and PR, but negative for AFP.

Key Words : Ovary; Yolk sac tumor; Endometrioid adenocarcinoma; Endodermal sinus tumor

A yolk sac tumor (YST) is a malignant germ cell tumor that is characterized by endodermal differentiation and usually occurs in women younger than 30 years of age.[1] A YST coexisting with an endometrioid adenocarcinoma (EAC) is extremely rare.[2-9] It has been suggested that this rare tumor should be considered a variant of an EAC, because it occurs in the same age range as EAC and shows more aggressive behavior than a pure YST. Herein, we present two cases of ovarian EAC with a YST component.

CASE REPORTS

Case 1

A 47-year-old postmenopausal woman presented with lower abdominal pain and a palpable pelvic mass. The serum level of alpha-fetoprotein (AFP) was 82 ng/mL (normal value, <10 ng/mL). An exploratory laparotomy was done and a right ovarian cystic mass was found. It ruptured during the operation, with spillage of chocolate-colored bloody contents. A total hysterectomy with bilateral salpingo-oophorectomy and pelvic lymph node dissection was done. This was followed by three cycles of combination chemotherapy consisting of bleomycin, etoposide, and cisplatin. The serum level of AFP returned to normal six weeks after the operation. The patient has been followed up for three months with no sign of recurrence or progressive disease.

Grossly, the right ovarian tumor consisted of a unilocular cyst, measuring 12.0 cm at its largest diameter. The outer surface was smooth. Within the cyst, there was a protruding solid nodule measuring 6.0×5.0 cm. In addition, a relatively well circumscribed, soft, friable, brown-tan lesion with necrosis, measuring 2.5×2.4 cm was noted within the solid nodule.

On microscopic examination, the cystic part was covered mainly by columnar or cuboidal single-layer epithelial cells and contained foci of endometriosis. The solid nodule was composed of two distinct histologic components. The major component was an endometrioid tumor composed of a mixed benign and borderline adenofibroma with squamous metaplasia. Sections from the brown-tan necrotic lesion were a YST, showing a combination of papillary, reticular and glandular patterns (Fig. 1A). The

