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Cytologic features of ascitic metastasis from a granulosa cell tumor

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Abstract : Previous history of the patient is sometimes very helpful in cytologic diagnosis. We report a case of peritoneal metastasis of an adult-type granulosa cell tumor (AGCT) of the ovary, forming ascitic fluid. The patient was a 58-year-old woman who was diagnosed with a granulosa cell tumor of the ovary 13 years previously. She admitted to the hospital because of 3 days of lower abdominal pain. Several masses were in the lower abdominal cavity as well as culdesac, measuring 7.0 cm in maximum length in computerized tomography (CT) scan. Aspiration cytology of ascitic fluid demonstrated irregular sheets, loose aggregates or tight clusters of small, relatively uniform neoplastic cells with round or oval nuclei and scant cytoplasm. Nuclear grooves and indentations were noted in a small number of cells. Tumor cells arranged in follicular pattern mimicking Call-Exner bodies were identified. The cytopathologic diagnosis of the ascitic fluid was made to be a metastatic granulosa cell tumor. Although the granulosa cell tumor is the most common malignant sexcord stromal tumor, practically, they comprise only 2-3% of all ovarian tumors. Because of rarity of the disease and presentation in the metastatic sites, the diagnosis of AGCT may not be easy. An understanding the quiet characteristic cytological features, such as monotonous cells, microfollicular pattern, and nuclear grooving, is necessary to avoid false diagnoses of a recurrent neoplastic lesion by aspiration cytology.

Key Words : ascite, aspiration, cytology, granulosa cell tumor, ovary

Introduction

Previous personal history of a patient is frequently very helpful in cytologic diagnosis.

We report a case of the peritoneal metastasis from the ovarian adult-type

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granulosa cell tumor, which forms fluid collection in the abdominal cavity. The patient was a 58-year-old woman who presented with gradually increase of the abdominal girth and left lower abdominal pain for three days.

The abdominopelvic computed tomography (CT) scan revealed multiple intrapelvic masses in the cull de sac and left lower pelvic cavity, which measures 7.0 cm in the largest length. Explo-laparotomy was performed and obtained ascitic fluid for cytology. Cytologic features of the ascitic fluid demonstrated irregular sheets, loose aggregates or tight clusters consisting of small, relatively uniform neoplastic cells with round or oval nuclei and scant cytoplasms.

A review of the earlier microscopic sections, when she presented with a left ovarian mass in 1996, confirmed the presence of an adult-type granulosa cell tumor. The current intrapelvic masses in the cull de sac and left lower peritoneum had similar histologic findings to the previously resected GCT (granulosa cell tumor) in the left ovary.

Although cytologic diagnosis of a metastatic adult-type granulose cell tumor have been described in a limited cases, the careful recognition of characteristics in cytologic preparation should, together with the clinical findings, lead to a correct cytologic diagnosis of AGCT.

Case Report

The patient was a 58-year-old woman who presented with gradually increase of the abdominal girth and left lower abdominal pain for three days. She had a history of left oophorectomy because of GCT (granulosa cell tumor) in 1996 when she was 45 years old. The current clinical event was the detection of multiple intrapelvic masses in the cull de sac and left lower quadrant of pelvic cavity, which measures 7.0 cm in the largest diameter by CT scan (Fig. 1).

Debulking operation with obtaining ascitic fluids was performed. The microscopic findings of ascites showed numerous irregular sheets, loose aggregates or tight clusters consisting of small, relatively monomorphic cells with round or oval, coffee bean-shaped nuclei and small nucleoli. The tumor cells arranged with follicular pattern mimicking Call-Exner bodies were identified. Admixed among these cells were macrophages with finely vacuolated cytoplasm as well as hemosiderin-laden macrophages (Fig. 2). A review of the previous microscopic sections confirmed the presence of an adult-type granulose cell tumor when she presented left ovarian mass in 1996. The tumor in the left ovary, resected in 1996, had a microfollicular, macrofollicular, trabecular, and solid architectures, composed of cells relatively with the presence of folds or grooves in the nuclei, referring to as "coffee-bean" appearance. The current intrapelvic masses in the cull de sac and left lower quadrant of pelvic cavity had similar histologic findings to the previously resected GCT in left ovary (Fig. 3). Immunohisto-chemical stains revealed that the tumor cells were strongly and diffusely positive for vimentin and CD99, and focally positive for inhibin. However, they were negative for the epithelial markers, cytokeratin, epithelial membrane antigen, CAM5.2, and calretinin.

