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Torsion of Granulosa Cell Tumor of the Ovary in a Preschool Patient: A Rare Cause of Acute Abdomen

Authors' Contribution:

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Conflict of interest: None declared

Patient: Female, 5-year-old
Final Diagnosis: Granulosa cell tumor of the ovary
Symptoms: Abdomen distension • abdominal mass • abdominal pain
Medication: —
Clinical Procedure: Diagnostic tests, surgical treatment and chemotherapy
Specialty: Pediatrics and Neonatology

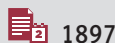
Objective: Rare disease
Background: Granulosa cell tumor of the ovary is very rare in childhood; its most common clinical manifestation is isosexual precocious puberty. Clinical presentation as acute abdomen due to pain and ovarian torsion is rare, but a granulosa cell tumor must be suspected in a patient with this acute presentation and signs of early puberty. Adult-type granulosa cell tumor is an even rarer occurrence in children.

Case Report: We report a case of torsion of adult-type granulosa cell tumor of the ovary in a 5-year-old patient with acute abdominal pain and ovarian torsion and highlight the importance of histological diagnosis of this tumor for the therapeutic plan and progression of these patients.

Conclusion: Precocious puberty, pain, abdominal distension, and an ultrasonography with suspicion of ovarian torsion are warning signs that may indicate the presence of a gonadal stromal tumor in pediatric patients seen at an emergency unit. These patients require long-term follow-up by a pediatrician and gynecologist because of the potential for late recurrence.

MeSH Keywords: Abdomen, Acute • Child • Granulosa Cell Tumor • Ovarian Neoplasms • Puberty, Precocious • Torsion Abnormality

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Background

Malignant ovarian tumors, which correspond to less than 1% of pediatric neoplasm cases, may originate from different components of the ovarian tissue. Germ cell tumors are the most common, occurring in 60% to 80% of these cases [1]. Epithelial tumors represent approximately 20% and are extremely rare before menarche. Sex cord-stromal tumors, which are hormonally active tumors, occur in only approximately 5% of cases, and may be classified as granulosa cell tumors that produce estrogens, Sertoli-Leydig cell tumors that produce androgens or undifferentiated tumors [1].

Granulosa cell tumors may be classified into 2 subtypes, juvenile and adult, according to clinical and histopathological presentation [2]. Only 5% of granulosa cell tumors of the ovary occur before puberty; when this happens, the tumors are most often of the juvenile type [1,2]. The occurrence of adult-type granulosa cell tumor is extremely rare in childhood [1,2].

The main clinical presentation of granulosa cell tumor is isosexual precocious puberty. The clinical manifestation as acute abdomen due to ovarian torsion is rare in childhood [3]. We report a case of adult-type granulosa cell tumor in a 5-year-old patient with acute abdominal pain and ovarian torsion.

Case Report

A 5-year-old patient was seen due to abdominal pain in the right iliac fossa lasting 3 days and progressively worsening. Her parent also reported anorexia and 2 food vomiting episodes in this period. She had no history of fever.

On physical examination, the patient had normal weight and was lethargic and discreetly pale, with good peripheral perfusion. Her respiratory and cardiovascular systems were unremarkable. The abdomen was globular, tender to light and deep palpation, with no palpable masses and/or visceromegaly and no signs of peritoneal irritation. The patient had signs of precocious puberty, with onset of thelarche and pubarche consistent with M2 and P2 Tanner stages, respectively.

Laboratory results were: red blood cells count: 4.23 million/mm³ (reference range [RR] 4.00–5.10×10¹²/L); hemoglobin: 11.5 g/dL (RR 11.4–14.3 g/dL); hematocrit: 34.6% (RR 34–42%); white blood cells count: 22 500 million/mm³ (RR 4.4–12.9×10⁹/L) and differential with 89% neutrophils (RR 50–62%), 4% band neutrophils (RR 3–6%), 3% lymphocytes (RR 25–40%), 4% monocytes (RR 3–7%), eosinophils and basophils 0%; platelets: 290 000/mm³ (RR 187–445×10⁹/L); erythrocyte sedimentation rate: 58 mm/hour (RR up to 10 mm/hour); C-reactive protein: 165.1 mg/dL (RR up to 0.8 mg/dL); alpha-fetoprotein:

1.7 IU/mL (RR up to 7.3 IU/mL); quantitative beta-human chorionic gonadotrophin: 1.2 IU/mL (negative up to 5 IU/mL); lactate dehydrogenase: 642 U/L (RR 313–618 U/L).

An ultrasonography of the entire abdomen and pelvis identified a small amount of free fluid in the peritoneal cavity, with debris and thin septa in the right iliac fossa and a mass of heterogeneous echogenicity in the pelvis measuring 5.7×5.5 cm, with small central anechoic areas, regular and well-defined margins, and minimal blood flow, which caused compression and anteroinferior displacement of the bladder. The ovarian parenchyma had small peripheral follicles, in addition to large-caliber vessels, some of them with a coiled appearance and a significant increase in blood flow. The ultrasonography of findings indicated a large solid mass in the right ovary associated with torsion (Figure 1A). A computed tomography (CT) scan of the upper abdomen and pelvis found that the right ovary was enlarged in volume, measuring 6.8×6.7×6.0 cm and occupying the pelvic midline, with a twisted vascular pedicle suggestive of ovarian torsion (Figure 1B).

