Bulletin of the *Transilvania* University of Braşov
Series VI: Medical Sciences • Vol. 13 (62) No. 1 – 2020
https://doi.org/10.31926/but.ms.2020.62.13.1.5

"COFFEE BEAN" NUCLEI IN A RARE CASE OF OVARIAN ADULT GRANULOSA CELL TUMOR

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Abstract: *Granulosa cell tumors represent only 1% of the total number of ovarian tumors. "Coffee bean" nuclei represent an extremely rare feature of these tumors. We presented the case of a 66 year-old patient that was hospitalized for abdominopelvic pain, lately to be diagnosticated with an Adult Granulosa Cell Tumor. The histopathological analysis revealed Call-Exner corpuscles and Coffee Bean" nuclei. Positive S100 marker was a particular finding in the immunohistochemical profile. Treatment strategy for this kind of cases should include surgery and adjuvant treatment and a strict follow-up of the patient for at least 5-10 years.*

Key words: *Coffee bean nuclei, adult granulosa cell tumor, ovary.*

1. Introduction

In 1855, Rokitansky described for the first time. Despite the fact that there is no common concept for the pathogenesis of these tumors, the majority of researchers in this field claim that they have a mesenchymal origin, due to the fact that they are composed of granulosa cells, theca cells and also fibroblasts in different stages of development [2].

Although the granulosa cell tumors only represent 1% of the total number of ovarian tumors [13], they represent the most common subtype of "ovarian sex-cord tumors" (70%) [8].

From the pathology point of view, there are two types of granulosa cell tumors identifiable: the adult type (AGCTs), most commonly occurring among older patients and the juvenile type (JGCTs)[1] which occurs, in 75% of the cases, prior the puberty period, due to high levels of estrogen. Their clinical features are also distinct; the juvenile ones cause hirsutism, amenorrhea, clitoral hyperplasia and acne and the adult ones cause endometrial hyperplasia and menstrual disorders. Due to the clinical presentation, the chances of making an early diagnosis are high [10].

2. Case report

A 66 year-old female patient has been admitted in the department of Obstetrics and Gynecology with severe pelvic-abdominal pain. Following the anamnesis, the general and gynecological clinical examinations, an ultrasound examination was performed, which revealed a tumoral

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mass occupying the right uterine adnexa in the pelvic-abdominal area of 90x60 mm.

Grossly, the right adnexa was described as composed of the Fallopian tube (60x15x15 mm) and the tumorally transformed ovary (90x17x40 mm) with its unaltered capsule. The cross-section of the ovary reveals a whiteish compact aspect.

The examination of the uterine body revealed an intramural nodular mass, with fasciculate appearance of 4 mm. No macroscopic pathological modifications have been discovered in the omentum.

Microscopically, we identified a tumor proliferation with a mixed architectural pattern. Tumor cells are arranged either diffusely, forming dense cell plaques, or with a follicular appearance forming Call-Exner corpuscles that inside have an eosinophilic material (figure 1) and in some places the tumor cells form micronodules and macronodules with diffuse arrangement or organized in island; separated by a fibrous stroma.

All of the tumor cells were described as round or oval, with reduced cytoplasm, elongated nuclei and in some places had the appearance of "Coffee bean" nuclei (figure 2). Mitosis was also identified with a mitotic index of 8 mitoses/10HPF (ob. 40x).

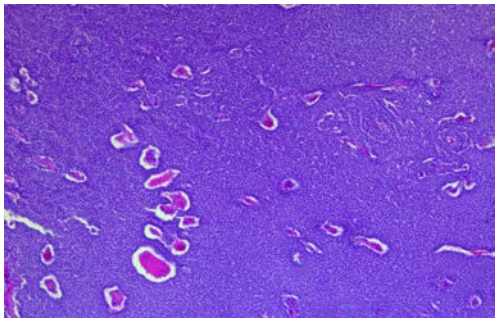

Fig. 1. *Call-Exner corpuscles, AGCTs, ovary, HE staining, 50x magnification*

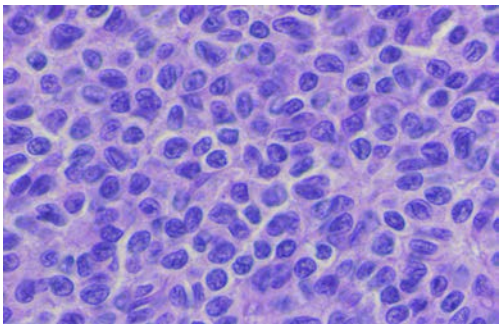

Fig. 2. *"Coffee bean" nuclei, AGCTs, ovary, HE staining, 630x magnification*

The immunohistochemical profile was a real challenge in the diagnostic process due to the fact that some cell groups were positive for Calretinin (figure 3), Vimentin and Inhibin, while focal groups of CD56 and S100 (figure 4) positive tumor cells were identified as well. Tumor cells were also negative for SMA, EMA, CD99, CTK7 and CTKHM markers.