Cytologic diagnosis of the ascitic fluid was reported as metastatic granulosa cell tumor.

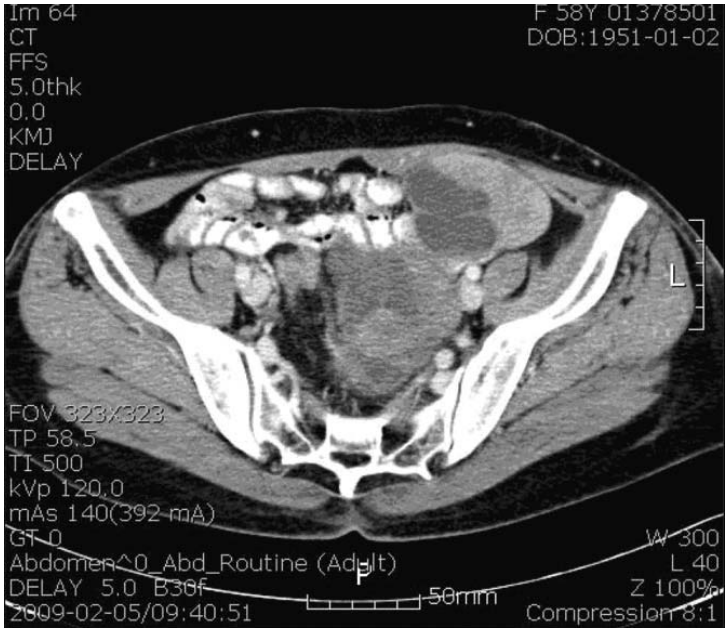

Fig. 1. Pelvic CT scans showed multiple complex masses in the cul de sac and left lower quadrant of pelvic cavity.

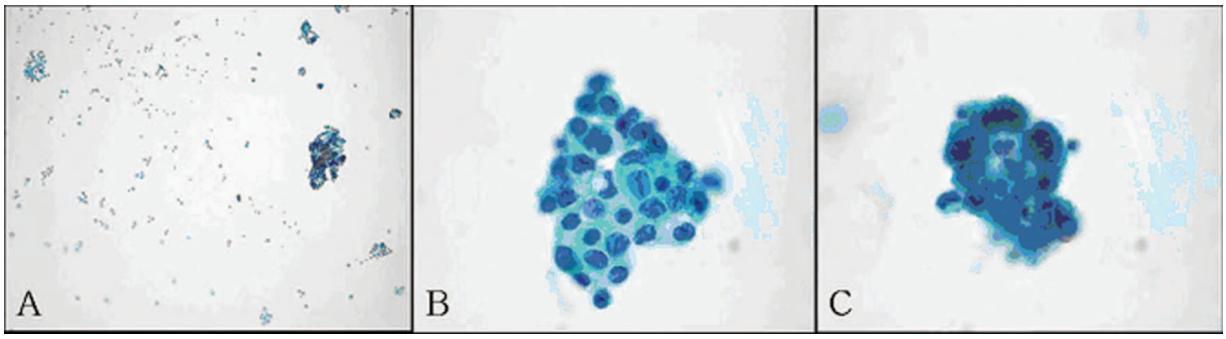

Fig. 2. Cytologic features represented numerous cell clusters composed of relatively uniform cells with nuclear grooves and indentations.(A x100, B x400) Microfollicular pattern (Call-Exner bodies) are identified.(C x400) (Papanicolau stain).

Pathologic diagnosis of the current intrapelvic masses was confirmed as recurrent granulosa cell tumor.

Discussion

Adult-type granulosa cell tumors (AGCTs) account for 1-2% of all ovarian neoplasms and approximate 5-8% of primary ovarian malignancies [1]. GCTs are derived from the granulosa cell, a hormonally active part of the ovarian stroma that is responsible for estradiol production, therefore, are referred to as an ovarian sex cord-stromal tumor [2]. GCTs can occur at any age but most commonly presents during the perimenopausal or early postmenopausal

