Gynecologic Oncology Reports 10 (2014) 13–15

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gore

Ovarian mucinous epithelial neoplasm showing immunohistochemical pattern of lower gastrointestinal origin with stromal minor sex-cord elements: A case report

Taeko Ueda *, Hitomi Nakagawa, Toru Hachisuga

Department of Obstetrics and Gynecology, University of Occupational and Environmental Health School of Medicine, Japan

ARTICLE INFO

Article history:
Received 10 June 2014
Accepted 15 August 2014

Keywords:
Ovary
Sex-cord
Mucinous
Endometrial carcinoma
Immunohistochemistry

Introduction

Ovarian stromal tumors with minor sex-cord elements are a rare neoplasm, first reported in a case series by Young and Scully (1983). This tumor is composed of predominantly stromal cells with scattered minor sex-cord elements in less than 10% of the tumor area. Only 12 cases of stromal tumor with minor sex cord elements have been reported in the literature, and 4 of the 12 cases coexisted with uterine endometrial cancer (Young and Scully, 1983; Lee and Ahmed, 2003; Kumar et al., 2013). The presence of endometrial cancer suggests hormone production by the ovarian tumor.

Mucinous neoplasm coexisting with a stromal tumor with minor sex-cord elements of the ovary is an exceedingly rare pathology that has only been reported once by Yang et al. (2001) Herein, we report a case of mucinous neoplasm with stromal proliferation with minor sex-cord elements occurring simultaneously with uterine endometrial cancer.

Case

A 65-year-old, gravida 3, para 3, Japanese woman presented with increasing discharge from the vagina and a feeling of abdomen distension for 6 months. The patient's menopausal age was 53 years and she was not obese (body mass index [BMI]: 24.1). Although the patient had essential hypertension, she was not taking any medication. On examination, a palpable, elastic, solid mass was identified in the lower abdomen extending to the umbilicus. On vaginal examination, uterus size could not be determined and a large abdominopelvic mass was palpable. Bloody discharge from the vagina was also noted. Abdominal ultrasonography revealed a normal sized uterus with endometrial thickness of 25 mm and a major axis of 130 mm cystic mass in the pelvis and lower abdomen. The left ovary was not identified and there was minimal ascites. The patient underwent endometrial curettage and the tumor was confirmed as an endometrioid adenocarcinoma. Chest and abdominal enhanced computed tomography (CT) did not identify the presence of distant metastasis nor para-aortic or pelvic lymph node metastasis. Pelvic magnetic resonance imaging revealed a 13 cm unilocular cystic mass without solid component in the domain of the right adnexa. Endometrial thickening with defect of the junctional zone was observed, which is suggestive of the presence of endometrial cancer (Fig. 1). Serum CA-125, carcinoembryonic antigen and CA-19-9 levels were within normal limits. Routine preoperative laboratory studies revealed that only fibrinogen was elevated (474 mg/dL). Preoperative stored blood was examined for hormone levels: estradiol was 14.7 pg/mL, follicle stimulating hormone (FSH) was 66 mIU/mL, luteinizing hormone (LH) was 39.6 mIU/mL, and anti-Müllerian hormone (AMH) was <0.16 ng/mL.

During the operation, we found a 14 × 14 × 10 cm smooth tumor attached to an average sized right ovary with 720° of torsion. The uterus, left ovary, bilateral fallopian tubes, and vermiform appendix appeared normal. Bilateral salpingo-oophorectomy, total hysterectomy, pelvic lymph node dissection, and para-aortic lymph node biopsy were all performed.

The external surface of ovarian tumor was smooth, and the cut surface was gray–white with a large cyst.

Microscopically, the ovarian tumor was a monolocular large cystic tumor with a local solid component in the cyst wall. The solid component was composed of hyperplastic stromal cells with edema appearing as scattered nests or gland-like sex-cord elements (Fig. 2). Stromal cells and the cells composed of sex-cord elements included inhibin-α and calretinin positive cells. The sex-cord component accounted for less than 10% of the tumor. The tumor had small cysts filled with mucus without destructive stromal invasion. The cells that composed the cyst wall were positive for cytokeratin (CK) 20 and negative for CK7 (Fig. 3). Sections from the uterine endometrium showed features of moderately differentiated endometrioid adenocarcinoma (International

* Corresponding author. Tel.: +81 93 603 1611; fax: +81 93 691 9337.
E-mail address: uedataeko@med.uoeh-u.ac.jp (T. Ueda).

