SEX CORD - STROMAL TUMOR: OVARIAN ADULT TYPE GRANULOSA CELL TUMOR - A CASE REPORT.

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Abstract

Granulosa cell tumors (GCT) are low grade indolent malignant neoplasm originating from granulosa cells of the ovarian follicles, accounting for approximately 10% of all sex cord stromal tumors of the ovary (1). Among the two distinct clinical and histological subtype, adult granulosa cell tumors (AGCT) are more common, 95% than the juvenile counterpart 5%. Adult GCT account for approximately 1% of all ovarian tumors and frequently occur in postmenopausal women with peak incidence between 50 to 55 years. AGCTs have low malignancy potential and rarely metastasize 5–30 years after the initial diagnosis.

GCTs usually present with features of hyperestrogenism, which symptoms depend on the woman′s menstrual status (2). The most common symptoms include early puberty for affected young girls, an increase in abdomen size or irregularities of menstrual cycles in premenopausal women, and abnormal uterine bleeding in postmenopausal women. They are often diagnosed on the histopathological examination following surgery. The exact cause of granulosa cell tumors is unknown.

Key words: *Adult-type granulosa cell tumor; ovarian cancer; ex cord-stromal tumor; prognostic factors*

Introduction

GCTs are a malignant entity originating from sex cord stromal cells and accounts for 2–5% of all ovarian cancers (1). They were first described by Rokintansky in 1855. The classification used is separating them in adult or juvenile pattern by clinical presentation and histologic characteristics, and Adult GCT accounts for 95% of all cases. The adult type occurs in peri- (4-45 years) and post-menopausal women (>45 years) with peak incidence 50-55 years. Juvenile GCTs are rare neoplasm comprising 5% of all GCTs occurring in the prepubertal age group (2). The clinical manifestations are mainly endocrine and are related to oestrogen hypersecretion resulting in endometrial hyperplasia, leiomyomas and irregular menstrual abnormalities. Small group may present with infertility due to unregulated inhibin and virilizing features due to androgen production.

Case presentation

We present a case of 44- year female admitted with severe abdominal pain to the Obstetrics and Gynecology Department. The ultrasonogram investigation revealed left adnexal cystic mass. The right ovary was normal. Abdominal hysterectomy and bilateral salpingo-opharectomy with preservation of the cervix was performed.

Material and Methods: Histological analysis of the tissues was performed using automatic tissue processor „DIAPATH EN ISO 9001:2000" and 4-5 μm formalin-fixed paraffin-embedded tissue sections underwent routine staining with hematoxylin-eosin (HE) to determine the presence of individual histological features.

Gross description: A solid tumor formation with a diameter of 6 cm, with a different density, cystic areas and whitish-yellow colour was found in the left ovary. Right ovary was without

pathological changes. Uterine body – endometrium was polypoid and thickened with a thickness of 2 cm, and a subserous leiomyoma with a diameter of 3 cm was also found.

Microscopical examination of the ovarian mass revealed diffuse and gyriform pattern of tumor cells with fine chromatine, round to oval nuclei with single, small nucleus. Some nuclei, showed longitudinal grooves, known as coffee-bean nuclei (Figures 1-3). Mitotic activity is not brisk (< 3/10 high power fields). The histological observation found leiomyoma with no increase of the mitotic activity or atypia (Figure 4) and polypoid hyperplasia with stromal pseudo decidualization (Figure 5). In some areas were detected endometrial glands with hypersecreting features, like Arias-Stella change, some showing cytological atypia and squamous metaplasia with suspection for carcinoma "in situ" (Figure 6-8). The morphological features of the ovarian tumor and the related hormonal induced changes of the endo- and myometrium supported the final diagnosis of GCT – adult type.

Discussion

GCT accounts for 2% of all neoplasms of ovary and is the 2nd most common sex cord-stromal tumors after thecomas and fibromas. Adult-type granulosa cell tumor is a clinically unique type of ovarian cancer. These tumors originate from the stromal cells of the ovarian germ line. The majority of adult-type granulosa cell tumors are diagnosed at an early stage with an indolent prognosis (3). They account for most of the hormonally active ovarian neoplasms (4). GCT usually produce oestrogens and cause symptoms and signs of oestrogen excess, such as endometrial hyperplasia in 50% of cases and adenocarcinoma of the uterus in 5–15% of cases; mainly in perimenopausal and postmenopausal women (4). Literature search reveals excessive estrogenic stimulation leads on to endometrial hyperplasia in 25-50% and subsequent development of endometrial carcinoma in 5-13% of cases. In patients with this ovarian tumour the risk of breast cancer development secondary to exposure to high oestrogen is also increased (3). Some cases may present with acute abdomen due to rupture of tumour's cyst. Some chromosomal abnormalities have also been associated with GCT like trisomy 12 and monosomy 22 (5). Few tumor predisposition syndromes associated with GCT are Peutz Jeghers syndrome and Potters syndrome. Ollier disease and Maffucci disease are associated with juvenile GCT (2). In the case we present, we are not aware of any genetic abnormalities associated with the GCT.

