

Adult Granulosa Cell Tumor in a Young Woman: A Case Report and Literature Review

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Abstract

Granulosa cell tumors belong to the group of stromal and sex cord tumors of the ovary. The adult type is the most common type and usually occurs during the perimenopausal period while the juvenile type mostly affects young women. This is a report of a 26 years old woman who presented an adult type of granulosa cells tumor, with review of the literature. She complained abdominal pain and distension associated with abundant ascites and underwent a right adnexectomy. The pathology examination diagnosed an adult granulosa cell tumor. The two entities of granulosa cell tumors (juvenile and adult types) are distinguished by their characteristic morphological aspects on histological examination allowing diagnostic orientation.

Keywords

Ovary, Stromal and Sex Cord Tumors, Granulosa Cell Tumors

1. Introduction

Granulosa cell tumors are rare ovarian neoplasms, represent 2% - 5% of malignant ovarian tumors. They are classified as sex cord-stromal tumors [1] and divided into 2 groups: adult and juvenile types. The adult form represents the most frequent type and is characterized by an indolent evolution and late recurrences; the rate of recurrence can reach 54% [2]. The diagnosis is made on histologic examination and based on morphological data [1]. We report a case of an adult granulosa cell tumor in a young woman.

2. Observation

She was 26-year-old who had enlarged abdomen with abdominal pain. Ultrasound revealed the presence of a right ovarian cyst associated with peritoneal effusion. Right adnexectomy was performed and the specimen underwent histological examination. On gross findings, the ovary was multilobate; its diameter was $16 \times 10 \times 8$ cm with smooth external surface. The sectioned surface was mostly cystic. The diameter of the cysts varies from 0.5 cm to 6.7 cm and contained a clear or mucoid liquid. The internal surface was smooth, without vegetation (**Figure 1**). Histological examination revealed a tumor proliferation of small round cells in the ovarian parenchyma. Cells are monomorphic, with a pale and scanty cytoplasm, with pale “coffee bean” nuclei. It was organized into compact clusters, microfollicular, or macrofollicular formations. Numerous Call-Exner bodies and some figures of mitosis have been observed (**Figure 2**). The tubal wall has a normal structure without tumor invasion.

3. Discussion

Granulosa cell tumors are classified into two entities: the adult form and the juvenile form. They belong to the group of the sex cord-stromal tumors (pure sex cord tumors) [3]. The juvenile type is characterized by a relatively younger age of onset, more pronounced morphological malignancy signs and a higher risk of recurrence [1]. It occurs in women under 30 and mainly in prepubescent girls [4] [5]. In the series by D. Pectasides *et al.*, the juvenile form was diagnosed in patients under 30, 20 and 10 years of age in respectively 90%, 80% and 50% of the cases [6]. Although very rare, the juvenile type can be observed in adults and the adult type in children [7]. The adult type constitutes approximately 1% of all



Figure 1. Ovary, adult granulosa cell tumor gross section showing multilocular cyst with smooth external (a) and internal surfaces, containing mucoid substances and clotted blood (b). Source: Department of Pathology, Joseph Ravoahangy Andrianavalona, Antananarivo Madagascar.

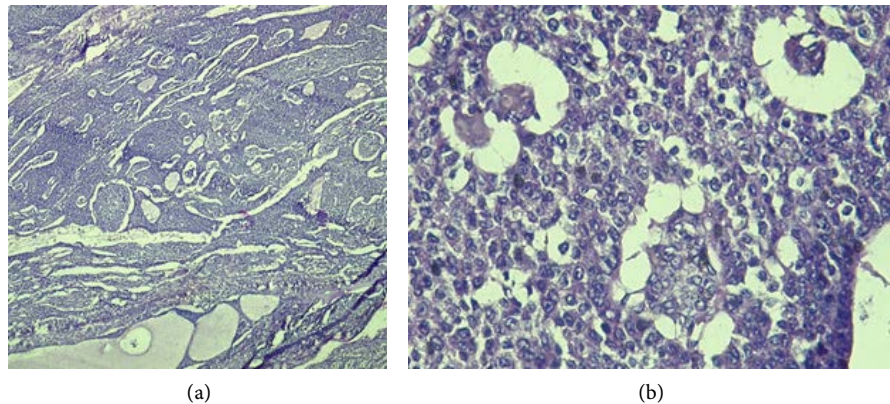


Figure 2. Adult granulosa cell tumor with monomorphic small round cells, organized into compact clusters or microfollicular or macrofollicular formations with Call-Exner bodies (a), with a pale and scanty cytoplasm, pale “coffee bean” nuclei (b). HE $\times 40$ (a), HE $\times 400$ (b). Source: Department of Pathology, Joseph Ravoahangy Andrianavalona, Antananarivo Madagascar.

ovarian tumors and is the most common form of granulosa cell tumors [8] and accounts for 90% to 97% of cases [9]. It can occur throughout life [7] but most often in the peri-menopausal or post-menopausal period with a peak frequency around 50 to 55 years [1] [10]. They are rare before 30 years of age and occur in the pre-pubescent period in 5% of cases [6]. Our patient was in the age groups whose occurrence is rare.