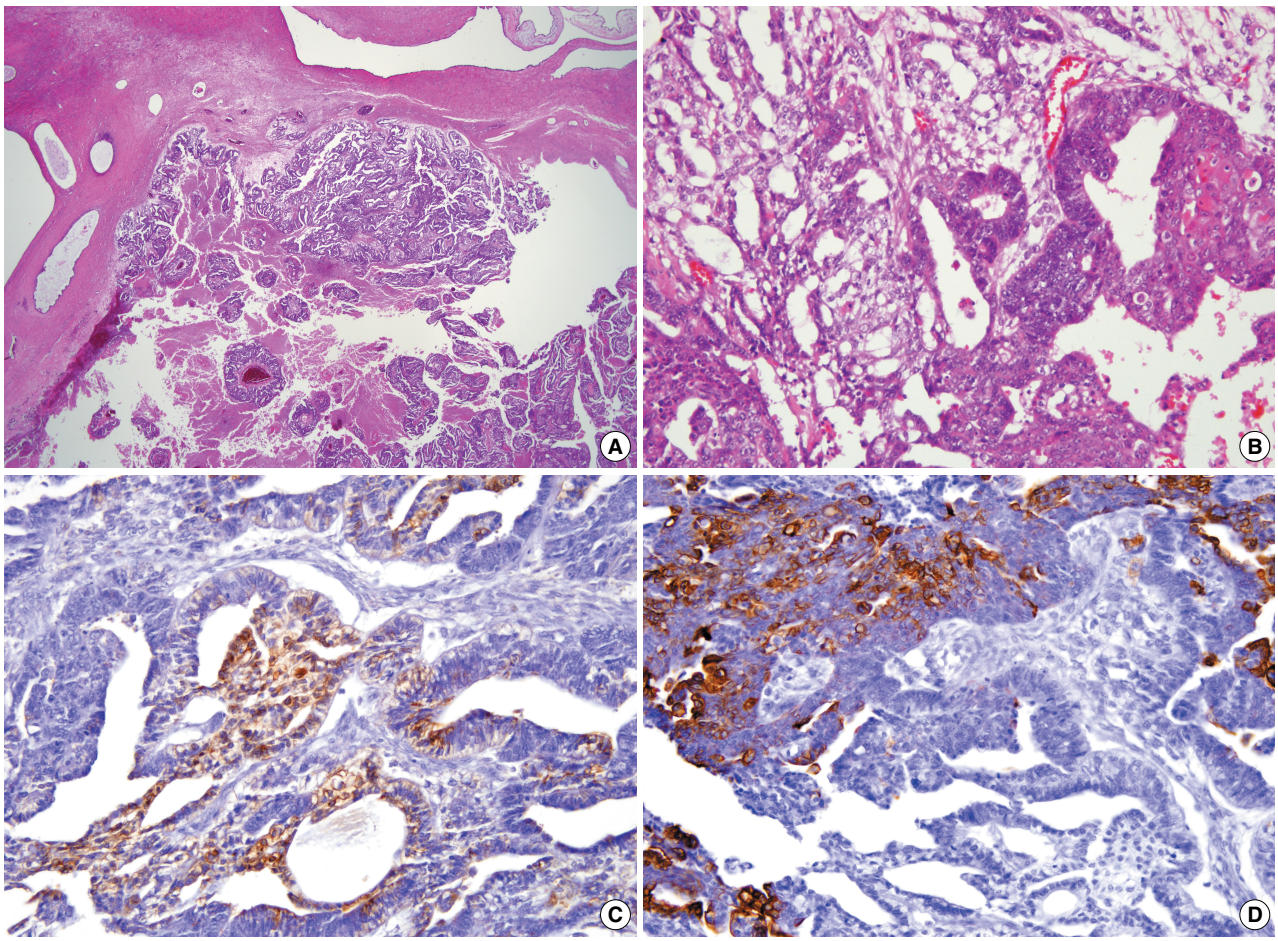

Fig. 1. Low-power view reveals endometrioid adenocarcinoma (EAC) with yolk sac tumor (YST) component in the background of endometrioid adenofibroma (A). Interfaces between YST and EAC are noted. The EAC component shows squamous metaplasia (B). YST components show positive immunoreactivity for alpha-fetoprotein, while EAC components show negative reactivity (C). EAC components are positive for cytokeratin 7 (D).

YST component was irregularly intermingled with the EAC and was in direct continuity with the EAC (Fig. 1B). Immunohistochemically, the YST component was positive for AFP (Fig. 1C), but entirely negative for cytokeratin 7 (CK7), epithelial membrane antigen (EMA), estrogen receptor (ER), and progesterone receptor (PR). In contrast, the endometrioid component stained positive for CK7 (Fig. 1D), EMA, ER, and PR, but negative for AFP.

Case 2

A 39-year-old woman was referred to our hospital because of a palpable pelvic mass. Serum levels of CA-125 and CA 19-9 were elevated up to 1,760.2 U/mL (normal value, <35 U/mL) and 138.5 U/mL (normal value, <37 U/mL). On exploratory laparotomy, bilateral ovarian masses were found, and total hysterectomy combined with bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, and omentectomy was performed. The patient received five courses of postoperative chemotherapy consisting of paclitaxel and carboplatin and has remained without clinical evidence of recurrent disease for three months.

Grossly, the right ovary was replaced by a solid and cystic tumor, 10.0×10.0 cm in size. The outer surface was smooth. The solid area measured 7.0×4.0 cm. The left ovarian tumor consisted of a multilocular cyst with a smooth outer surface measuring 7.0×7.0 cm. There was a solid area measuring 3.5×3.0 cm. The uterus had two leiomyomatous nodules up to 15.0×10.0 cm in size.

On microscopic examination of the right ovary, the cyst was covered by a single layer of benign-looking endometrial-type epithelial cells, and an old hemorrhage was noted in the under-