The patient underwent surgical treatment by laparotomy, which confirmed the presence of a solid mass approximately 8 cm in diameter in the right ovary, compatible with a tumor, with twisted vascular pedicle and uterine tube (Figure 2). We collected peritoneal fluid, which had a serious appearance, and performed a right salpingo-oophorectomy. The patient progressed without complications and was discharged from the hospital on the third postoperative day.

Cytological examination of the peritoneal fluid indicated the presence of neoplastic cells. On gross examination, the right ovary had a tumoral appearance, weighing 110 g and measuring 7.5×7.0×5.0 cm. Histological sections of the ovary revealed neoplasm consisting of cells with eosinophilic cytoplasm, sometimes vacuolated, and ovoid or round regular nuclei, some of them hyperchromatic or depolarized. No mitotic figures were found. The neoplastic cells were arranged into small clusters or strands isolated by fibrous stroma in a trabecular pattern and microcystic arrangement, involving hyaline material and forming frequent Call-Exner bodies. There were large areas of coagulative and liquefactive necrosis, as well as hemorrhage. These findings were consistent with adult-type granulosa cell tumor.

According to the International Federation of Gynecology and Obstetrics (FIGO), tumor stage was IC, since it was limited to the ovary but there were neoplastic cells in the peritoneal fluid. The patient received 4 cisplatin-based chemotherapy cycles. The patient remains under clinical/oncological follow-up, with normal tumor markers (inhibin B) and serial ultrasonography examinations in 2 years of follow-up. The clinical signs of precocious puberty regressed after surgical treatment.

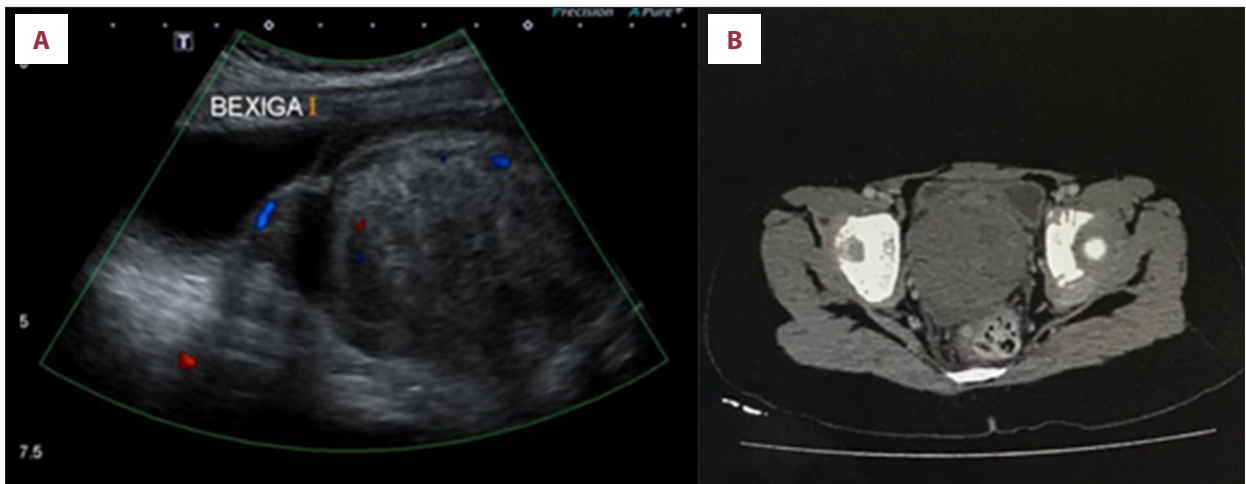


Figure 1. (A) Ultrasonography showing a large mass in the right ovary and anterior displacement of the bladder, and (B) computerized tomography scan showing a large ovarian mass in the pelvis.



Figure 2. Intraoperative photograph showing torsion of the ovary and right uterine tube, with a large tumor mass in the ovary.

Discussion

Granulosa cell tumors are the most frequent cause of precocious puberty in childhood and represent most tumors of the ovarian gonadal stroma. They are classified as juvenile or adult type according to clinical and histopathological data [1,2].

Juvenile-type tumors correspond to only 5% of granulosa cell tumors and are more common before menarche and in young women [2,4]. In this type, the main clinical manifestations derive from hyperestrogenism, with precocious puberty or vaginal bleeding before puberty or menorrhagia and intermenstrual bleeding in reproductive-age women.

In adult-type granulosa cell tumors, which are more frequent and are usually found in 50- to 55-year-old women, the main clinical manifestation is vaginal bleeding [2–6]. They very rarely occur in childhood. In the case reported, a 5-year-old patient presented clinically with precocious puberty and the histopathological pattern of adult-type granulosa cell tumor.

Due to a high level of estrogen, and therefore increased tumor vascularization, granulosa cell tumor may also cause hemoperitoneum due to rupture, and manifest as acute abdomen. This occurs in approximately 10% of cases [7]. It may also manifest as pain or palpable abdominal mass.

