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Juvenile granulosa cell tumor associated with Maffucci syndrome in pregnancy: A case report

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ABSTRACT

Juvenile granulosa cell tumor (JGCT) is an extremely rare ovarian tumor that has been associated with Maffucci syndrome. It both secretes hormone and has been postulated to grow in response to hormone. We present a case of a 33-year-old G1P0 asymptomatic woman with a history of Maffucci syndrome found to have a left adnexal mass on routine ultrasonography at 13 weeks gestation. This case demonstrates the sonographic and magnetic resonance imaging (MRI) features of JGCT, as well as the natural progression of the tumor during pregnancy. A follow-up ultrasound 3 weeks after initial diagnosis demonstrated marked growth in size and vascularity of the tumor, prompting unilateral salpingo-oophorectomy. Histopathological findings confirmed the diagnosis of JGCT.

1. Introduction

A granulosa cell tumor (GCT) is a rare type of sex cord-stromal tumor arising from the granulosa cells of an ovarian follicle, accounting for < 5% of all malignant ovarian tumors [1]. GCT is divided into two distinct types: adult granulosa cell tumor and JGCT, with JGCTs representing 5% of all GCTs [2]. JGCT usually occurs in prepubertal girls and young women, with 97% occurring in the first three decades of life [2]. GCTs are estrogen-producing tumors and can manifest as precocious puberty in pediatric patients [3].

JGCTs have been reported in association with both Ollier disease and Maffucci syndrome, rare inherited disorders characterized by enchondromas, in addition to hemangiomas in the case of Maffucci syndrome. While the genetic underpinning of this association is unclear, mutations in the isocitrate dehydrogenase (IDH) 1 and 2 genes identified in the enchondromas in both Ollier disease and Maffucci syndrome have been proposed to account for the initiation of the tumorigenesis in JGCTs [4].

Few cases of JGCTs have been reported in pregnancy. It has been demonstrated that the hormonal environment associated with pregnancy alters the histological and biological features of JGCT, inducing tumor cells to synthesize steroid [5]. HCG, with its FSH-like properties, may also induce more rapid growth in GCTs [2]. It has also been postulated that pelvic congestion during pregnancy can promote tumor growth and malignant transformation [1].

2. Case report

A 33-year-old woman, gravida 1, para 0, diagnosed with Maffucci Syndrome at age 21, with a past medical history significant for only the syndrome's characteristic enchondromas and hemangiomas, was found to have a left adnexal mass on routine obstetrical ultrasonography at 13 weeks gestation. A pelvic ultrasound performed in the radiology department for further characterization revealed a well-defined, minimally heterogeneously isoechoic left ovarian mass measuring 5.2 × 4.1 × 3.9 cm (Fig. 1). The lesion demonstrated peripheral and minimal internal color Doppler flow with posterior acoustic enhancement, possibly related to a cystic component. A pelvic MRI was recommended for further evaluation.

Given her pregnancy status, a non-contrast enhanced pelvic MRI was performed 7 days later and demonstrated a solid left adnexal lesion with peripheral and internal cystic components. The solid components of the mass demonstrated T2 hyperintensity (Fig. 2a) and T1 hypointensity (Fig. 2b) without fat. Benign and malignant etiologies were postulated, and surgical consultation was advised. Incidental note was made of multiple T2 hyperintense, lobulated osseous lesions throughout the pelvis, consistent with enchondromas.

Interval laboratory studies revealed elevated CA-125 (60 U/ml; normal range ≤ 30.1 U/ml), anti-Mullerian hormone (180 ng/ml; normal range 0.66–8.75 ng/ml for females 31–35 years-old), and inhibin B levels (> 4325 pg/ml; normal < 290 pg/ml), with a normal CA 19–9 level (7 U/ml; normal range 0–37 U/ml).

