



Caso Clínico

## Precocious Menarche: Functional Ovarian Cystadenoma?



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### A B S T R A C T

Precocious menarche is rare and should be investigated when not consistent with pubertal development.

Seven-years-old girl with painful bilateral breast button and menarche. Analytically with slightly elevated estradiol, normal endocrinological study and negative tumor markers. Ultrasound showed a large right ovary cystic lesion compatible with an ovarian cystadenoma. Magnetic resonance imaging showed an enlarged right ovary with a medullary cystic lesion and parenchymal preservation, suggestive of an ovarian cystadenoma. Multidisciplinary follow-up showed breast reduction, absence of vaginal hemorrhages or other signs of puberty. One year later, ultrasound showed spontaneous resolution of the ovarian cystadenoma.

This case describes a large functional cystadenoma with spontaneous resolution. Non-invasive approach may be safe but clinical close surveillance is imperative.

### Menarca Precoce: Cistoadenoma Funcionante do Ovário?

#### R E S U M O

A menarca precoce é uma condição rara que deve ser investigada quando ocorre em não consonância com o desenvolvimento pubertário.

Menina de 7 anos com botão mamário doloroso bilateral e menarca. Analiticamente com estradiol ligeiramente elevado, estudo endocrinológico normal e marcadores tumorais negativos. Ecografia apresentou lesão cística de grandes dimensões do ovário direito compatível com cistoadenoma do ovário. Ressonância magnética revelou ovário direito aumentado com lesão medular cística e preservação do parênquima, sugestiva de cistoadenoma do ovário. Seguimento multidisciplinar com redução do tamanho da mama, ausência de hemorragia vaginal ou outros sinais de puberdade. Repetiu ecografia um ano depois onde se constatou resolução espontânea do cistoadenoma do ovário. Este caso descreve um cistoadenoma funcionante do ovário de grandes dimensões com resolução espontânea. A abordagem não invasiva pode ser segura, mas é necessário a vigilância apertada.

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## Introduction

Precocious puberty (PP) in caucasian girls is defined as the development of secondary sexual characteristics before the age of 8 years and may range from normal variants of pubertal development to pathological processes.<sup>1</sup> Most cases of PP are due to normal variants of pubertal development and do not require treatment. All cases of PP should be carefully evaluated, mainly those occurring at younger age. Vaginal bleeding before the age of 8 years or not consistent with pubertal development requires additional evaluation and prompt referral to a pediatric endocrinologist.

Pediatric cystic abdominal masses have several etiologies and can occur in almost every intra-abdominal organ. Differential diagnosis should be made with abscess, teratomas and necrotic or cystic changes in tumors.<sup>2</sup>

In girls, pediatric tumors of the genital tract are rare, and among them, ovarian tumors are the most frequent.<sup>3</sup> Its incidence increases with age, and most cases are benign or physiologic, such as functional cysts.<sup>3-5</sup> Germ cell tumors are the most frequent ovarian tumors in children, and within these, about 10%-17% are epithelial tumors.<sup>4-6</sup> The majority of ovarian epithelial tumors are mucinous or serous cystadenomas.<sup>2</sup> Childhood epithelial tumors are usually unilateral, and a minority (12%) can be malignant.<sup>2</sup> Malignant tumors can be up to 10% of ovarian masses and are more frequent during premenarchal age.<sup>3,4</sup>

Ovarian tumors usually present with abdominal pain, increased abdominal volume, nausea, vomiting or symptoms that result from surrounding compression of urinary or intestinal organs. Rarely, they can present with PP or menarche due to hormonal disorders. Ovarian cysts can also present as asymptomatic abdominal mass or incidental imaging finding.

After the diagnosis of an ovarian mass, it is important to establish the malignant potential since it will determine the therapeutic approach and consequently the prognosis. The diagnosis is based on ultrasound and magnetic resonance image (MRI). Ultrasound criteria can differentiate benign from malignant tumors. Tumor markers, such as, cancer antigen 125 (CA-125), alpha-fetoprotein ( $\alpha$ -FP), beta-human chorionic gonadotropin ( $\beta$ -hCG), carcinoembryonic antigen (CEA), inhibin, lactate dehydrogenase (LDH) and cancer antigen 19-9 (CA 19-9) are useful, but nonspecific.<sup>3,4</sup> The presence of tumor markers, along with abdominal ultrasound data such as size, homogeneity, and presence of solid components, raise the suspicion of malignancy. The absence of tumor markers does not exclude the diagnosis since they can be positive in only 54% of cases.<sup>3</sup>

Treatment of ovarian epithelial tumors, such as cystadenomas, remains controversial. The therapeutic approach of ovarian tumors is mostly surgical and should be evaluated by a multidisciplinary team that includes Pediatrics, Gynecology and Pediatric Surgery. The preservation of the ovary is very important to maintain fertility.