The clinical manifestation as acute abdomen due to ovarian torsion, as in the case reported, is very rare in children and adolescents. In a comprehensive study carried out by Oltmann et al., of 707 patients with ovarian torsion, only 1.8% had a malignant tumor [3]. Most torsions of ovarian tumor described in the literature are caused by germ cell tumors, which is explained by the fact that this is the most common malignant tumor in this age group [7].

A clinical diagnosis of ovarian tumor is usually confirmed by tumor markers. Granulosa cell tumor is not associated with an increase in alpha-fetoprotein and human chorionic gonadotropin, but it may produce inhibin A and B, which is the main marker of the ovarian stroma. Inhibin B is more specific. Although serum levels of inhibin are used for following patients with granulosa cell tumor in many institutions, its role has not been completely explained, especially in childhood [1,2,4]. It is also not clear if there are any benefits in monitoring serum estradiol levels during follow-up of these patients [2].

Imaging is therefore essential for therapeutic planning, because it provides information on the presence of a tumor in the ovary

affected by torsion, in addition to information on the contralateral ovary, uterus, and other abdominal organs. Ultrasonography is the most frequently used imaging technique to confirm ovarian torsion, especially because it provides vascular flow data through Doppler, and for examining acute abdomen. If a diagnosis of ovarian tumor is suspected, a CT scan may complement the imaging assessment. Nuclear magnetic resonance imaging may be used as an alternative exam, or when the ultrasonography of diagnosis is still unclear, because it provides an excellent image without ionizing radiation [8].

Definitive diagnosis of granulosa cell tumor of the ovary and type classification, either as adult or juvenile, can be only be achieved through histopathology. Usually, granulosa cell tumor appears as a large unilateral ovarian mass, with solid and cystic areas. Morphologically, the juvenile type shows characteristic rudimentary follicles (macrofollicles filled with mucinous fluid), with hyperchromatic and oval nucleus, rare or absent Call-Exner bodies, no nuclear indentations, and more immature-appearing nuclei. The cells have an abundant eosinophilic cytoplasm and tend to form strands or nodules, with a variable proportion of follicular and cystic structures. The adult type has a different morphology, with hypochromatic round nuclei, infrequent cellular atypia or mitosis, nuclear indentations, and frequent Call-Exner bodies [2,9].

Currently, the best surgical approach for children and adolescents with ovarian torsion is under discussion. The recommendation is detorsion and preservation of the ovarian tissue with the goal of preserving fertility, because most preserved ovaries have been shown to retain viability after detorsion, since arterial perfusion may be maintained for several days. These patients are followed up through ultrasonography of every 3 months to assess the presence of tumor and follicles or ovarian viability. This recommendation does not apply if there is evidence of a malignant tumor. In these cases, the consensus is the performance of a salpingo-oophorectomy [10], as in the present case, which had a solid mass of ovary that showed the presence of a tumor and torsion of its vascular pedicle.

In ovarian tumor cases, it is essential to collect peritoneal fluid and also examine the contralateral ovary, or to stage the tumor following FIGO guidelines [2]. In the case reported, the tumor was staged as IC, because it was limited to the ovary and the capsule was intact, but the peritoneal fluid cytology revealed

the presence of tumor cells. In these cases, FIGO recommends that tumor excision be followed by 4 cisplatin-based chemotherapy cycles. In most children with granulosa cell tumor, the condition is localized, that is, it has a stage I diagnosis and a favorable prognosis. Recurrence is rare and, when it occurs, it is usually within the first 2 to 3 years post-surgery [4,11]. In the adult type recurrence may occur later, up to 10 years later [4].

For patients in stage IC, if the tumor ruptures or the cytology is equivocal, both histology and mitotic count are very important for therapeutic planning. Children with the juvenile type and surgical rupture and low mitotic count may be followed up by imaging studies and tumor markers (inhibin B) alone. If the mitotic rate is high, chemotherapy is needed [9,11].

Quarterly ultrasonography examinations in the first 3 years after diagnosis are performed, with a longer interval between examinations after that, but follow up should be long-term, because the tumor may recur many years later [4,9,11].

Since this is a type of tumor that is very rare in childhood, its management is highly controversial. Clinical and imaging diagnoses must be accurate, since the current recommendation for a patient with ovarian torsion is a conservative treatment involving detorsion and preservation of the ovary. For a patient with ovarian torsion and malignant ovarian tumor, however, the treatment should be the removal of the affected ovary. Given the intraoperative evidence of a malignant ovarian tumor, salpingo-oophorectomy is indicated. Histopathological diagnosis is also extremely important, since it guides the postoperative plan that will be decisive for prognosis or progression.

Conclusions

Precocious puberty, pain, and abdominal distension, in addition to an ultrasonography with suspicion of ovarian torsion, are signs that may indicate the presence of a gonadal stromal tumor in pediatric patients seen at an emergency unit. These patients need long-term follow-up by a pediatrician and gynecologist because of potential late recurrence.

Conflict of interest

None.

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