http://dx.doi.org/10.1016/j.gore.2014.08.003

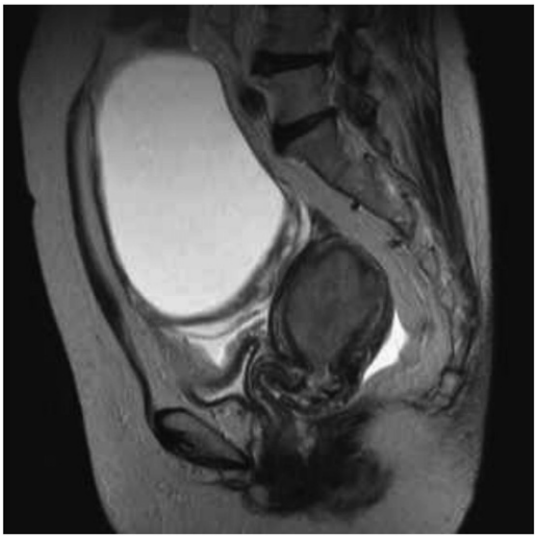

Fig. 1. T2-weighted magnetic resonance imaging of the pelvic cavity revealed a unilocular cystic mass without a solid component in the domain of the right adnexa. Endometrial thickening with defect of the junctional zone was observed.

Federation of Gynaecology and Obstetrics [FIGO] Grade 2) with superficial myometrial invasion. Lymph node metastases were not found.

After the operation, upper and lower gastrointestinal tract endoscopy revealed no specific abnormalities and her estradiol levels decreased to <5 pg/mL.

Discussion

We searched the literature using the following databases: MedLine and Web of Science. Each database was searched from its inception date to June 2014 using "minor sex-cord elements" "mucinous" and "ovary" as keywords. We found only one previous report of a mucinous cystadenoma coexisting with a stromal tumor with minor sex-cord elements and proliferation of stromal cells existing as nodule of a cystic tumor with smooth walls (Yang et al., 2001). In the present case, the point of difference was the form of the stroma with sex-cord elements: our case had diffusely proliferating stroma enclosing a large mucinous cystadenoma instead of forming a nodule as in the previous case.

In this case, the solid and hollow tubule-like sex-cord structures, more specifically the Sertoli cell elements, were widespread in the stroma. Immunohistochemistry supported the theory that the solid and hollow tubules were representative of true sex-cord differentiation; tubule cells were positive for calretinin and inhibin-α, the two markers most commonly used for the diagnosis of sex-cord elements (Rabban and Zaloudek, 2013; McCluggage, 2001).

Young et al. reported 36 cases of Sertoli–Leydig cell tumors that contained heterologous elements in the form of gastrointestinal epithelium. All of the 36 cases contained solid areas, unlike the present case that contained monolocular cysts without an obvious solid component (Young et al., 1982). In addition, one case of heterologous granulosa cell tumor with mucinous epithelial tumor has been previously reported (McKenna et al., 2005). These two studies reported that all cases formed nodular sex-cord stromal tumors separately from the heterologous epithelial tumor, which is similar to the case with minor sex-cord elements previously reported by Yang, but dissimilar to our case (Yang et al., 2001). We speculate that the appearance of sex-cord elements is

