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Case Report

Ovarian yolk sac tumor with epithelial tumor component in a postmenopausal woman - case report and literature review

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Abstract: Ovarian yolk sac tumors are common germ cell tumors usually arising in young women. Yolk sac tumors in elderly women are infrequently encountered and most of them are combined with other epithelial tumor components including endometrioid carcinoma or serous carcinoma. Here, we report an extremely rare case of a yolk sac tumor with mucinous tumor and large cell neuroendocrine carcinoma components in a postmenopausal woman, which is the third yolk sac tumor case with a neuroendocrine tumor element in an elderly woman. An 82-year-old female visited our hospital due to abdominal distention. Abdominal computed tomography (CT) demonstrated a solid and cystic mass, measuring about 9.0 cm in the largest diameter. A total hysterectomy with bilateral salpingo-oophorectomy and excisional biopsy of the peritoneal metastatic lesions was performed. Histologic evaluation revealed a malignant ovarian tumor composed of a variety of tumor components, including a yolk sac tumor, a mucinous tumor with multifocal mucinous carcinomatous areas, and a large-cell neuroendocrine carcinoma. After surgery, the patient refused further treatment and the disease recurred in the pelvic peritoneum and a left supraclavicular lymph node nine months later.

Keywords: Composite tumor, ovarian yolk sac tumor, adult

Introduction

Ovarian yolk sac tumors (YSTs) are the second most common malignant germ cell tumors, usually occurring in young women under 20 years of age. YSTs in postmenopausal women are extremely rare [1]. The majority of YSTs arising in old age tend to concurrently accompany variable types of somatic epithelial neoplasms [2]. Among them, endometrioid carcinomas are the most common malignancies in ovarian YST-associated epithelial neoplasms [3]. Interestingly, germ cells are not identified in the ovaries of postmenopausal women. Therefore, YSTs in postmenopausal patients may have different pathogenesis than those in younger women. One hypothesis suggested that YSTs in old age may originate from an epithelial neoplasm through the processes of neometaplasia or retrodifferentiation [4].

Herein, we report an additional case of a YST combined with a mucinous tumor and large-cell neuroendocrine carcinoma arising in a postmenopausal woman. As far as we know, this is the third case of a YST with a neuroendocrine carcinoma component in a postmenopausal woman. We review the pathogenesis and clinicopathologic characteristics in previous reports of YSTs in elderly women.

Case report

An 82-year-old postmenopausal woman was admitted to our hospital for abdominal distention and discomfort for one month. There was no remarkable personal history. The computed tomography (CT) detected a mixed solid and cystic mass with heterogeneous enhancement in the left ovary. The preoperative serum tumor marker levels were CA125: 44.51 U/mL (normal, 0-35 U/mL), CA19-9: 152.00 U/mL (normal, 0-34.0 U/mL) and CEA: 5.66 ng/mL (normal, 0-5.0 ng/mL). Under suspicion of ovarian epithelial malignancy, the patient underwent a total abdominal hysterectomy with bilateral sal-

