# Androgenic juvenile granulosa cell tumor of the ovary with cystic presentation: a case report

**R.S. Nomelini[1], A.M.R. Micheletti[2], S.J. Adad[2], E.F.C. Murta[1]**

*[1]Research Institute of Oncology (IPON)/Discipline of Gynecology and Obstetrics,*
*[2]Discipline of Special Pathology, Federal University of Triângulo Mineiro (UFTM), Uberaba-MG (Brazil)*

**Summary**

Granulosa cell tumors account for approximately 1-2% of all ovarian tumors. There are two types: adult granulosa cell tumor and juvenile granulosa cell tumor. Juvenile granulosa cell tumors constitute 5% of this histological subtype, and the prognosis is good because the majority present as Stage I tumors. The treatment can consist of conservative surgery. Androgen production is rare and produces virilization in women. These tumors are usually solid or predominantly solid. We describe the case of a 13-year-old girl with androgenic manifestations and increased abdominal size. Her plasma testosterone level was elevated. A left adnexal cyst (14.4 x 9.1 x 9.7 cm) was revealed at pelvic ultrasonography. The patient underwent an exploratory laparotomy, revealing a left ovarian cystic tumor. Diagnosis was juvenile granulosa cell tumor.

*Key words:* Granulosa cell tumor; Adolescent; Testosterone; Ovarian Neoplasms; Hyperandrogenism.

## Introduction

Granulosa cell tumors (GCTs) are rare, accounting for roughly 1-2% of all ovarian tumors. Two types have been distinguished: adult granulosa cell tumor (AGCT) and juvenile granulosa cell tumor (JGCT). AGCT is the most common, and occurs mainly in peri and postmenopausal women. JGCT constitutes 5% of GCTs occurring in the first two decades of life [1-6].

JGCTs are interesting because of their hormonal effects. The majority of these tumors produce estrogenic effects: pseudoprecocious puberty and endometrial bleeding [4, 7]. Androgen production is infrequent (only 4%), and produces virilization in women. Most of the virilizing granulosa cell tumors present a solid and uncalcified gross appearance [8]. Nonetheless, a few cases of cystic appearance have been reported in cases of GCT [8, 9].

We present an unusual case of androgenic juvenile granulosa cell tumor in a 13-year-old patient with a cystic aspect. Our case report corroborates that rare JGCT are unilocular cystic with androgenic manifestations.

## Case Report

A 13-year-old girl (gravida 0, para 0, menarche at age 12) was admitted to the hospital complaining of amenorrhea of six months duration. Three months later she developed hirsutism, increased abdominal size, abdominal pain and deepening of the voice.

On examination, the patient presented a moderately sized abdominal and pelvic mass, palpable just below the umbilicus (10 x 7 cm). The tumor was painless and had a cystic consistency. The patient's blood pressure was normal and there was an increase of facial and abdominal hair, both with a male pattern of distribution. Breast volume was reduced. On vulvar examination the clitoris measured 1.5 x 0.7 cm.

The plasma testosterone level was 386 ng/ml. A left adnexal cyst (14.4 x 9.1 x 9.7 cm) was found at pelvic ultrasonography. Figure 1 shows a computed tomography (CT) scan of the abdomen and pelvis. There was no ascites.

The patient underwent exploratory laparotomy, revealing a left ovarian cystic tumor. The uterus, tubes and right ovary were normal. The left ovarian mass was removed by oophorectomy along with the uterine tube. Peritoneal washing cytology did not show altered cells. The postoperative course was uncomplicated. Serum testosterone was normal after 50 days. Virilizing symptoms regressed and her voice was normal after one year. Now she is fine, has no symptoms of recurrence and the testosterone level is normal.

Anatomopathological examination showed a cystic unilocular tumor measuring 15 x 12 x 3 cm and weighing 480 g; the uterine tubes were unaltered. The external surface of the cystic lesion was white and smooth, and the inside was filled with yellow-citrine fluid. The thickness of the wall was from 0.1 to 0.2 cm, firm and white and generally smooth, except for the area near the tubes, where it was slightly yellowish with a slightly folded aspect and a thickness of up to 0.5 cm in an area of 3 x 2 cm (Figure 2). Intrasurgical examination (cytology and frozen section) showed hypercellular smears constituted by cells of small or medium nuclei, rounded or spindle-shaped, with well distributed thin chromatin, but generally without folds or clefts in the karyotheca and scarce or non-evident cytoplasm. Paraffin-embedded ovarian tumor specimens consisted of a cystic lesion covered by an inner layer of rounded cells with small or medium nuclei and well distributed thin chromatin, without pleomorphism, generally without clefts or folds in the karyotheca and scarce cytoplasm, compatible with granulosa cells, surrounded by a rim of cells with luteinization (Figure 2). There was one mitotic figure per 50 high power fields. Diagnosis was juvenile granulosa cell tumor.