Concerning the clinical features, granulosa cell tumors have different clinical manifestations due to their ability to produce estrogens [7]. According to In Ho Lee *et al.*, estrogen production leads to the development of symptoms such as abnormal vaginal bleeding (45%), and abdominal pain or abdominal bloating (10% - 20%) [11].

In premenopausal patients, adult granulosa cell tumor usually causes irregular bleeding or amenorrhea and more rarely infertility. The most common clinical presentation in post-menopausal patients is abnormal bleeding with unilateral ovarian mass. Ascites is rarely present in the early stage (10% of patients) [6]. In 8% to 15% of cases, the tumor is ruptured and manifests as an acute abdominal pain with hemoperitoneum [7]. In our study, the patient has abdominal pain with ascites and abdominal distension. The diagnosis of granulosa cell tumors is made on histologic findings and based essentially on morphologic data [1]. Juvenile type has different histological characteristics compared to the adult form [4]. On gross examination, the size of the adult type tumor varies according to the literature. In Ho Lee *et al.* [11] noted an average diameter of 9.7 cm with extremes of 3 and 24 cm. The tumor can have different aspects. According to the study by Inada Y *et al.* [4], it is cystic in 30.3%, solid in 27.8 or solid and cystic in 41.7%. The tumor can be ruptured but usually the outer surface is intact and smooth [8]. These are solid tumors that are soft or firm, depending on the relative amount of neoplastic cells and the fibrothecomatous stroma they contain. They are yellow or gray, depending on the amount of intracellular lipids in the

lesion. On gross section, the classic appearance is a solid, cystic tumor. The cysts are multilocular or unilocular, with a smooth internal surface and are generally filled with serous fluid [6] or with fluid or coagulated blood, or with ill-defined areas of hemorrhage, separated by solid tissue [8]. Our case was cystic, multilocular with a smooth internal surface and clear liquid content.

On microscopic examination, the architecture varies, microfollicular, trabecular, tubular solid or diffuses. The tumor is often made of a mixture of these architectures and consists of small cells with a high nucleo-cytoplasmic ratio, “coffee bean” nuclei sometimes with a discrete nucleolus [5]. The morphological aspects can pose differential diagnoses. Sometimes granulosa cell tumors of diffuse architecture can be confused with undifferentiated carcinoma as extemporaneous. The appearance of the nucleus can be very useful in making a positive diagnosis. Adult granulosa cell tumors may be difficult to distinguish from undifferentiated carcinomas, adenocarcinomas and carcinoid tumors. Each of these tumors has a very different prognosis. A characteristic aspect is the appearance of the nuclei. The oval or angular nuclei, uniform and pale, grooved (coffee bean appearance) are typical of granulosa tumors. The nuclei of undifferentiated carcinomas are often hyperchromatic, not grooved, and of uneven size and shape. Nuclear atypia and multiple mitotic figures are also less frequent in granulosa tumors but more frequently observed in undifferentiated carcinomas. The presence of Call-Exner bodies is also important criteria of diagnosis [6]. In our study, the presence of proliferation of small round cells with “coffee bean” nuclei associated with Call-Exner bodies had made to orient the diagnosis in favor of adult granulosa cell tumor.

Estrogen production can also lead to endometrial abnormalities, according to the literature, the incidence of endometrial carcinoma varies from 3% to 22%, and endometrial hyperplasia varies from 32% to 85% [11]. Kitamura S *et al.* [12] found, in their series, 8 cases (out of 16) of endometrial hyperplasia and one case of endometrial carcinoma associated with granulosa cell tumors adult type. In our study, the patient underwent right adnexectomy only and the endometrium could not be assessed.

4. Conclusion

Adult type of granulosa cell tumors is rare before 30 years of age. Our study is characterized by the early onset of this tumor. The age of onset of granulosa cell tumors can point towards the suspicion of the adult form or juvenile form but the morphological characteristics of each tumor entity guide the diagnosis. An endometrial assessment should be performed once the diagnosis of granulosa cell tumors is confirmed.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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