

# Pediatric ovarian tumors, a challenge for pediatrician and gynecologist

## Three case reports (CARE compliant)

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### Abstract

**Rationale:** Ovarian or adnexal tumors are very rare in patients below the age of 18 years, most of them being functional cysts, only 10% being malignant. We report 3 cases of ovarian tumors with the aim of revealing the particularities regarding the diagnosis and management of benign and malignant ovarian tumors in pediatric patients.

**Patient concerns:** The 1st case, a 9-year-old girl presented for diffuse abdominal pain, distended abdomen and rapid increase in abdominal volume. The 2nd case describes a 13-year-old female patient admitted for acute abdominal pain and nausea, and the 3rd one was an 18-year-old female teenager who presented for distended abdomen, intermittent diffuse abdominal pain and rapid increase in abdomen volume.

**Diagnoses:** The abdominal ultrasound revealed in all 3 patients suggestive signs for ovarian tumors.

**Interventions:** The 1st patient underwent laparotomy with adnexectomy, and the histopathological exam showed the diagnosis of *dysgerminoma*. The 2nd patient underwent laparoscopy with adnexectomy, and the histopathological exam revealed a *borderline tumor*. The 3rd patient benefited by a laparotomy with left ovariectomy, and the histopathological exam pointed out a *mature teratoma*.

**Outcomes:** The outcome was favorable in all 3 cases, but the patients with dysgerminoma and mature teratoma were further referred to the oncologist for proper assessment.

**Lessons:** Laparoscopy may represent the first choice for uncomplicated ovarian masses. The diagnosis and the therapeutic plan must be based on symptoms, pelvic ultrasound, the time of menarche and the potential serum markers.

**Abbreviations:**  $\alpha$ -FP = alpha fetoprotein,  $\beta$ -HCG = beta human chorionic gonadotropin, CA = cancer antigen, FIGO = International Federation of Gynecology and Obstetrics, LDH = lactate dehydrogenase, PID = pelvic inflammatory disease.

**Keywords:** benign tumors, laparoscopy, malignant tumors, ovarian tumors, pediatric patients, surgical intervention

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Ovarian or adnexal tumors are very rare in patients below the age of 18 years, most of them being functional cysts, only 10% being malignant.

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## 1. Introduction

Ovarian tumors are rare in children. The incidence increases with age, from 0.43 in 100,000 cases at 1 year of age to 152 in 100,000 cases in 35-year-old patients.<sup>[1,2]</sup> The studies including surgical intervention under the age of 18 years indicate benign tumors in most of the cases, such as functional cysts. Nevertheless, up to 10% of adnexal tumors are malignant.<sup>[3]</sup> Malignant tumors are more frequent during premenarche in comparison to the afterward period.<sup>[1]</sup>

The referring symptoms for these patients are acute or continuous abdominal, other symptoms as a result of the compression on surrounding organs, such as urinary or bowel transit disorders, nausea, vomiting, increase of abdominal volume, and much rarer early puberty or vaginal bleeding.<sup>[4]</sup> The differential diagnosis in pediatric patients includes benign and malignant lesions. The first ones include gynecological disorders, such as: functional cysts, corpus luteum cysts, hydrosalpinx, paratubal/paraovarian cysts, endometrioma, mature cystic teratoma, cystadenoma, ectopic pregnancy, pelvic inflammatory disease (PID), tubo-ovarian abscess, müllerian anomalies, while the malignant ones comprise germ cell tumors, sex cord-stromal tumors, epithelial ovarian tumors, metastatic tumors, lymphomas, and other tumors.<sup>[5]</sup> There are also other organs related pathologies that must be taken into account for the