Revised manuscript accepted for publication September 28, 2006

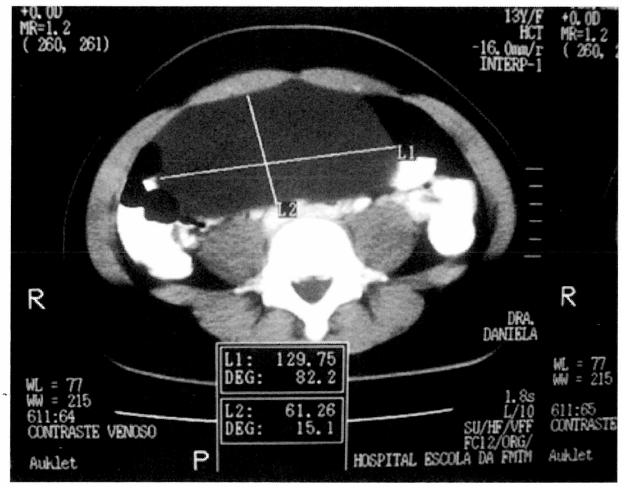


Figure 1. — Computerized tomography scan of the abdomen and pelvis. A large cystic mass, most likely of ovarian origin, measuring 12.9 x 6.1 cm can be seen.

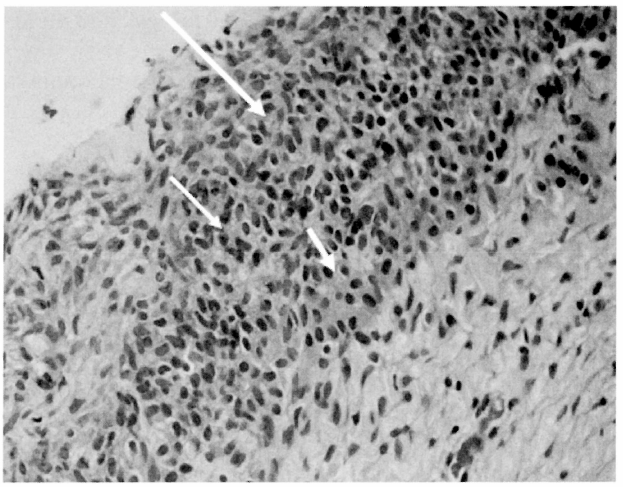

Figure 2. — The cyst is covered by an inner layer of granulosa cells (very large arrow) surrounded by a rim of luteinized theca cells (large and small arrows) (H&E x 40).

## Discussion

We describe an unusual case of androgenic juvenile granulosa cell tumor with a cystic gross aspect in a 13-year-old patient. To our knowledge, few cases of virilizing granulosa cell tumors have been reported in young women under 20 years old [2, 8, 10-12]. This is a rare case of JGCT accompanied by virilization with a cystic aspect and unilocular to macroscopy and to frequent luteinization of the stromal cells of the tumor.

The most common clinical manifestations seen in patients with androgenic granulosa cell tumor include hirsutism, clitoromegaly, increased abdominal size, amenorrhea, deepening of the voice and a male escutcheon, and less commonly, baldness, vaginal bleeding, acne, abdominal mass, oligomenorrhea, irregular menses, pubic hair in childhood and reduction of breast volume. Other rare associations with Ollier's Disease (enchondromatosis), Maffucci's syndrome, and abnormal karyotypes with ambiguous genitalia have been described [13-17]. In children, the clinical manifestations of elevated testosterone are heterosexual precocity, accelerated growth, hirsutism and acne [18]. Our case presented hirsutism, clitoromegaly, an abdominal mass, amenorrhea, deepening of the voice and reduction of breast volume. Her testosterone serum level decreased rapidly after tumor extirpation and virilizing symptoms regressed. Hirsutism and voice deepening may persist in some cases [11, 19, 20]. In our case, the testosterone level regressed after two months but deepening of the voice continued until one year after the extirpation of the tumor. The normal range of plasma testosterone is 0.8 to 3.2 pg/ml. Testosterone level is a good tumor marker during the follow-up.