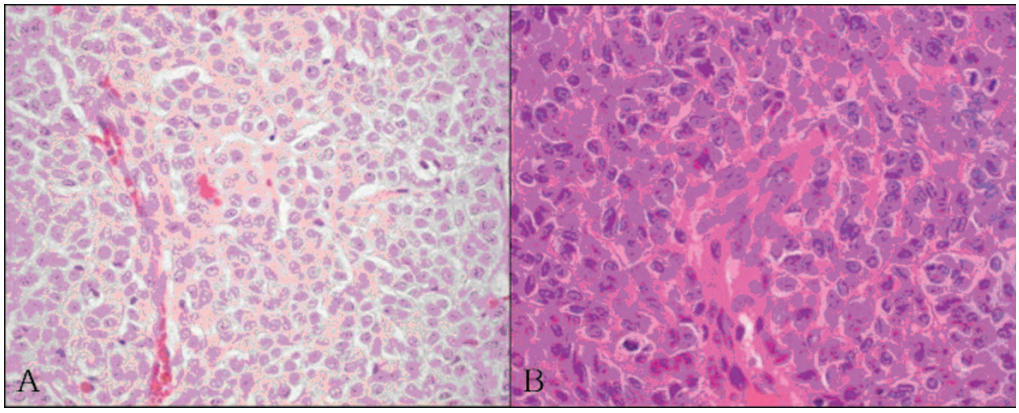

Fig. 3. Histopathologic features showed a microfollicular, macrofollicular, trabecular, and solid architectures, composed of relatively uniform cells with the presence of folds or grooves in the nuclei, referring to as "coffee-bean" appearance, which presented with a left ovarian mass in ovarian mass in 1996.(A x200) The current intrapelvic masses in the cull de sac had similar histologic findings.(B x200) (H&E stain).

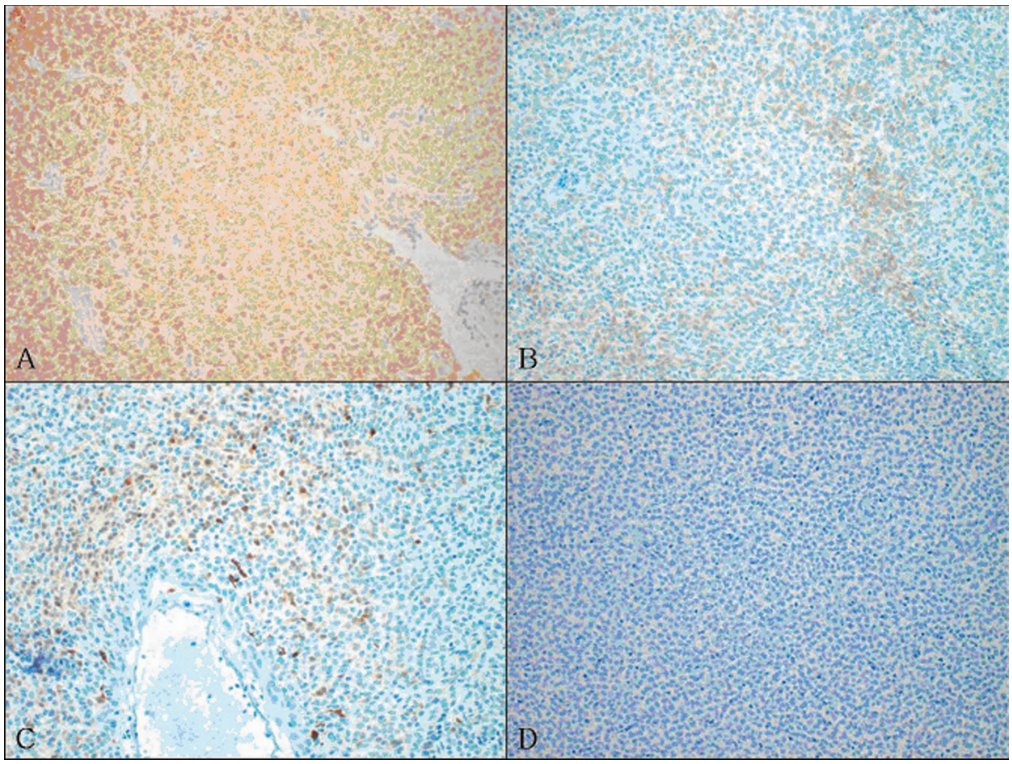

Fig. 4. Immunohistochemistry of ascitic fluid showed positive for vimentin(A x100) and inhibin(B x100), whereas negative for calretinin(C x100) and CAM5.2 (D x100).

period, with a median age of diagnosis between 50 and 54 year in most series [2]. These tumors are regarded as malignancies, although a low grade type in most GCTs (70-80%) [2,3].