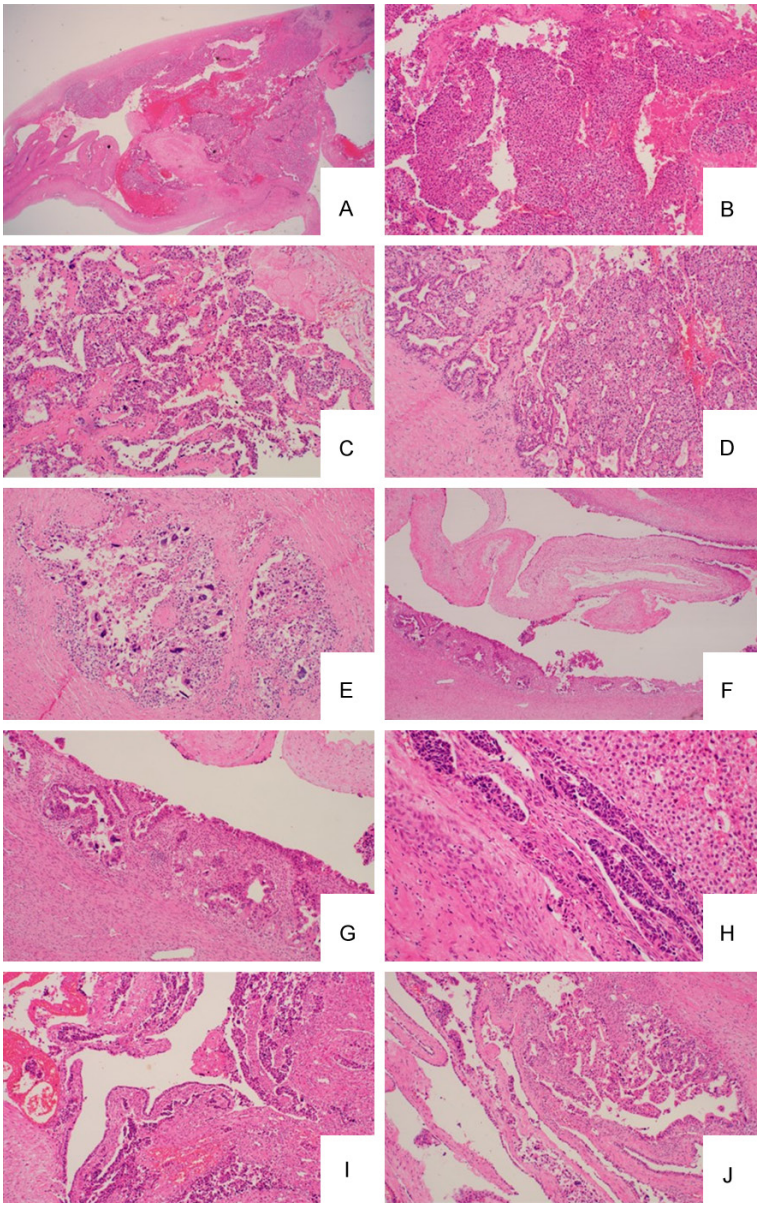

Figure 1. Microscopic features of the ovarian tumor. (A) The ovary showed a solid and cystic mass with multifocal hemorrhage. (B-D) The YST component exhibited a variety of histologic features, including solid sheet-like (B), papillary (C), and glandular patterns (D). (E) There were markedly pleomorphic cells in some areas. (F) The mucinous tumor component showed a cystic appearance. (G) Stromal invasion was noted in the mucinous tumor, suggesting mucinous carcinoma. (H) A large-cell neuroendocrine carcinoma component was also found in focal areas. (I and J) There were transitional regions between the mucinous tumor and the neuroendocrine tumor components (I) and between the mucinous tumor and the YST components (J).

pingooophorectomy, partial omentectomy, and metastatic tumor resection in the right and left para-rectal areas. On gross examination, the left ovary was replaced by a solid and cystic mass with a multinodular contour, measuring 9.0 × 8.5 × 7.0 cm. The cut surface displayed a variegated appearance with multifocal hemorrhagic and necrotic areas.

Microscopic examination revealed that the tumor in the left ovary showed both yolk sac tumor components and epithelial tumor components (**Figure 1A**). The YST component occupied about 85% of the total tumor volume. The YST area displayed a predominantly solid-sheet growth pattern with focal papillary and glandular patterns (**Figure 1B-D**). Multifocal hemorrhage and necrosis were frequently noted in this area. Although some tumor cells were pleomorphic, forming multinucleated giant cells (**Figure 1E**), most of the tumor area consisted of relatively monotonous polygonal cells with pale to eosinophilic cytoplasm and a centrally located round nucleus. The second most common component of this tumor was a mucinous neoplasm, including a mucinous cystadenoma and a mucinous cystadenocarcinoma, which occupied about 10% of the total tumor volume (**Figure 1E** and **1F**). Mucinous neoplasm appeared in many cystic parts of the tumor. Most of the component was benign mucinous cystadenoma, but there were multiple small foci of cellular atypia and proliferation with stromal invasion (**Figure 1G**). As a third component, cord-like structures were noted in a focal area estimated at about 5% of the tumor. The tumor cells in the area had modest eosinophilic cytoplasm and irregular pleomorphic nuclei with coarse chromatin patterns, suggesting large-cell neuroendocrine carcinoma (**Figure 1H**). Mitotic activity was frequently seen, up to 10/10 high-power fields. Among each component, a mor-