The aim of this paper was to describe the presentation of a benign tumor of the ovary and its evolution to spontaneous resolution. Written informed consent was obtained from the patient's legal guardian for the publication of this case.

## Case Report

We report the case of a 7-years-old caucasian girl referenced to Pediatric Endocrinology consultation due to suspected precocious puberty. The child's mother reported the appearance of painful bilateral breast button with 1-month-evolution but without

pubic or axillary hair, without apocrine odor and without capillary or cutaneous oil. Menarche occurred in the previous week with a catamenium duration of 4 days. There was no phytosterols intake, consumption of medicines or use of cosmetic products

There was a maternal notion of increase in growth velocity, but there were no measurements to prove it.

The child was lactose intolerant and had previous complaints of abdominal pain and diarrhea that resolved with lactose-free milk. Her growth was regular, with height at 75<sup>th</sup> percentile and weight at 25-50<sup>th</sup> percentile. There was no family history of puberty alterations. Her target family height was 169.5 cm (75-90<sup>th</sup> percentile). Remaining past history was unremarkable.

At the consultation, she presented the following anthropometric data: weight 22.8 kg (50<sup>th</sup> percentile), height 127.3 cm (75-90<sup>th</sup> percentile) and body mass index of 14.5 kg/m<sup>2</sup> (15-50<sup>th</sup> percentile). On examination, there were no dysmorphia, breasts were palpable bilaterally with 2-3 cm of diameter and without nipple elevation or enlargement, and there were no vulvar alterations. The remaining examination was unremarkable.

Bone age was similar to chronological age. Pelvic ultrasound showed the presence of an image adjacent to the right ovary with 40x27 mm, convex and with anechoic morphology, suggestive of a cystic formation. Analytically: normal blood count, normal erythrocyte sedimentation rate, LDH 442 U/L (reference range 142-290 U/L), normal lipid profile and transaminases. Endocrinological study: normal thyroid function, estradiol 22.3 pg/mL (reference value <15 pg/mL), FSH <0.3 mUI/mL, LH <0.1 mUI/mL, total testosterone <20 ng/dL and normal cortisol (13.7 ug/dL). Four days later, she repeated the pelvic ultrasound that confirmed the presence of a 51x25 mm cystic lesion in the right ovary in relation to a probable ovarian cystadenoma (Fig. 1). Uterus with

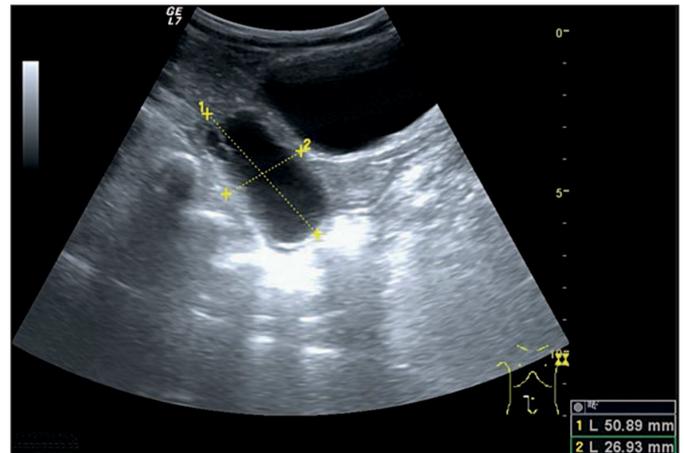


Figure 1. Ultrasound showing cystic lesion in the right ovary

preserved morphology, measuring 24x12x40 mm (TxAPxL), left ovary with normal morphology, without adnexal lesions. Tumor markers, such as CA-125, prolactin,  $\alpha$ -FP,  $\beta$ -hCG and CEA were within the normal limits. Two months later, a pelvic MRI was performed, and showed an enlarged right ovary with a cystic lesion measuring 19x22x33 mm centered on the medullary region of the ovary, with preservation of the ovarian parenchyma, suggesting an ovarian cystadenoma (Fig. 2). Left ovary and uterus with dimensions and morphology appropriate to the age group.

