Extraovarian Granulosa Cell Tumor

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A 54-year-old woman was admitted to our hospital complaining of postcoital bleeding. Sonography of the abdomen showed a 8.2 × 8.9 cm-sized solid heterogeneous mass occupying the cul-de-sac, which appeared to be in no way connected with the ovary. On exploratory laparotomy, the tumor mass protruded from the posteriora retroperitoneum of the pelvic cavity and severely replaced the uterus and adnexa with the outer surface being grossly intact. It grossly measured 10 cm in maximal diameter. The histologic features closely resembled those of ovarian granulosa cell tumor. The primary extraovarian granulosa cell tumor is extremely rare such that in the English literature only 7 cases have been reported to date. Of those granulosa cell tumors are especially rare and only two cases have been reported to arise from retroperitoneum.

We herein present a case of retroperitoneal granulosa cell tumor with special regard to differential diagnosis from other solid tumors with similar histology.

Key Words: Extraovarian granulosa cell tumor, retroperitoneum

INTRODUCTION

Granulosa-theca cell tumors embrace ovarian neoplasms composed of varying proportions of granulosa and theca cell differentiation. These tumors are composed almost entirely of granulosa cells or a mixture of granulosa and theca cells.

With very few exceptions, granulosa cell tumors are usually found in the ovary. In the literature, several cases of extraovarian granulosa cell tumors were reported.¹⁷ Concerning extraovarian granulosa cell tumor, especially granulosa cell tumor of retroperitoneum, only two cases have previously been reported in the literature.¹⁷ We present a third case and discuss its preoperative diagnostic difficulty and clinical significance.

CASE REPORT

A 54-year-old woman, gravida 3 para 3, was referred to Department of Obstetrics and Gynecology from a local clinic because of a postcoital bleeding. She had ceased menstruating four years ago. Nine years previously she had received right oophorectomy. The ovary excised was histologically examined as non-neoplastic cyst in a commercial pathologic laboratory. The physical examination disclosed a large lower abdominal mass. Sonography of the abdomen showed some ascites and a 8.9 × 8.2 cm sized heterogeneous mass in cul-de-sac. Computerized tomography (CT) revealed a 7.5 × 8.8 cm sized, large solid lobulated mass between urinary bladder and uterus with evidence of multiple necrosis. The mass displaced rectum and sigmoid colon posterolaterally (Fig. 1). Cervical cytology was within normal limit.

The results of serological tumor markers of CEA and CA19-9 were within normal range, but CA125 was increased to 83.08 U/ml. The other laboratory results were unremarkable. With the presumptive diagnosis of ovarian malignancy, the patient underwent exploratory laparotomy. An exploratory laparotomy showed a large bulging solid tumor to protrude from the retroperitoneum into the pelvic cavity and it was covered by peri-
toneum, giving the impression of a sarcoma of retroperitoneum origin. Externally, it was grayish red and smooth with a row of adipose and fibrous tissue tags along one surface. The left ovary, both fallopian tubes and uterus were grossly unremarkable except for partial adhesion of the right fallopian tube and the posterior surface of uterus to the tumor. The sigmoid colon was displaced posteriorly and leftward by the tumor. Hysterectomy with left salpingo- oophorectomy were followed by complete extirpation of the retroperitoneal tumor with a little difficulty caused by focal adhesion to mesocolon and peritoneum.

Pathology

The tumor was ovoid, and fully encapsulated. The cut surface was composed of pale yellowish grey soft tissue with foci of necrosis.

Microscopic examination revealed small, cuboidal to polygonal neoplastic cells growing as anastomosing cords, sheets, or strands only granulosa cells growing predominantly in insular, trabecular and focally microfollicular patterns (Fig. 2). The microfollicular pattern was characterized by the occasional presence of small, distinctive, gland-like structures filled with an acidophilic material recalling immature follicles (Call-Exner bodies) (Fig. 3).