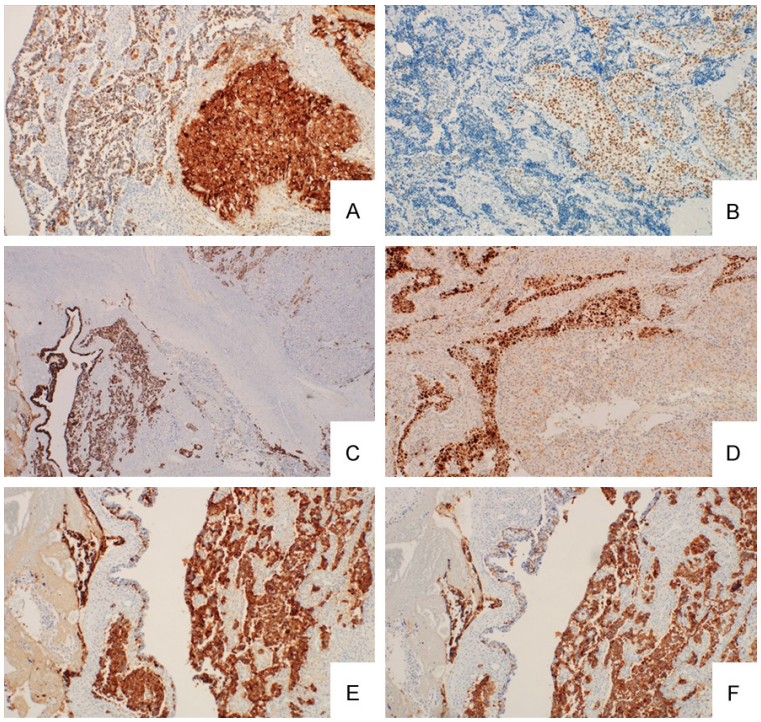

Figure 2. Immunohistochemical staining for glypican-3 (A) and SALL4 (B) were positive mainly in YST areas and immunohistochemical staining for CK7 (C) and Pax8 (D) was positive mainly in the somatic epithelial tumor areas. Chromogranin A (E) and synaptophysin (F) showed immunoreactivity in the large-cell neuroendocrine carcinoma areas.

phologically overlapping transition region was observed, which gradually changed into another component (**Figure 1I** and **1J**).

Immunohistochemistry for alpha-fetoprotein (AFP), a specific YST marker, was focally positive in the YST component and negative in the mucinous tumor and large-cell neuroendocrine carcinoma components. Other YST markers including glypican 3 and SALL4, showed diffuse positivity in the YST area and focal patchy positivity in the mucinous tumor and neuroendocrine carcinoma areas (**Figure 2A** and **2B**). CK7 and PAX8, ovarian somatic epithelial tumor markers, were diffuse and strongly immunoreactive in the mucinous tumor and neuroendocrine carcinoma areas, whereas they were focally positive in the YST area (**Figure 2C** and **2D**). Representative neuroendocrine markers, including synaptophysin, chromogranin A, and CD56, showed diffuse and intense immunoreactivity in the neuroendocrine carcinoma area and focal immunoreactivity in the YST and mucinous carcinoma areas (**Figure 2E** and **2F**). Although the tumor components mainly expressed typical immunophenotypes according to their histologic features, the markers of other components were focally expressed in all components. Metastatic lesions with histology similar to the primary tumor were identified in the right ovary and serosa of the uterus and peritoneum. After the pathologic diagnosis, the serum AFP level was measured and it had increased to 488.30 ng/mL (normal, 0-7.99 ng/mL). The patient refused any chemotherapy and the tumor recurred at the left pelvic side wall and right supraclavicular lymph node nine months later.