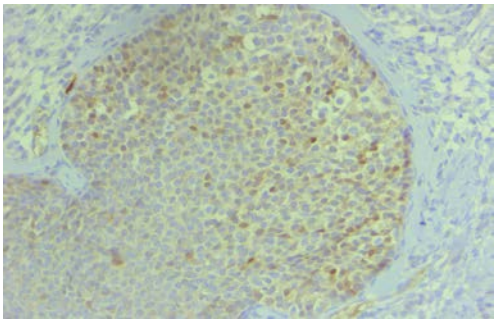

Fig. 3. *Microscopy of Calretinin immunostaining, 200x magnification*

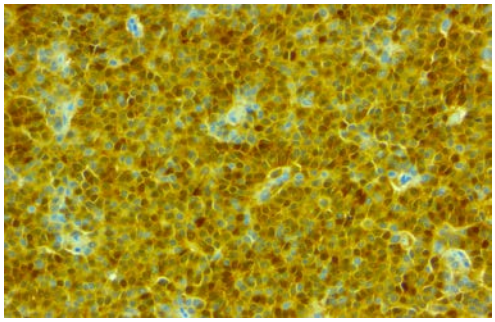

Fig. 4. *Microscopy of S100 immunostaining, 200x magnification*

At the level of the uterine body, the endometrial mucosa was atrophied, intramural being observed a well delimited formation, consisting of a proliferation of smooth muscle fibers, without atypia, arranged in intersecting bundles, with multiple areas of endometrial glands and stroma without atypia.

In the section of the omentum we found normal structure of connective and adipose tissue without the presence of tumor cells. Based on the microscopic appearance and immunohistochemical profile, the patient was diagnosed with low-grade malignant adult granulosa cell tumor, pT1aNxMx, FIGO IA.

Postoperative, the patient progressed accordingly, with no early nor late complications. She was discharged few days later. It is desired to follow-up the patient at 6 and 12 months, by clinical examination and ultrasonography exam to identify possible recurrences or metastasis.

3. Discussions

AGCT it is considered one of the most common malignant ovarian sex cord-stromal tumors. It is well known that metastasis and recurrences occur late, often in over 10 years after diagnosis. While the clinical evolution between the primary neoplasm and the metastasis and recurrences is similar, most patients develop more aggressive forms and they will finally die due to the neoplasm [12].

In over 70% of cases the recurrences were identified at the pelvic level, 9% at the abdominopelvic level, 6% retroperitoneally, 6% were cases with both pelvic and retroperitoneal recurrences and only 3% were represented by simultaneous recurrences in the retroperitoneum and abdominopelvic cavity [3].

Grossly, both AGCTs and JGCTs can be described as solid, cystic or solid and cystic. Although JGCTs could present much different clinical and histological features compared to AGCTs, the two types have similar MR imaging due to similar gross appearance. The most common MR imaging features for GCTs are sponge-like appearance with numerous cystic spaces and solid areas on T2-weighted MR images, high signal intensity of haemorrhagic areas on T1-weighted MR images [5]. Often the size of AGCTs is described as greater than 10 cm, but the size of the specimens found in the literature varies from small nonpalpable lesions to giant tumours, 3 to 27 cm [7].

"Coffee bean" nuclei are considered an exceptional feature of AGCTs, most often being identified in cytology examinations of ascites or pleural fluids [9]. In terms of immunohistochemical profile, ACGTs are positive for Inhibin, Calretinin, FOXL2, SF-1, WT1 and CD56; but in some isolated cases the positive result of the CD99 and S100 markers were also described, as we identified in our case the positive reaction for S100.

The gold standard method of treatment is surgery and should achieve complete resection of the tumor, without any residual evidence of tumor and negative margins. Incomplete surgical staging for fertility preservation can be perform safely among young women with early-stage diseases. Some studies have reported no significant difference in five-year survival rates of women with stage I disease after complete vs incomplete surgery [6].

The role of adjuvant chemotherapy is also debatable as it was shown to improve survival rates, but it is only recommended for advanced, recurrences or metastatic diseases.

The dissection of lymph nodes remains controversial, only 3% are positive [4].

Due to the high risk of recurrences or metastases, the recommend follow-up period is between 5 and 30 years [11].

4. Conclusions

Adult granulosa cell tumors are a rare form of ovarian neoplasm and despite the correctly applied surgical and adjuvant treatment, metastases or recurrences occur.

The "coffee bean" nuclei are an extremely rare aspect of these tumors, a feature that has been poorly identified and described to date.

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