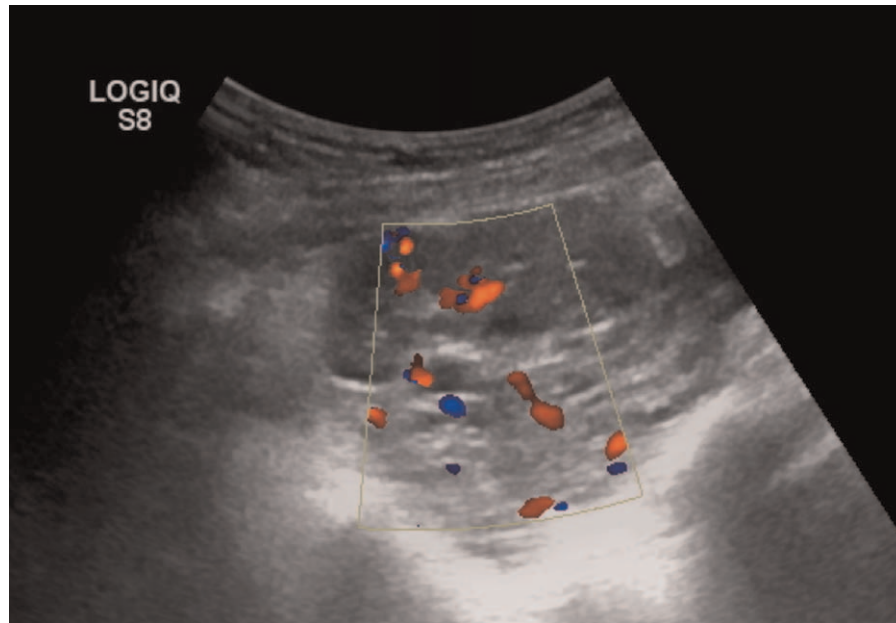


Figure 1. Ultrasound aspect of the disgerminoma.

differential diagnosis like: peritoneal/retroperitoneal inclusion cysts, appendicitis/appendicular abscess, and renal ectopy/urological anomalies.<sup>[5]</sup> The risk of malignancy is reduced in newborns, presenting a peak around 6 years of age, and afterward it decreases to under 10% at the age of 14 years.<sup>[2]</sup> Hermans<sup>[1]</sup> states that these percentages are related to the cases of adnexal tumors that benefited from surgery, and therefore, most likely the percentage of malignant tumors at any age is smaller than in their study. Post menarche, the risk of malignancy of only 2% to 4%.<sup>[2]</sup>

The diagnosis of ovarian tumors is based on pelvic ultrasound and abdominal-pelvic MRI.<sup>[6]</sup> The ultrasound criteria suggesting a benign tumor are: unilocular cysts, smooth multilocular tumors, solid component of under 7mm, the lack of acoustic shadow and Doppler signal.<sup>[6]</sup> On the other hand, the criteria that indicate a malignant mass are: solid unregulated tumor, multilocular solid mass >10cm in diameter,  $\geq 4$  papillary structures, the presence of ascites, and high Doppler signal.<sup>[6]</sup> A diagnostic algorithm for predicting the character of ovarian tumors was proposed and it comprises a combination between age, menarcheal status, tumor markers and the 'simple rules' mentioned above.<sup>[1,6]</sup>

*The useful tumor markers*<sup>[1]</sup> for the diagnosis of adnexal masses in children are: CA-125 for epithelial tumors,  $\alpha$ -FP and  $\beta$ -HCG for germ cell tumors in newborns, CA-125,  $\beta$ -HCG, inhibin for granulosa cell tumors, LDH for dysgerminomas,<sup>[1]</sup> and CA 19-9 for immature teratoma.<sup>[5]</sup>

The treatment consists in laparotomy in case of malignant tumors, pelvic adhesion syndrome, hemodynamic instability and other comorbidities, or laparoscopy, especially in young girls, even though the tumor sizes overpass 25cm, but are considered benign.<sup>[5]</sup> Nevertheless, pediatrician's and gynecologist's communication skills are essential in order to create a partnership with the parents and patient and to obtain the best outcome.<sup>[7]</sup>

*The aim* of this paper was to reveal the particularities regarding the diagnosis and management of benign and malignant ovarian tumors in pediatric patients.

The written informed consent was obtained from the patients' mothers (legal guardians) for the publication of these cases.

## 2. Case series description

### 2.1. Case 1

**2.1.1. Presenting concerns, clinical findings, and diagnostic focus.** We present the case of a 9-year-old female patient who presented diffuse abdominal pain, distended abdomen and rapid increase in abdominal volume. The onset of the symptoms was approximately 1 month before the admission. The patient was premenarche at the time of diagnosis. The laboratory tests revealed only mild anemia. The abdominal ultrasound pointed out a left ovarian mass which appeared as a mixt tumor (most solid, but also with a small amount of fluid content), moderately vascularized (Fig. 1).

**2.1.2. Therapeutic focus and assessment.** Based on the ultrasound findings, the patient underwent laparotomy with adnexectomy. The histopathological exam established the diagnosis of *dysgerminoma*, and the patient was transferred in the Oncology Department in order to receive appropriate chemotherapy.

**2.1.3. Follow-up and outcome.** The postsurgical evolution was favorable as well as the postchemotherapy one with no tumor recurrence within the next 2 years.