Discussion

Combined germ cell tumor and somatic epithelial malignant tumors occur in various sites, including the lung, breast, and colon, as well as in female reproductive organs [5-9]. Particularly, YSTs with carcinomatous components have been described in the endometrium and ovary [2, 9]. Since Rutgers et al. reported the first case in 1987, less than 30 cases of mixed ovarian tumors in perimenopausal and postmenopausal women have been reported in the English literature [1, 3, 10]. The common forms of YST-associated somatic neoplasms in the ovary are serous carcinoma and endometrioid carcinoma. Interestingly, our case showed two distinct epithelial tumor components of mucinous neoplasm and large-cell neuroendocrine carcinoma that were proven by histology and immunohistochemical staining. Notably, to date, there have been only two reports describing neuroendocrine tumors as the somatic epithelial neoplasms element in these ovarian mixed tumors [2, 11].

The pathogenesis of the simultaneous presence of YST and ovarian carcinoma is still obscure because there are no germ cells in the ovaries of postmenopausal women [3]. Clarification of the pathogenesis is important for correctly understanding the disease nature, as well as establishing appropriate therapeutic

Table 1. Clinicopathologic characteristics of adult yolk sac tumor with neuroendocrine tumor component

	Author	Age	Tumor size (largest diameter)	Tumor site	Stage	Histology	Chemotherapy	Outcome
1	Boussios S et al. and McNamee et al. [2, 11]	59	40 cm	Right ovary	II	YST and LNEC	Not received after first surgery Carboplatin and etoposide after recurrence	Recurrence 1 year later, Died 21 months after initial diagnosis
2	McNamee et al. [2]	72			IC	YST, IT, CT and EC	NA	NA
3	Present case	82	9.0 cm	Left ovary		YST, MC and LCNEC	Not received	

plans and chemotherapeutic regimen [2]. Some studies reported that the YST component could originate from somatic epithelial cells by the processes of neometaplasia or retrodifferentiation and pure YSTs in elderly women could be explained by the replacement of epithelial tumor elements into rapidly-growing YST elements [1-3]. In the case reported here, transitional histologic features were identified between the YST, mucinous tumor, and large-cell neuroendocrine tumor components (**Figure 1I** and **1J**). Additionally, the PAX8, glypican-3, and SALL4 immunoreactivity patterns were observed in morphologically overlapping areas of all these tumor components. We believe these findings could support the possibility of a shared origin of these different morphologic phenotypes.

The biologic behavior and prognostic significance of a mixed YST and neuroendocrine tumor in the ovary are unclear due to the limited case numbers and insufficient clinical information. In one case of a mixed YST and neuroendocrine tumor, the neuroendocrine tumor component was a large-cell neuroendocrine carcinoma and the YST component showed glandular and solid patterns in its histology. The disease recurred one year after surgical treatment and the patient died 21 months after the initial diagnosis [11]. The other case was an ovarian tumor composed of complex elements of YST, immature teratoma, endometrioid carcinoma, and a carcinoid tumor. The YST area showed microcystic and reticular features. Unfortunately, the clinical information, including disease recurrence and the patient outcome, could not be obtained [2] (**Table 1**). In our case, the tumor consisted of three histologic components, including YST, a mucinous tumor, and a large-cell neuroendocrine carcinoma. The patient suffered from disease recurrence and metastasis in the supraclavicular lymph node and pelvic peritoneum nine months after surgery. YST with a neuroendocrine component is often associated with a poor clinical outcome.

Here, we report an extremely rare case of a YST combined with an epithelial tumor composed of a mucinous neoplasm and a neuroendocrine carcinoma in an elderly woman. We also review the pathogenesis of ovarian YSTs in postmenopausal women and the clinicopathologic features of previous cases of YSTs with neuroendocrine tumor components. Based on the previous cases and this case, a YST with a neuroendocrine tumor component is associated with an unfavorable prognosis. However, it is necessary to collect and analyze more cases.

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Disclosure of conflict of interest

None.

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