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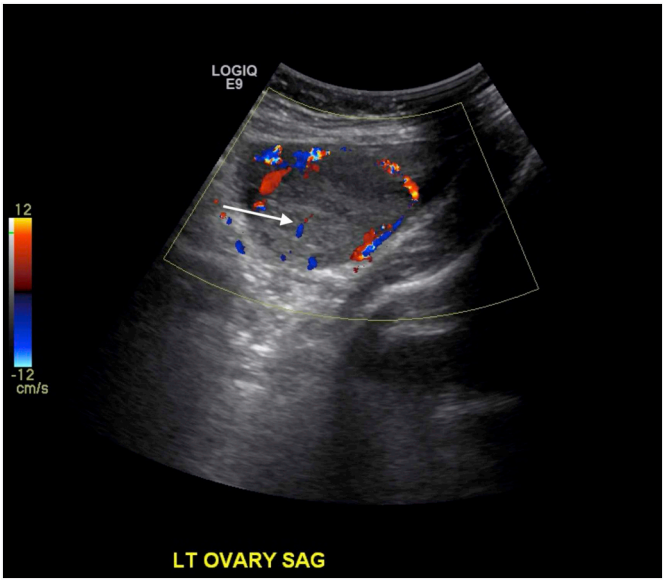

Fig. 1. Pelvic ultrasound with sagittal image of the left ovary demonstrates a predominantly solid isoechoic mass with mild posterior acoustic enhancement and minimal internal color Doppler flow (arrow).

Three weeks after the initial ultrasound, at 16 weeks gestation, a follow up pelvic ultrasound demonstrated increased size and vascularity of the predominantly solid left ovarian lesion, measuring 7.5 × 5.1 × 6.6 cm (Fig. 3). Color-flow Doppler imaging revealed a low resistance arterial waveform. Given the interval enlargement and dense peripheral vascularity of the mass, the patient proceeded to surgery later the same day.

Laparoscopic findings included a left ovarian mass replacing the entire left ovary, measuring approximately 8.0 cm, as well as straw-colored abdominopelvic ascites. Other pelvic organs, including the uterine tubes, right ovary, and gravid uterus, appeared free of disease. The peritoneal washing was negative for malignant cells. The patient underwent a left salpingo-oophorectomy and the post-operative fetal heart rate was normal.

Histologic examination of the ovarian mass revealed a nodular tumor consisting of round-to-oval cells with ample eosinophilic-to-amphophilic cytoplasm (Fig. 4a and b). The tumor was positive for inhibin and calretinin (Fig. 4c and d), while negative for EMA on immunohistochemical staining. Beta-catenin showed membranous staining. A reticulin special stain highlighted fibers surrounding clusters of tumor cells. The morphologic and immunohistochemical findings were consistent with JGCT.