### 2.2. Case 2

**2.2.1. Presenting concerns, clinical findings, and diagnostic focus.** The 2nd case describes a 13-year-old female patient admitted for acute abdominal pain and nausea. The onset was approximately 2 days before the admission and the symptoms

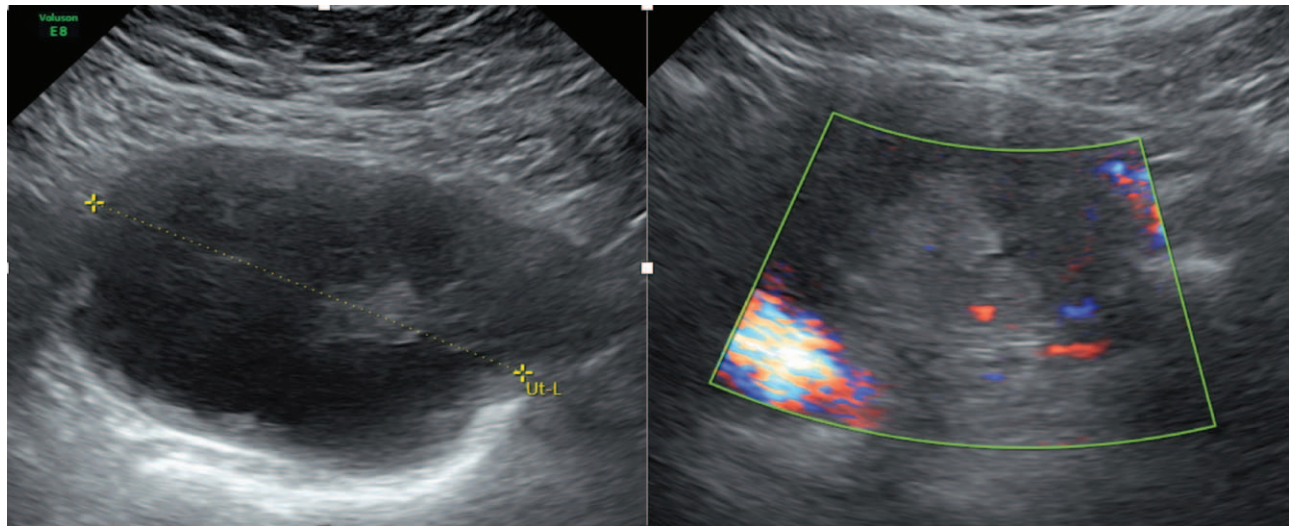


Figure 2. Ultrasound aspect of borderline tumor.

worsened despite the symptomatic treatment. The laboratory tests were within normal ranges. The abdominal ultrasound pointed out a right ovarian tumor—a cystic mass, but in periphery we observed a solid area with high number of vessels in Doppler examination (Fig. 2). Nevertheless, the exam was partially hindered by the fact that the patient was obese weighting approximately 90 kg.

**2.2.2. Therapeutic focus and assessment.** The patient underwent laparoscopy with adnexectomy. The histopathological exam revealed a *borderline tumor*.

**2.2.3. Follow-up and outcome.** The patient was closely monitored, and she did not present any signs of relapse after approximately 3 months from the surgical intervention. Moreover, we repeated the CA-125 but it remained negative.

### 2.3. Case 3

**2.3.1. Presenting concerns, clinical findings and diagnostic focus.** Our 3<sup>rd</sup> case reveals a 18-year-old female teenager who presented distended abdomen, intermittent diffuse abdominal pain and rapid increase in abdomen volume. The onset of the symptoms was approximately 2 months before the admission

with chronic abdominal pain. Our patient was postmenarche. The laboratory tests were within normal ranges. The abdominal ultrasound revealed a left ovarian mass—solid, inhomogeneous, vascularized mass (Fig. 3).

**2.3.2. Therapeutic focus and assessment.** A laparotomy was performed and the patient underwent left ovariectomy. The histopathological exam pointed out a *mature teratoma*.

**2.3.3. Follow-up and outcome.** The patient's evolution after the surgery was favorable. Based on the histopathological results, she was admitted in an Oncology Department in order to receive the appropriate treatment.

### 3. Discussions

Young patients with ovarian tumors often complain of acute or chronic abdominal pain, vomiting, nausea, increase of abdominal volume or other symptoms induces by the compression on surrounding organs.<sup>[4]</sup> All our 3 patients complained of abdominal pain, while the patient diagnosed with borderline tumor also associated nausea and rapid increase of abdomen volume and abdominal distension was noticed in both dysgerminoma and mature teratoma patients.