The microfollicles were separated by well-differentiated granulosa cells that contain scanty cytoplasm and pale, oval or angular nuclei with longitudinal groove. These cells were arranged haphazardly in relation to one another and were supported by a delicate connective tissue containing numerous capillary blood vessels. The tumor cells were immunoreactive for inhibin and were focally weakly reactive for vimentin. The tumor cells were negative for NSE, synaptophysin, and EMA. There was no evidence that the neoplastic granulosa cells had undergone luteinization. The mesenteric nodules also showed similar histopathologic features indicating metastasis from retroperitoneal tumor mass.
Ultrastructural findings

The tumor cells show high nuclear-cytoplasmic ratio with occasional deep nuclear indentations. They are tightly adhered to one another with desmosomes. The cytoplasm contains relatively few organelle with only a small number of mitochondria, rough endoplasmic reticulum, and free ribosomes. Occasional lipid droplets are also present but glycogen particles are scant. The nuclei with or without indentations reveal evenly distributed chromatin with rather prominent single nucleoli. Basal lamina or Call-Exner bodies are not noted. These findings are in part consistent with that of granulosa cell tumor. The most important and diagnostic findings, Call-Exner body with basal lamina, is not present, however. These results could be considered as supportive but not confirmative evidence in the diagnosis of this unusual tumor of retroperitoneum as an extraovarian granulosa cell tumor.

DISCUSSION

Adult granulosa cell tumors accounts for approximately 1-2% of all ovarian tumors. They occur more often in menopausal and postmenopausal than premenopausal women with a peak age incidence between 50 and 55 years, but they may be seen at any age. They are the most common ovarian tumors with estrogenic manifestation. Granulosa-theca cell tumors have clinical importance for two reasons: (1) their potential elaboration of large amounts of estrogen and (2) the small but distinct hazard of malignancy in the granulosa cell forms. In adult women, they may be associated with endometrial hyperplasia, cystic disease of the breast, endometrial carcinoma. It is difficult, from the histologic evaluation of granulosa cell tumors, to predict their biologic behavior. The estimates of clinical malignancy (recurrence, extension) range from 5% to 25%. In general, malignant tumors pursue an indolent course in which local recurrence may be amenable to surgical therapy. Recurrence within the pelvis and abdomen may appear many years (10 to 20) after removal of the original tumor. Distant metastasis are rare, but have been reported in many sites. In one series the mean time from diagnosis to death was 10.5 years and the median time was 7.5 years. No clinical follow up studies of extraovarian granulosa cell tumor have been undertaken, and such a follow up of this extraovarian granulosa cell tumor is warranted.

In the literature, 7 cases of extraovarian granulosa cell tumor have been reported to date. Four of them was originated from broad ligament and only two were retroperitoneal origin. The remainder was adrenal origin. The present case represents a very rare extraovarian granulosa cell tumor arising in the retroperitoneum. Microscopic and ultrastructural features of the tumor cells were similar to those reported in granulosa cell tumor cells. But, no biologic assay for estrogen content of the patient’s urine or blood, nor of the tumor tissue was attempted, because the nature of the tumor was not suspected until it was removed.

The histogenetic origin of extraovarian sex cord-stromal tumors is reviewed through the many literature. It is considered to be ectopic gonadal stromal tissue. Sex-cord stroma, specialized mesenchymal tissue of the gonads, is induced after the primordial germ cells migrate to the gonadal ridge. Rare but definite demonstration of supernumerary ovaries has provided evidence of the formation of ovarian sex cord stroma at extragonadal sites. In recent years, several investigators have claimed that the sex cords may originate from the mesonephros. A dualistic theory of both the celomic epithelium and the mesonephros in the origin of the pregranulosa cells has also been proposed. Accordingly, the mesonephros itself or at least its functional influence seems to be necessary for creating the sex cords. This is consistent with gonad formation being limited to the gonadal ridge and may explain why the sites of the origin of extraovarian sex cord-stromal tumors or supernumerary ovaries are limited to the broad ligament, retroperitoneum, and adrenal gland, all of which differentiate close to the mesonephros and mesonephric duct.

Several other histologically similar tumors, including undifferentiated carcinoma, small cell or neuroendocrine carcinoma, endometrial stromal sarcoma (especially with sex cord-like differentia-
tion), thecoma, carcinoid, malignant melanoma and intrabdominal desmoplastic small cell tumor can be difficult to distinguish from granulosa cell tumors. The use of a reticulin stain and antibodies to inhibin, S-100, synaptophysin, chromogranin, pan-keratin, estrogen receptors, and progesterone receptors determines a pattern specific for granulosa cell tumor, thereby confirming the diagnosis of granulosa cell tumor and excluding alternative diagnoses. Especially, a positive immunoreactivity for inhibin is useful in differential diagnosis of granulosa cell tumor.

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REFERENCES