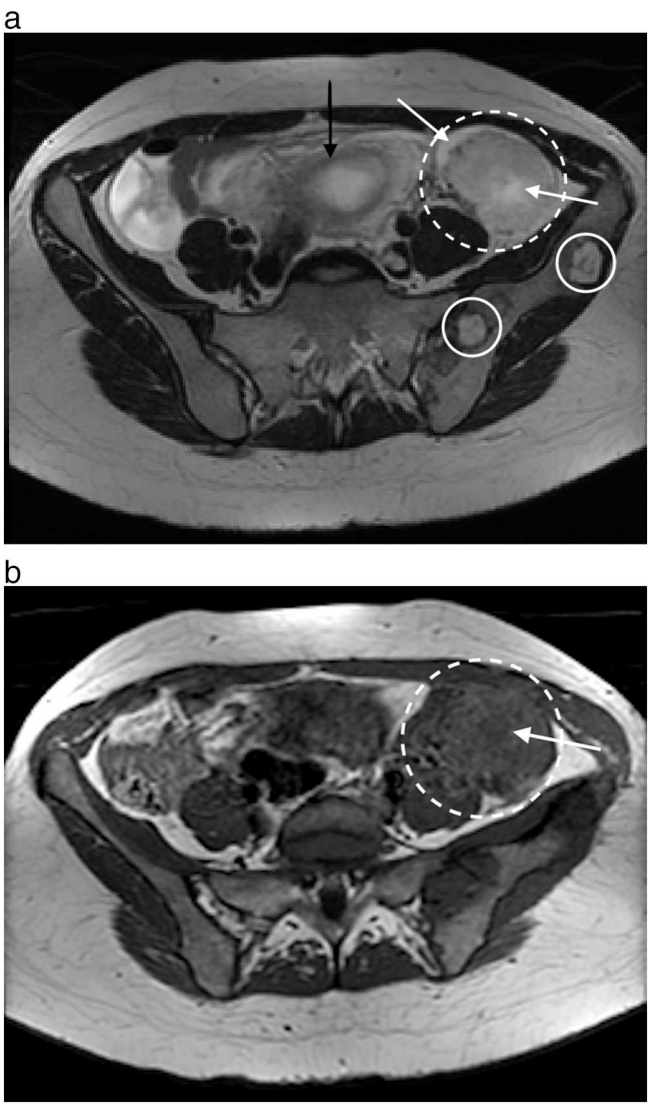

Fig. 2. a. Pelvic MRI with axial T2-weighted image demonstrates T2 hyperintense left pelvic mass (dashed circle) with internal and peripheral cystic components (white arrows). Lobulated hyperintense lesions incidentally noted in the left iliac bone are consistent with enchondromas (solid circles). The gravid uterus is partially seen (black arrow). b. Pelvic MRI with axial T1-weighted image demonstrates corresponding T1 isointensity of the left pelvic mass (dashed circle) with internal hypointensity consistent with cystic component seen on T2-weighted images (white arrow). No macroscopic fat is identified within the mass.

3. Discussion

In general, GCTs are considered to be low grade tumors, usually unilateral and confined to the ovary [6]; however, some patients with JGCTs have rapid tumor recurrence and metastases [1]. The rapid growth rate of the tumor demonstrated in the present case supports the concern that JGCTs may be more aggressive during pregnancy. Tumor markers have to be interpreted with caution during pregnancy. For example, CA-125 levels can be elevated during pregnancy, especially during the first trimester [7]. As a result, imaging plays an important role in the diagnosis of JGCT.

On MRI, JGCTs can appear entirely solid or cystic, the majority containing both solid and cystic components. They are typically large, unilateral, and sponge-like with cystic components and solid areas of high T2 signal intensity and homogeneous contrast enhancement [3,8]. The sonographic appearance of GCTs is nonspecific, including solid and cystic masses, solid masses with a spongiform appearance, and completely solid masses, but the juvenile forms typically demonstrate a dominant solid component [9,10]. Signs of estrogen secretion can also be seen, such as thickening of the endometrial stripe [9].

As demonstrated by the present case, pregnant patients with an ovarian mass and history of Ollier disease or Maffucci syndrome should raise suspicion for JGCT. Imaging evaluation and recognition of this association is key in facilitating early diagnosis and optimizing timing for resection, given the tumor's evolution during pregnancy and its potential, albeit low likelihood, for malignant behavior.