On ultrasound, much like it was in the case we presented, they are seen as multi-cystic mass with variable solid component, none of which are diagnostic. The median mass for Adult GCT is 20cm (4-33). In our case it was 6 cm. Juvenile GCT average around 12.4 cm (5–26 cm).

Histologically, GCTs are typically characterized by Call-Exner bodies and coffee bean nuclei. On pathology, the solid and cystic masses had GCTs with macrofollicular and microfollicular patterns. The classic features of Adult type GCT on histological examination include Call-Exner bodies and "Coffee-bean" nuclei, along with a low mitotic rate. Call-Exner bodies are gland-like structures that appear similar to those of ovarian follicles. "Coffee-bean" nuclei are pale, round, and longitudinally grooved (6). The Call Exner bodies are seen in 30 % of cases (2). In the case we present the nuclear features were very prominent and easily distinguishable. We were also able to see the effects of the hyper-production of oestrogen - detected endometrial glands with hypersecreting features, like Arias-Stella change, some showing cytological atypia. In contrast, JGCTs have only a few typical findings. JGCTs have fewer Call-Exner bodies, and gland-like structures resembling ovarian follicles are irregular in size and shape (2,5-7).

It is rare for this unusual diagnosis to pose any difficulty, especially for an experienced pathologist. However, if this happens, especially in the poorly differentiated forms (about 39% of all Adult type GCT), immunohistochemistry (IHC) can help with the diagnosis. GCT is alpha inhibin and calretinin positive. These tumours on IHC are non-specifically positive for

CD99, CAM 5.2, AE1/AE3, CD10, S100, WT-1, smooth muscle actin and desmin. They are negative for CK7 and EMA (2). In our case, due to the easily recognizable pattern, no immunohistochemistry was needed.

The majority of patients are diagnosed in early stages of disease and overall prognosis is favourable. The initial treatment of choice is surgery, which is necessary for histological diagnosis, appropriate staging, and debulking. Postoperative treatment for patients who remained without disease includes radiotherapy, combination of chemotherapy and radiotherapy and other regiments very rarely. Patients with recurrent disease are seen very rarely mostly in patients with diffuse pattern and with significant atypia and mitoses (8).

Conclusion

Granulosa cell tumors of the ovary are a rare finding. They are the most common estrogenic ovarian tumors. Mainly affected of the excessive hormone stimulus is the uterine body, responding with simple endometrial hyperplasia that usually exhibits some degree of pre-cancerous atypia. The incidence of associated endometrial carcinomas is around 5%.

Therefore, there must be clinical suspicion of hormone depended endometrial pathology any time that a diagnosis of granulosa cell tumor is made.

The timely diagnose followed by surgical treatment results has a very good prognosis.

Conflict of interests

The authors state no conflict of interest.

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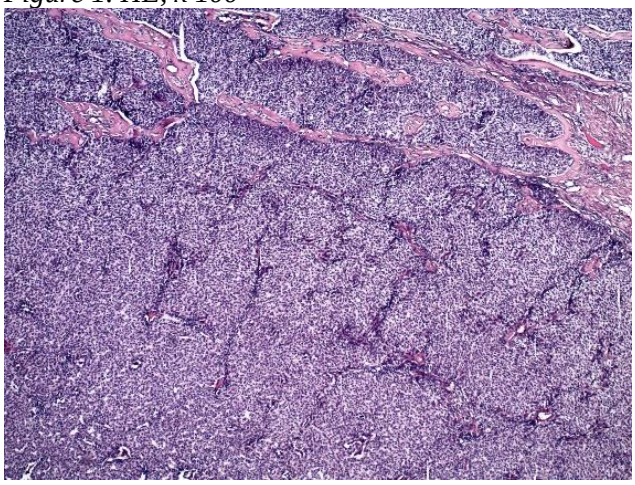
Legends to figures:

Figure 1. HE, x 100



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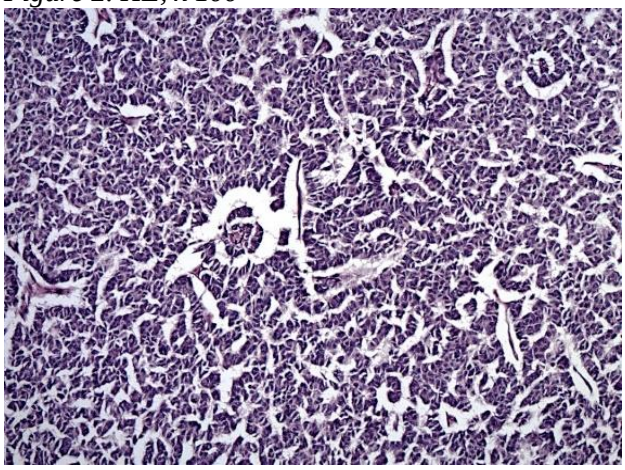