Clinically and morphologically, the GCTs

can be subdivided as the more frequent adult type (AGCTs) and the less frequent juvenile type (juvenile GCT). Juvenile GCT represents only 5% of this tumor type and usually occurs in prepubertal girls and young women [2]. AGCTs are hormonally active neoplasms that secrete high level of estrogen, which can lead to abnormal uterine bleeding (menorrhagia or metrorrhagia), endometrial hyperplasia (50-60%) and ultimately adenocarcinoma (5-10%) [2].

Histologically, there can be a variety of growth patterns in AGCT, including microfollicular, macrofollicular, trabecular, insular, solid, gyriform, and diffuse [2,4].

The tumor cells were relatively monomorphic with nuclear grooves. The distinct nuclear appearance is one of the hallmark features of ovarian AGCT [2]. Call-Exner bodies have been demonstrated in 30-60% of AGCT.

There are relatively few studies to date reporting the findings of cytologic features in the diagnosis of GCTs from peritoneal metastasis. The quiet characteristic cytologic features represent monotonous cells, microfollicular pattern, and nuclear grooves [1,2,5,6]. Also bright purple round bodies with fibrillary structure referred as Call-Exner bodies may be identified. Differential diagnoses include Brenner tumor, sex cord tumor with annular tubules (SCTAT), poorly differentiated carcinoma, papillary transitional cell carcinomas (PTCC), and mesothelial hyperplasia [2].

Proliferating Brenner tumor and SCTAT are two other primary ovarian tumors that are characterized by the presence of prominent nuclear grooves which are indistinguishable in the basis of cytology alone. Proliferating Brenner tumor and SCTAT have small nucleoli, which can be helpful in differentiating from AGCT. Immunoreactivity for inhibin and CD99 of AGCT can be useful in the differential diagnosis [2,6]. Occasionally, AGCT with a diffuse pattern can be mistaken for a poorly differentiated carcinoma. The nuclear appearance can be very helpful for differentiating the two entities. AGCT nuclei are normally uniform and pale and are often grooved, whereas the nuclei of un-differentiated carcinomas are often hyper-chromatic, without grooves, and pleomorphism. Nuclear atypia and multiple mitotic figures are less common in AGCT [2,4]. The differential diagnoses to PTCC and mesothelial hyperplasia are made of cafeful examination and immunohistochemistry.

Patients with GCTs require longterm clinical followup because of the known, yet unpredictable, recurring or metastasizing behaviors many years after a diseasefree interval even in those with low clilnical stages of the tumor at diagnosis [1-3,5].

To conclude, although the granulosa cell tumors are the most common malignant sexcord stromal tumor, practically, they comprise only 2-3% of all ovarian tumors. Because of rarity of the disease and presentation in the metastatic sites, the diagnosis of AGCT may not be easy.

We observed that the cytologic features of GCTs is fairly impressive and include monotonous cells, microfollicular pattern, nuclear grooves and Call-Exner bodies. Understanding the cytological features and obtaining the clinical information are necessary to avoid false diagnoses of a recurrent neoplastic lesion by aspiration cytology.

References

1. Stewart CJ, Brennan BA, Crook ML, Doherty DA, Hammond IG, Leuverink E, *et al*. Comparison of proliferation indices in primary adult-type granulosa cell tumors of the ovary and their corresponding metastases: an analysis of 14 cases. *Int J Gynecol Pathol* 2009;**28**:423-31.
2. Ali S, Gattuso P, Howard A, Mosunjac MB, Siddiqui MT. Adult granulosa cell tumor of the ovary: fine-needle-aspiration cytology of 10 cases and review of literature. *Diagn Cytopathol* 2008;**36**:297-302.
3. Ylagan LR, Middleton WD, Dehner LP. Fine-needle aspiration cytology of recurrent granulosa cell tumor: case report with differential diagnosis and immunocytochemistry. *Diagn Cytopathol* 2002;**27**:38-41.
4. Shimizu K, Yamada T, Ueda Y, Yamaguchi T, Masawa N, Hasegawa T. Cytologic features of ovarian granulosa cell tumor metastatic to the lung. A case report. *Acta Cytol* 1999;**43**:1137-41.
5. Lal A, Bourtsos EP, Nayar R, DeFrias DV. Cytologic features of granulosa cell tumors in fluids and fine needle aspiration specimens. *Acta Cytol* 2004;**48**:315-20.
6. McCluggage WG, Young RH. Non-neoplastic granulosa cells within ovarian vascular channels: a rare potential diagnostic pitfall. *J Clin Pathol* 2004;**57**:151-4.