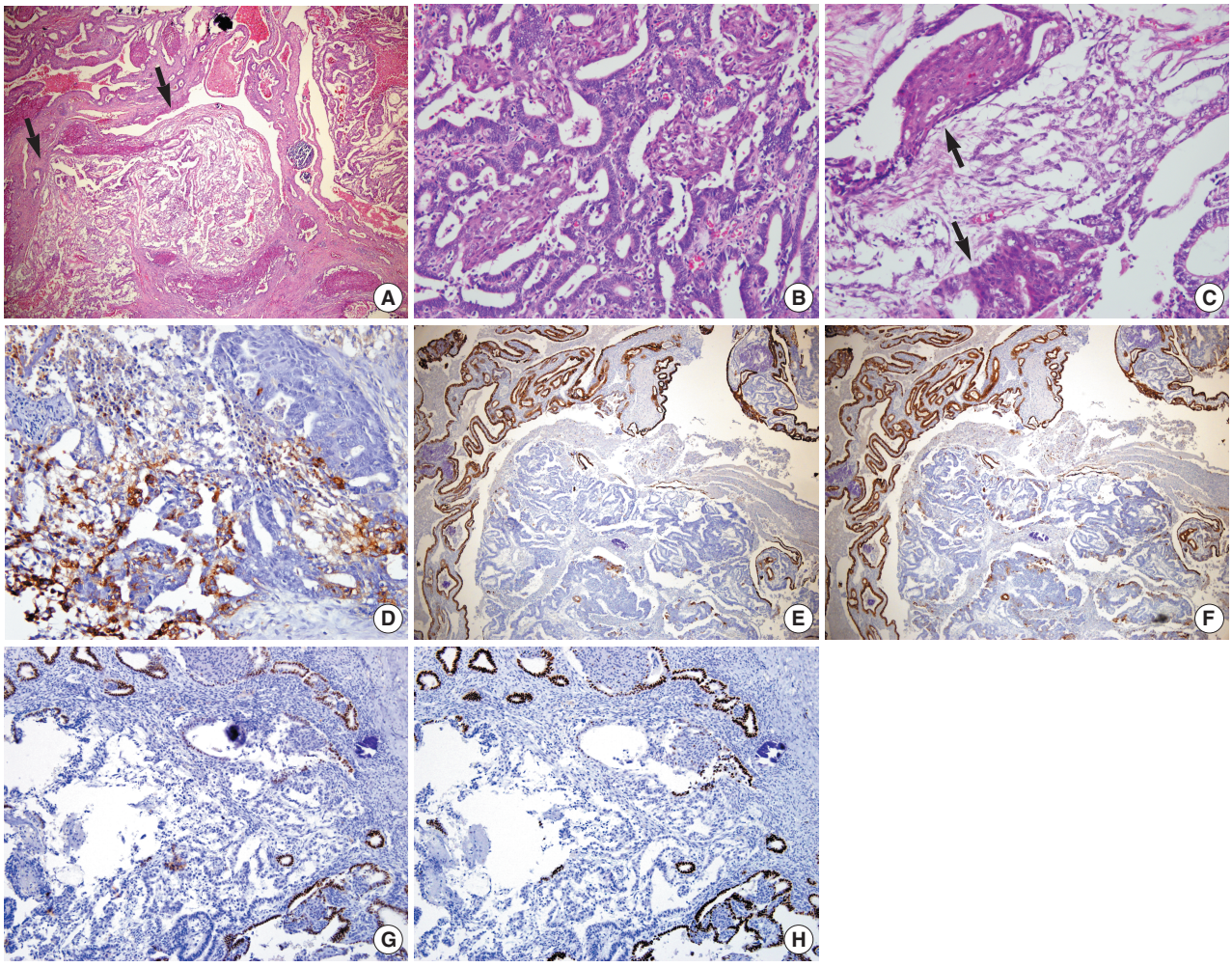

Fig. 2. Low-power view reveals a yolk sac tumor (YST, arrows) in the background of a borderline endometrioid tumor (A). The endometrioid adenocarcinoma (EAC) component shows squamous morules protruding into the lumina of neoplastic glands (B). YST components are irregularly intermingled with those of the EAC (arrows) (C). On immunohistochemical stain, YST components are positive for alpha-fetoprotein, while EAC components are negative (D). Endometrioid tumor components reveal positive immunoreactivity for cytokeratin 7 (CK7) (E), epithelial membrane antigen (EMA) (F), estrogen receptor (ER) (G), and progesterone receptor (PR) (H). In contrast, YST components are negative for CK7 (E), EMA (F), ER (G), and PR (H).

lying endometrial stroma. There were two different types of histologic components within the solid area (Fig. 2A). The major component was an endometrioid tumor containing a well-differentiated EAC in the background of a borderline tumor. Many squamous morules were seen protruding in the lumina of neoplastic glands (Fig. 2B). The other component was consistent with a YST. The predominant feature was a reticular or microcystic pattern composed of a meshwork of clear cells. YST components were irregularly intermingled with those of the EAC (Fig. 2C). Overall histologic and immunohistochemical features were similar to Case 1 (Fig. 2D-H). The left ovarian tumor was an endometrioid borderline tumor.