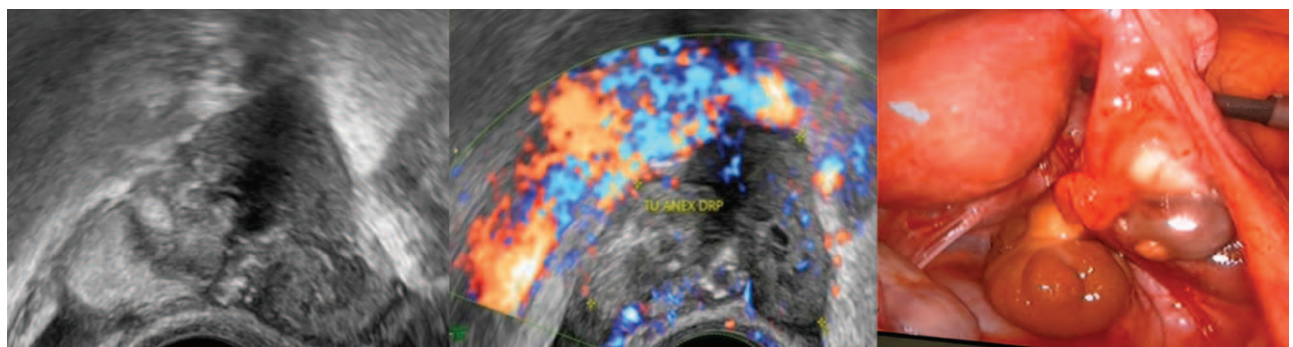


Figure 3. Mature teratoma.

Talma et al<sup>[8]</sup> underlined that pre-menarcheal girls with a more reduced hormonal secretion express an overall lower risk for benign ovarian tumors due to the fact that hormonal changes appear at the time of menstruation onset, but a particular higher risk for malignant adnexal tumors. Therefore, an assessment of an ovarian mass requires not only the girl's age, but especially her hormonal status.<sup>[8]</sup> Confusions may occur in case of a granulosa cell tumor that can induce puberty normally expected at that age. Therefore, it is mandatory to differentiate the menarche from the premenarche hemorrhage. Menarche occurs lately at younger ages being directly influenced by genetic factors, industrialization process and BMI.<sup>[8]</sup> Contrary to the previously mentioned study,<sup>[8]</sup> of our series of cases only the patient diagnosed with dysgerminoma was premenarche, the other 2 were postmenarche.

The imagistic tools are extremely useful in establishing the diagnosis of ovarian tumors and they usually consist in pelvic and abdominal ultrasound.<sup>[6]</sup> Ultrasound is widely used in the assessment of multiple pediatric pathologies, such as abdominal tumors,<sup>[9]</sup> inflammatory bowel diseases<sup>[10,11]</sup> (IBD-urile si SCAD-ul), but also cardiac malformations.<sup>[12]</sup> In certain cases, abdominal-pelvic MRI may also be required. The assess of the malignancy risk may be based on the simple ultrasound rules stated by Timmerman et al<sup>[6]</sup>, even though these were not validated for pediatric patients. The authors underlined that in cases where the simple rules cannot establish clearly the diagnosis of an adnexal tumor, the case must be referred to an ultrasound expert in order to indicate the most-likely diagnosis.<sup>[1,6]</sup> In our cases, the ultrasound exam was very suggestive for the diagnosis. Despite the fact that in the case of the patient with borderline tumor the ultrasound exam was hardened by the patient's excessive weight, it pointed out a solid adnexal mass, without Doppler flow and negative serum markers. Obesity is a major public health problem worldwide<sup>[13–21]</sup> that may result not only in diagnosing difficulties, but it can also burden the management of these patients. Moreover, Hermans et al proposes as a tool for risk prediction, a combination between the age, menarcheal status, tumor markers and the 'simple rules', previously mentioned.<sup>[1,6]</sup> Despite the rarity of malignant ovarian tumors in small ages, a screening program involving a routine abdominal ultrasound between 10 and 18 years of age would be very useful for their early detections resulting in a better outcome as in the case of other rare diseases.<sup>[22]</sup> The proper presurgical investigations are of major importance because they orientate the therapeutic plan, the surgical approach, the surgical team and the type of surgical intervention.

In another study performed by Hermans et al, on 111 patients with adnexal tumors, with the median age of  $10.2 \pm 5.6$  years, treated in a period of 15 years, who benefited by a surgical intervention in 83.1% cases, with 46.4% cases of oophorectomy and only 25.2% malignant tumors. The authors concluded that the presence of gynecologist in the therapeutic plan was the only factor that decreases the incidence of oophorectomy in benign masses,<sup>[23]</sup> as in our study. The same authors in a former study proved that in case of benign tumors, ovariectomy was more frequently performed during premenarche, and the ovary sparing was mostly during post-menarche.<sup>[2]</sup> Regarding our series of cases, we had only 1 case during premenarche whom underwent oophorectomy, whereas for the postmenarche tumors, unilateral oophorectomy or adnexectomy was performed in the remaining cases.