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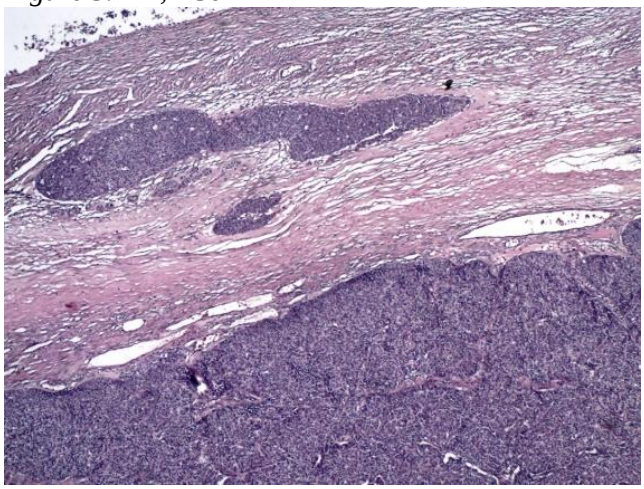

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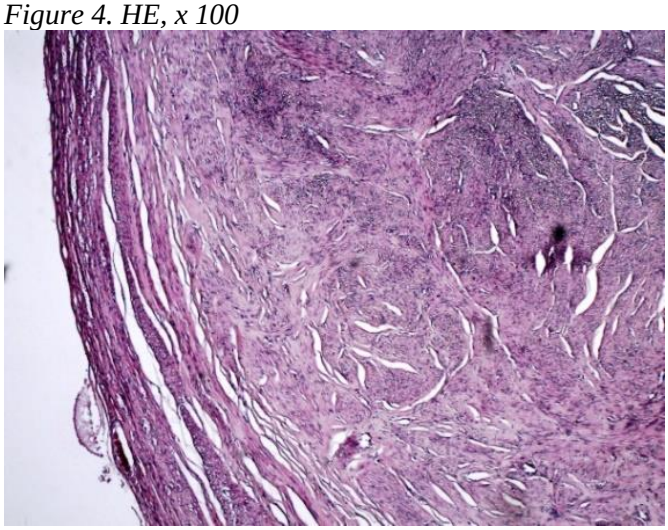

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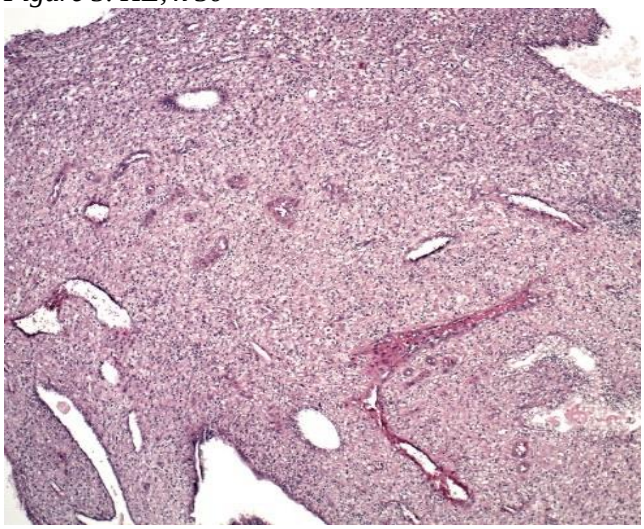

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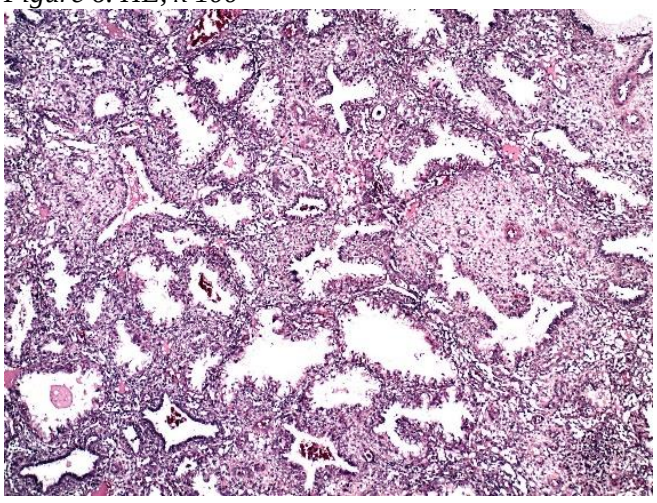

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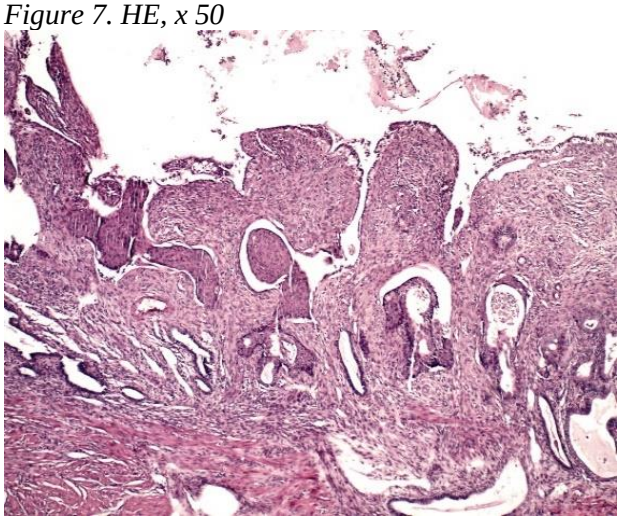

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