Due to the apparent size reduction of the cystic formation, surgery was postponed. Multidisciplinary follow-up was maintained

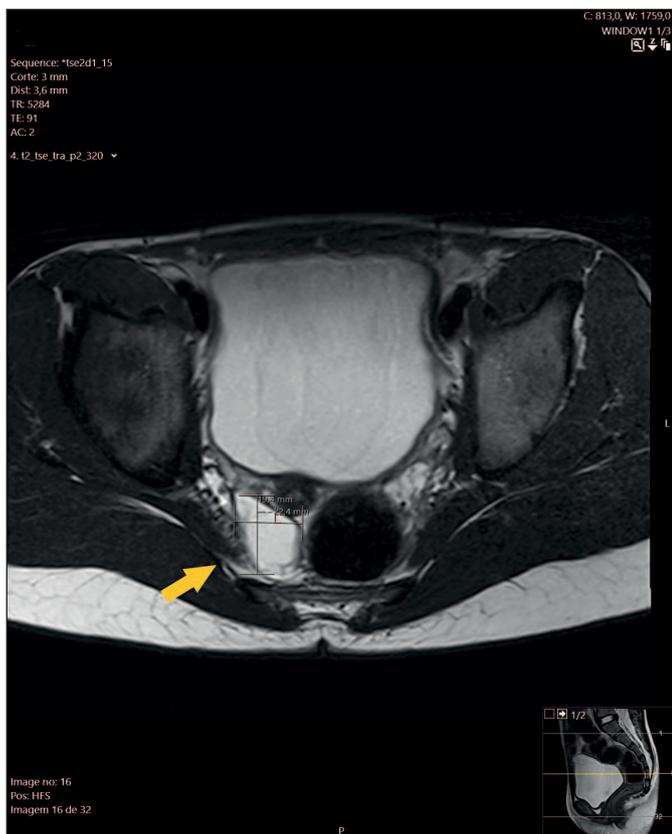


Figure 2. Pelvic MRI showing cystic lesion in the right ovary

with regular pediatric surgery and pediatric endocrinology consultations. During follow-up, she presented regular growth velocity, breast size reduction, and there were no new episodes of vaginal hemorrhage or other signs of puberty.

One year later, pelvic ultrasound was repeated and showed uterus with normal shape and dimensions for the age group, measuring 3.6x1.5 cm, and right ovary with 18 mm longitudinal diameter and left ovary with 16 mm, without any cystic formations. Analytical reassessment of the tumor marker CEA came back negative.

Despite the spontaneous regression and the presumptive diagnosis of a functioning ovarian cystadenoma, multidisciplinary follow-up was maintained.

## Conclusion

Ovarian masses may be cystic, complex, or solid. Most ovarian cysts, whether occurring in the prepubertal phase or in the pubertal phase, are physiological. Most ovarian tumors are benign, with cystadenomas being the most common type.<sup>8</sup> An early diagnosis of ovarian mass is necessary to reduce the risk of complications, such as ovarian torsion, and to improve the prognosis if a malignant neoplasm is diagnosed.

This case reports an unusual pathology in prepubertal girls, with clinical and imaging features suggestive of ovarian cystadenoma. Most pediatric ovarian cysts are functional and usually regress spontaneously.<sup>7</sup> According to the literature, ovarian masses measuring more than 8 cm rarely resolve spontaneously, with the majority requiring surgical removal.<sup>8</sup> This girl presented a cystic lesion compatible with cystadenoma, without unequivocal ultrasonographic criteria of functional cyst. Spontaneous resolution, particularly in large-volume lesions as in this case, is not

common, and is not described in the literature. This raises the hypothesis that an expectant attitude can be maintained if there are unremarkable clinical and analytical findings along with benign ultrasonographic characteristics. In those cases, an expectant attitude includes careful clinical follow-up and imaging control. However, if puberty continues to progress, surgery is mandatory, even if clinical, analytical or imaging findings are suggestive of benignity.

Ovarian masses can have a variable and nonspecific presentation, ranging from diffuse abdominal pain, increased abdominal volume, asymptomatic abdominal mass or hormonal disorders.<sup>5</sup> In this case, the initial presentation was a precocious puberty. The presence of bilateral breast button and the slightly elevated estradiol levels should raise the suspicion of either central or peripheral stimulation. Since gonadotropins are non doseable, the hypothesis of central stimulation is ruled out and the presence of an estradiol-secreting tumor or a physiologic cyst should be considered.

Although this girl has negative tumor markers, it is very important to maintain a careful clinical, analytical and imaging follow-up, since negative tumor markers do not exclude the existence of malignancy. Also, a small percentage of cystadenomas can become malignant.<sup>3</sup>

Pediatric population with adnexal tumors should be followed by a multidisciplinary team that includes Pediatrics, Gynecology and Pediatric Surgery. When necessary, surgery should be carefully programmed in order to preserve the ovary and maintain fertility.

The absence of follow-up protocols for this type of pathology makes research in this area important. Clinical and therapeutic approach should be based not only on individual experiences but on robust scientific evidence.

The presentation of this case aims to contribute to a better understanding of this unusual pathology in the pediatric age.

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