DISCUSSION

Ovarian EACs with a YST component are very rare and only 12 cases have been reported in the English literature.[2-9] The clinicopathologic features of those cases are summarized in Table 1. It is known that ovarian YSTs are most frequently seen in young females (average age of 19 years) and show a favorable response to chemotherapy.[1] However, a YST coexisting with an EAC differs from a pure YST in many respects. A YST with an EAC occurs within the same age range as an EAC (23-71 years), and does not respond to systemic chemotherapy. Eight of 12 patients having surgery and postoperative chemotherapy died of the tumor 3 to 14 months after surgery.[2-9]

Table 1. Clinicopathologic features of cases with ovarian endometrioid adenocarcinoma with yolk sac tumor component

Case	Patient age (years)	Clinical presentation	Treatment	Tumor side/size (cm)	Endometriosis	Stage	Serum AFP level (ng/mL)	Follow-up
1[8]	50	Abd fullness, pelvic mass	TAHBSO, omentectomy	L/11	Yes	IA	720	Recurrence, DOD 8 mo
2[2]	64	Increasing abd girth and chronic pain	TAHBSO	L/13	No	IA	>300	Recurrence, DOD 14 mo
3[2]	71	As above	TAHBSO	R/10	Yes	IA	N/A	Alive and well 12 mo
4[2]	71	As above	TAHBSO	R/11	No	III	N/A	DOD 3 mo
5[2]	40	As above	TAHBSO	L/25 R/15	No	IV	33	DOD 5 mo
6[2]	31	Aute abdomen	RSO, 2nd-look surgery	R/15	Yes	III	7,600	Recurrence, DOD 8 mo
7[3]	53	Pelvic mass, fever, lower abd pain	TAHBSO, omentectomy, pelvic LND	L/11	Yes	IA	2,842	DOD 6 mo
8[5]	54	Abd fullness	TAHBSO, omentectomy	R/20	Yes	IC	13,143	Alive and well 21 mo
9[7]	51	Lower abd swelling	TAHBSO, omentectomy	R/16	Yes	IC	37→12,000	DOD 10 mo
10[6]	23	Abd pain	TAHBSO, omentectomy	L	Yes	III	2,726	Alive and well 12 mo
11[9]	41	Lower abd pain	TAHBSO, omentectomy, paraaortic LND	L/21	Yes	IIB	N/A	DOD 11 mo
12[4]	52	Lower abd pain	TAHBSO, omentectomy, pelvic and paraaortic LND	L/10	No	IC	24,518	Alive and well 20 mo
Present case 1	47	Lower abd pain	TAHBSO, pelvic LND	R/12	Yes	IA	82	Alive and well 3 mo
Present case 2	39	Palpable pelvic mass	TAHBSO, omentectomy, pelvic and paraaortic LND	R/10	Yes	IA	N/A	Alive and well 3 mo

Abd, abdominal; TAHBSO, total hysterectomy and bilateral salpingo-oophorectomy; L, left ovary; DOD, died of disease; mo, months; R, right ovary; N/A, not available; RSO, right salpingo-oophorectomy; LND, lymph node dissection.

Making a diagnosis between an ovarian YST coexisting with an EAC and a so called endometrioid variant of a YST can be difficult, because of their striking morphological resemblance. An important clinical difference between these two tumors is the age of the patients. The coexistence of precursor lesions (benign and borderline endometrioid tumor) and associated squamous metaplasia are findings in keeping with the diagnosis of EAC.[2] Immunohistochemically, an endometrioid tumor differs from a YST in its positivity for CK7, EMA, ER, and PR and in its negativity for AFP, which is positive in the YST.[3,5,6,10] Our cases showed the coexistence of endometriosis and borderline endometrioid tumor with squamous metaplasia in the same ovary. Immunohistochemistry revealed positive staining for CK7, EMA, ER, and PR in the EAC component. Thus, diagnosis as an endometrioid variant of YST seemed inappropriate for the present tumors.

Mixed endometrioid and clear cell carcinoma (CCC) should be included in the differential diagnosis. CCC may resemble YST and show high association with endometriosis. The identification of a reticular pattern typically seen in YSTs when present, facilitate the diagnosis of YST. Immunohistochemical stains for AFP, CK7, and EMA may aid in the differential diagnosis. AFP is demonstrable in almost all YSTs, but is rarely found in CCCs. In contrast, both CK7 and EMA are stainable in almost all CCCs, but not in YSTs.[10]

In terms of histogenesis, several mechanisms have been proposed. It has been suggested that somatic carcinomas have the ability to acquire germ cell differentiation. This phenomenon could be explained by neometaplasia (aberrant differentiation), which appears to be the most reasonable explanation for the histogenesis of the tumor in these cases.[2-8]

In summary, we have described two unusual cases of ovarian EAC with a YST component. This tumor should be considered a variant of EAC and its recognition is very important in view of its unusually aggressive behavior and poor response to chemotherapy.

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