The surgical approach of adnexal masses can consist in either laparotomy or laparoscopy depending on factors related to both the tumor and the patient. The advantages of laparoscopic

approach consist in less perioperative discomfort and blood loss, minimal tissue trauma, decreased hospitalization period and lower overall related-care costs.<sup>[24,25]</sup> Postsurgical cosmetic results is another benefit of the laparoscopy being of particular importance in young ages, and it should be taken into account in the therapeutic decision of pediatric patients with adnexal masses.<sup>[26]</sup> Moreover, the complications rates between laparoscopic approach and laparotomy are comparable.<sup>[27]</sup> In our series of cases, we did not encounter any intra or post-surgical complications independently of the surgical approach. The first one is especially indicated in cases of malignancy suspicion, unstable hemodynamic status, with pelvic adhesion syndrome or those with other comorbidities (cardiac or pulmonary disorders) which may preclude abdominal insufflation.<sup>[5]</sup> Due to the rarity of malignant conditions in pediatric ages, laparoscopy became the first choice even for cystic lesions of up to 25 de cm considered benign,<sup>[5]</sup> being a viable option even in giant paraovarian cysts.<sup>[28]</sup> In case of malignant tumors stage IA–IC, when the cyst content is spilled into the peritoneal cavity, adjuvant treatment may be required or even laparotomy.<sup>[7]</sup> Nevertheless, Seckin et al<sup>[29]</sup> found strong correlation between the operative diagnosis and the histopathological exam underlining that under the circumstances of a thorough exploration of both tumor and pelvis, laparoscopic approach may be a safe procedure in adolescents. Therefore, careful tumor examination during the surgery may prevent misdiagnosis of malignant lesions, and laparoscopy achieved a sensitivity of 87.5% and specificity of 98% in this area.<sup>[30,31]</sup> The impact of the surgical approach on the further fertility is also of major importance. Thus, Quint et al reported in 1999 a rate of 85% for salpingo-oophorectomy, of whom 9 cases underwent bilateral oophorectomy.<sup>[5]</sup> Later, Eskander et al in 2011, showed on a study performed on 190 pediatric patients who underwent surgical intervention for malignant or benign adnexal tumors a percentage of ovary preservation of 50%, but oophorectomy was performed in all 12 cases found with malignant lesions.<sup>[32]</sup> Also, Bristow et al<sup>[33]</sup> assessed the impact of the surgical approach in ovary preservation in young women with adnexal masses, and proved that the rate of preservation was higher in case of surgical intervention performed by gynecologists in comparison to the cases where it was performed by surgeons.<sup>[33]</sup> Moreover, the conservation of the ovary whenever possible is essential also due to the possibility of cyst development in the contralateral ovary otherwise resulting in bilateral oophorectomy in the future.<sup>[34]</sup> In our series of cases, 1 patient underwent ovariectomy, and 2 of them adnexectomy. Also, Laparoscopic approach was chosen in the case of our patient with borderline tumor, while the dysgerminoma and mature teratoma patients underwent laparotomy.

The limitations related to the diagnosis or the management in the 3 cases presented above consisted in increased patient's weight (the borderline tumor patient) that hindered both the pre-surgical ultrasound exam and the surgical intervention, and the fact that in 2 of our cases the gynecologist was not present at the surgical intervention.

#### 4. Conclusions

Ovarian or adnexal tumors in pediatric patients are most of the time benign and can benefit from a laparoscopic approach as a first choice. The diagnosis, the intervention, and the therapeutic plan must be based on the symptoms, pelvic ultrasound and potential serum markers.

## Author contributions

Dr Mărginean Cristina Oana, Dr Mărginean Claudiu, Dr. Mărginean Maria Oana and Dr Meliț Lorena Elena conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr Chinceșan Mihaela, Dr Săsăran Vlăduț and Stud. Cristian Dan Mărginean designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript.

Dr Mărginean Claudiu was involved in the surgical management, designed the data collection instruments, coordinated and supervised data collection, and critically reviewed the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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**Validation:** Cristina Oana Mărginean.

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**Writing – review & editing:** Cristina Oana Mărginean, Claudiu Mărginean, Mihaela Chinceșan, Maria Oana Mărginean, Lorena Elena Meliț.

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