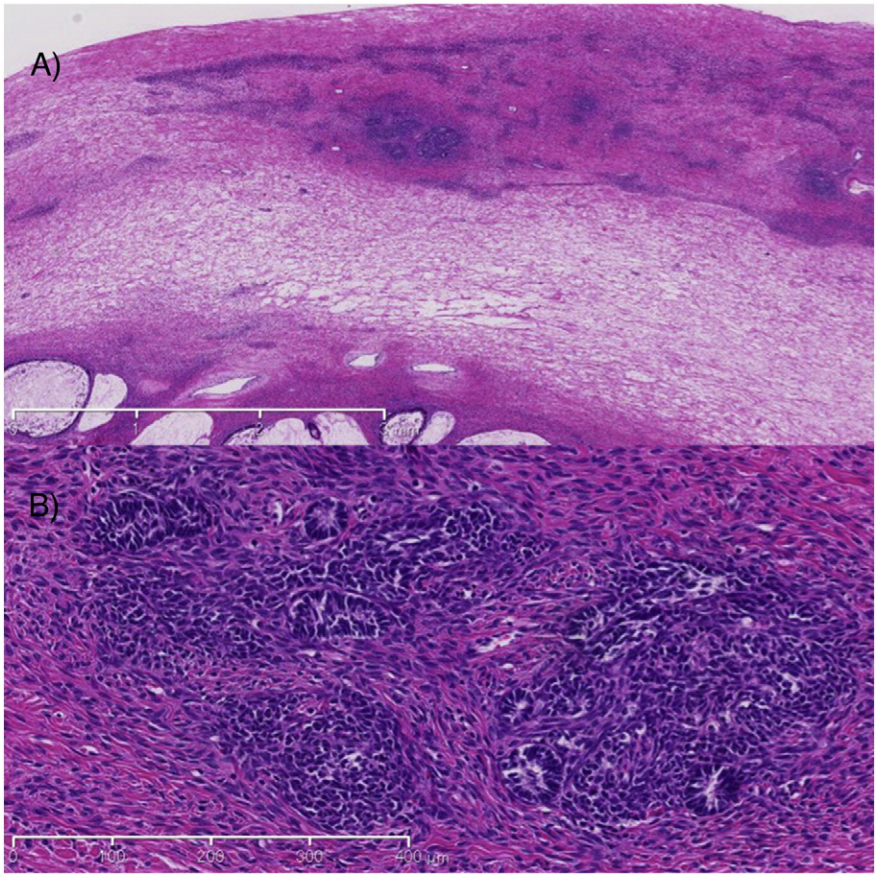

Fig. 2. Histopathological findings of the right ovarian tumor. A: The cyst is lined by a single row of uniform mucin-filled columnar cells with edematous stroma. B: The cyst wall shows a proliferation of stromal spindle cells with a small amount of gland-like structures.

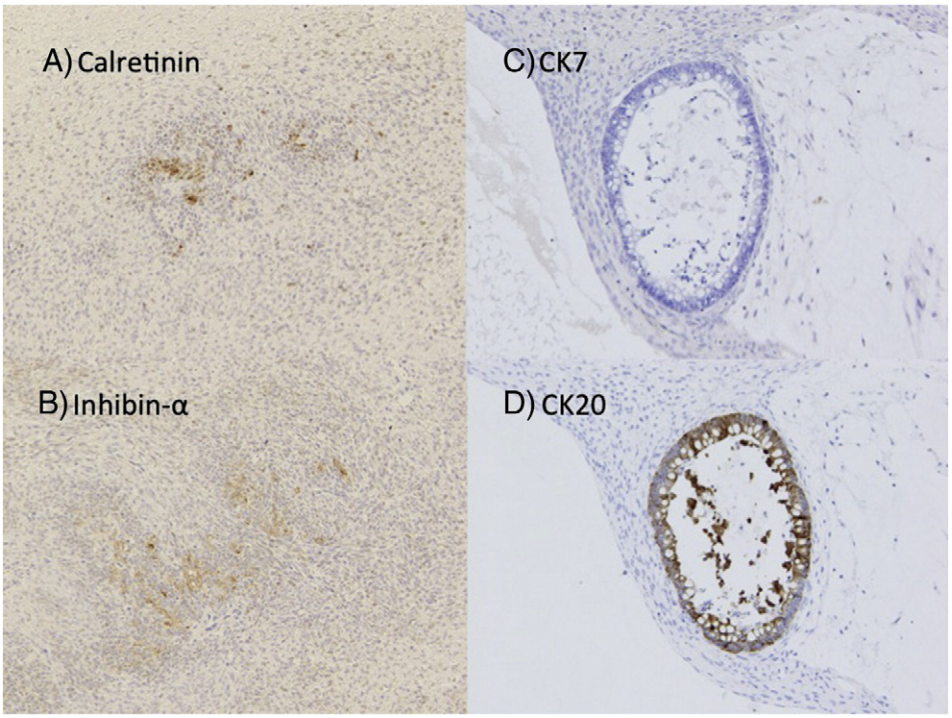

Fig. 3. Immunohistochemical findings of the right ovarian tumor. Cells of the gland-like structure and stromal cells show immunoreactivity for calretinin (A) and inhibin-α (B). Cells lining the cyst wall show strong immunoreactivity for cytokeratin 20 (D), but were negative for cytokeratin 7 (C).

caused by nonneoplastic reactive changes rather than neoplastic changes because the stromal cells under the mucinous epithelium were also comparatively numerous positive for calretinin and inhibin-α. This conjecture stems from a case reported by Dillon et al. in which a heterologous ovarian serous cystadenofibroma had stromal sex-cord elements (Dillon et al., 2006).