The majority of JGCTs are characterized by a benign clinical course. However, their histological features are associated with malignant behavior [21]. Most of the virilizing granulosa cell tumors present a solid and uncalcified gross appearance [8]. When they are virilizing, they can be cystic [8, 9]. Nonetheless, a few cases of cystic appearance have been reported in cases of GCT. The tumor in our patient was cystic and virilizing. In a study of 128 JGCTs, the gross appearances were: 57 solid and cystic, 47 solid, 16 with multilocular cysts, seven without an adequate gross description and one with a thin-walled unilocular cyst without virilization [2]. Cystic appearance is more commonly found in AGCT [8]. The average diameter of these tumors varies greatly (from 3 to 32 cm) with an average of 12.5 cm [2, 18].

Martinez *et al.* [22] reported a case of a solid granulosa cell tumor with stromal luteinized cells and associated virilization. Young *et al.* [23] presented four cases of luteinized granulosa cell tumors, but unlike our case, they were of the adult type, solid, and did not present virilization. Norris *et al.* [19] described two cases of cystic granulosa tumors associated with virilization, however multilocular, and only one showed focal luteinization. In the same paper, the authors described a review of 150 granulosa cell tumors from the AFIP (Armed Forces Institute of Pathology) files, where they found nine cystic tumors, one unilocular, seven tumors with stromal luteinized cells and only two associated with virilization, showing that these characteristics are generally uncommon in granulosa cell tumors.

However, Nakashima *et al.* [11] showed that in tumors associated with virilization, the cystic or partially cystic aspect is more common, as observed in our case. They reported 17 androgenic granulosa cell tumors, nine solid, one solid and cystic and seven completely cystic tumors (5 unilocular and 2 multilocular). Eleven tumors showed stromal luteinized cells. From the six juvenile-type tumors, only one was cystic and presented luteinized theca cells. Only one tumor presented malignant behavior and macroscopy showed this tumor to be cystic and unilocular. Although generally benign, these tumors should be differentiated from other ovarian cystic tumors, such as serous cystadenomas, because they rarely show malignant behav-

ior. Histologically, JGCTs show focal follicle formations and can have histologic features of malignancy (high mitotic rate and cellular atypias) [2]. Imaging findings reveal a multicystic mass with solid components, that is, a tumor with irregular septa, but predominantly solid [24].

Most JGCTs are in Stage I according to the International Federation of Gynecology and Obstetrics (FIGO) classification, with a survival rate of about 90% [4, 25, 26]. Therefore, they have a good prognosis and surgery remains the primary treatment. Contralateral ovarian involvement is rare. Although a complete abdominal cavity inventory was not performed in our case, we treated it as Stage IA. Tumors in advanced stages have a poor prognosis and treatment is surgery and chemotherapy [13-17, 21, 27]. The main factor determining the likelihood of recurrence is tumor stage, but other factors can increase the risk of recurrence (tumor size and DNA aneuploidy) [27]. The majority of JGCTs present as Stage I tumors [2, 15]. It is possible to preserve the contralateral ovary and the uterus, as our case shows. Chemotherapy is favored in patients with advanced and recurrent disease. Adjuvant cisplatin-based chemotherapy may be useful in advanced FIGO stages and recurrent or metastatic disease. Powell and Otis [15] reported the case of a 13-year-old girl with JGCT (Stage IIIC) treated with oophorectomy, omentectomy and six cycles of carboplatin and etoposide. The therapy for patients in advanced stages is a difficult decision; the uterus and contralateral ovary can be preserved if they are normal. Pregnancy after conservative treatment of advanced disease has been described [28]. The prognostic value of staging and early diagnosis of recurrence are important. Tumor stage forecasts recurrence, which is important factor in patient survival. However, conservative surgery is often performed in adolescents to preserve reproductive function [29].

In summary, JGCT with increased androgens and cystic aspects is rare. Pediatricians and gynecologists should keep this manifestation in mind to avoid misdiagnosis.

This paper was supported by FAPEMIG and CNPG.

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Address reprint requests to:
E.F.C. MURTA, M.D.
Research Institute of Oncology (IPON)
Discipline of Gynecology and Obstetrics,
Av. Getulio Guarita, S/N
Universidade Federal do Triângulo Mineiro (UFTM)
38075-440, Uberaba-MG, Brazil