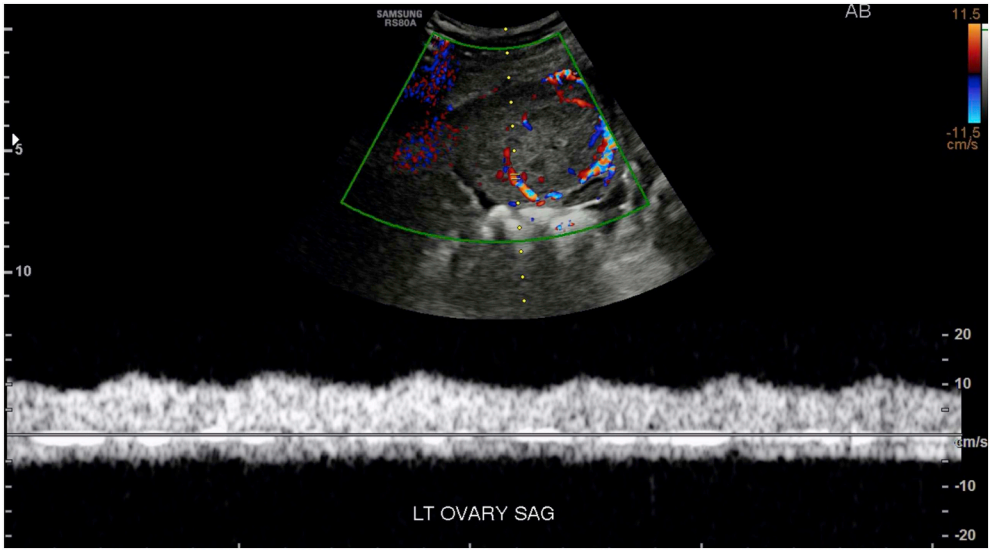

Fig. 3. Follow-up pelvic ultrasound with sagittal image of the left ovary demonstrates an interval increase in size and internal vascularity of the predominantly solid isoechoic mass with a low resistance arterial waveform.

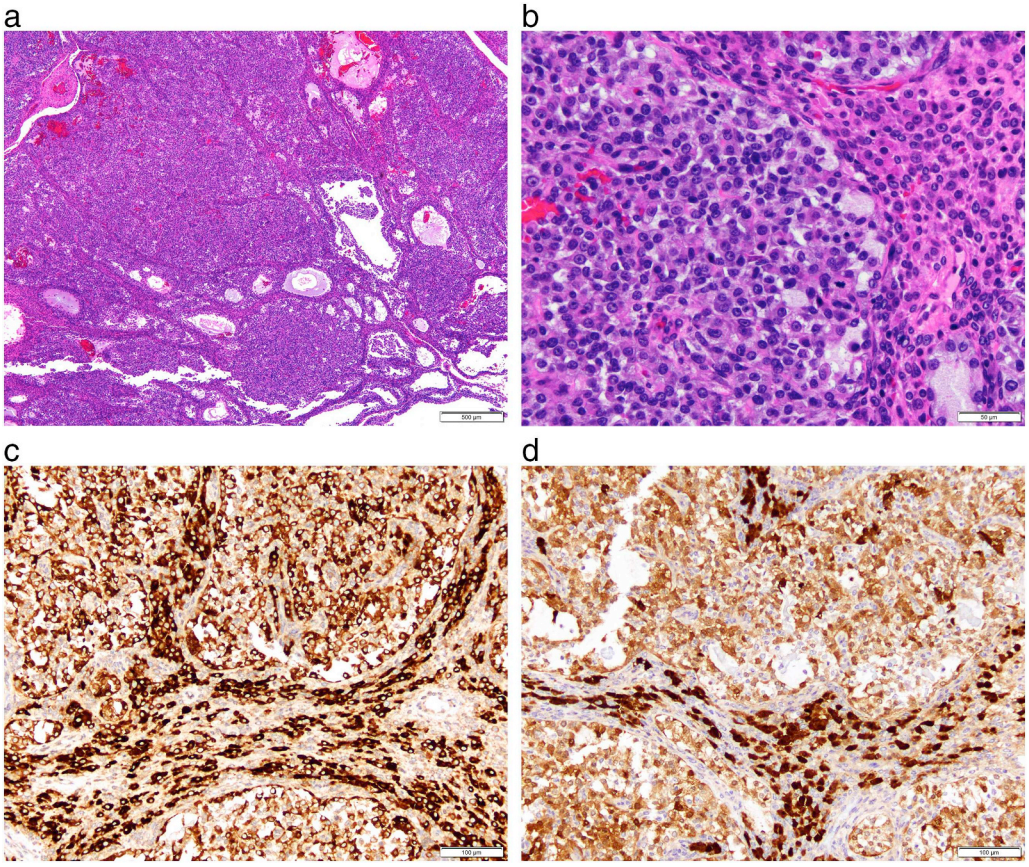

Fig. 4. a. Histopathology demonstrates solid nodules and variably sized follicular spaces. b. High power view shows round-to-oval granulosa cells with ample eosinophilic-to-amphophilic cytoplasm. The mitotic activity is brisk. Luteinized theca cells are present in the internodular septa. c. Immunohistochemistry for inhibin stains tumor cells. d. Immunohistochemistry for calretinin stains tumor cells.

Disclosure

No author has any potential conflict of interest.

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