Colorectal adenocarcinoma, the most common tumor that metastasizes to the ovary, is often difficult to distinguish from primary ovarian mucinous adenocarcinoma. Immunohistochemistry can be useful for this diagnosis; currently, CK7/CK20 is considered the standard panel for differentiation. Shin et al. reported that metastatic colorectal adenocarcinomas, in contrast to primary ovarian mucinous adenocarcinomas, were often negative for CK7 (82.9% versus 9.1%) and diffusely positive for CK20 (65.9% versus 9.1%) (Shin et al., 2010). In our case, immunohistochemical findings suggested that the mucinous epithelium was an intestinal type in spite of the absence of macroscopic colorectum findings, including the appendix in the operational view. Since we didn't do the appendectomy and pathological examination of appendix, we are not ready to consider the tumor genesis.

Young and Scully reported that two of seven ovarian stromal tumor cases with minor sex-cord elements had well-differentiated uterine endometrial cancer and one of these cases exhibited endometrial cystic hyperplasia. Furthermore, sex-cord elements might be estrogenic in half of the cases (Young and Scully, 1983). In our case, the uterine endometrium showed features of moderately differentiated endometrioid adenocarcinoma, which was perhaps secondary to estrogenic activity of the sex-cord elements. Estradiol was not highly elevated, but this might be the result of hormonopoiesis of the ovarian tumor as suggested by supporting evidence, such as menopause onset 12 years prior and that estradiol levels decreased following removal of the tumor. Recently, serum AMH was reported as a highly sensitive marker for granulosa cell tumor; however, AMH was not elevated in the present case (Long et al., 2000).

Conflict of interest statement

We declare that we have no conflict of interest.

References

Dillon, K., Boyde, A., Murphy, J.K., 2006. Case report. Ovarian serous cystadenofibroma with stromal sex cord elements: report of a unique case. Int. J. Gynecol. Pathol. 25, 336–339.

Kumar, S., Mathur, S., Singh, L., et al., 2013. Ovarian stromal tumor with minor sex cord elements with coexistent endometrial carcinoma. Indian J. Med. Paediatr. Oncol. 34, 44–46.

Lee, H.Y., Ahmed, Q., 2003. Fibrosarcoma of the ovary arising a fibrothecomatous tumor with minor sex cord elements. A case report and review of the literature. Arch. Pathol. Lab. Med. 127, 81–84.

Long, W.Q., Ranchin, V., Rey, R., et al., 2000. Detection of minimal levels of serum anti-Müllerian hormone during follow-up of patients with ovarian granulosa cell tumor by means of highly sensitive enzyme-linked immunosorbent assay. J. Clin. Endocrinol. Metab. 85, 540–544.

McCluggage, W.G., 2001. Value of inhibin staining in gynecological pathology. Int. J. Gynecol. Pathol. 20 (1), 79–85.

McKenna, M., Kenny, B., McCluggage, W.G., et al., 2005. Combined adult granulosa cell tumor and mucinous cystadenoma of the ovary: granulosa cell tumor with heterologous mucinous elements. Int. J. Gynecol. Pathol. 24, 224–227.

Rabban, J.T., Zaloudek, C.J., 2013. A practical approach to immunohistochemical diagnosis of ovarian germ cell tumors and sex cord-stromal tumours. Histopathology 62, 71–88.

Shin, J.H., Bae, J.H., Lee, K.Y., et al., 2010. CK7, CK20, CDX2 and MUC2 immunohistochemical staining used to distinguish metastatic colorectal carcinoma involving ovary from primary ovarian mucinous adenocarcinoma. Jpn. J. Clin. Oncol. 40 (3), 208–213.

Yang, S.W., Cho, M.Y., Kim, K.R., et al., 2001. Mucinous cystadenoma coexisting with stromal tumor with minor sex-cord elements of the ovary: a case report. J. Korean Med. Sci. 16, 237–240.

Young, R.H., Scully, R.E., 1983. Ovarian stromal tumors with minor sex cord elements: a report of seven cases. Int. J. Gynecol. Pathol. 2, 227–234.

Young, R.H., Prat, J., Scully, R.E., 1982. Ovarian Sertoli–Leydig cell tumor with heterologous elements. I Gastrointestinal epithelium and carcinoid: a clinicopathologic analysis of thirty-six cases. Cancer 50, 2448–2456.