Virilization and abdominal mass in a newborn female: A case report

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A B S T R A C T

We describe virilization in a newborn female secondary to bilateral congenital juvenile granulosa cell tumor (JGCT). The patient presented with abdominal mass and ambiguous genitalia at birth, and bilateral ovarian masses were discovered on further imaging. The patient underwent bilateral salpingo-oophorectomy in staged procedures, as it became apparent that we could not spare the ovaries. Diagnosis of JGCT was confirmed by surgical pathology. She required no adjuvant therapy and has no signs of recurrence at two-year follow-up.

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Virilization and ambiguous genitalia in a newborn female is an uncommon and complex problem with many possible causes. The most common cause for virilization in genetically female infants is congenital adrenal hyperplasia (CAH). Other conditions in the differential diagnosis include exposure to maternal androgens or exogenous hormones. We present a case of virilization secondary to bilateral congenital juvenile granulosa cell tumor (JGCT) with no other associated abnormalities.

1. Case report

A 5.2-kilogram 37-week gestation female was born to a 42-year-old G5P2202 woman by Cesarean section for failure to progress. Pregnancy was complicated by polyhydramnios and pregnancy-induced hypertension. Ultrasound at 20 weeks was consistent with a normal female fetus. APGARS at birth were 8 and 9. On physical exam, she was noted to have a palpable abdominal mass and ambiguous genitalia. The mid-abdominal mass was firm, mobile, nontender, and 8–10 cm in diameter. She had clitoromegaly with normal labia majora without evidence of posterior labial fusion. Her urethral and vaginal orifices appeared normal, and she had a patent anus. Basic metabolic panel was normal. Ultrasound demonstrated an abdominal mass with a cystic component. MRI revealed a normal uterus and bilateral cystic masses of the ovaries. On MRI, the larger mass measured 7.4 cm × 5.2 cm × 4.8 cm, and the smaller one measured 4.0 cm × 2.5 cm × 2.2 cm (Fig. 1).

Diagnostic laparoscopy demonstrated a large mass in the midline originating from the left ovary, as well as a smaller mass originating from the right ovary that had undergone torsion. Examination of the left ovary demonstrated multiple small cysts with no discernible ovarian tissue distinct from the mass. The right ovary was not ischemic and was detorsed. Surgical exploration was expedited before return of any laboratory values because of concern for torsion. With the evidently bilateral nature of the pathology, biopsies were obtained of the larger left mass in hopes that any normal ovarian tissue would be able to be preserved.

Pathology demonstrated juvenile granulosa cell tumor (JGCT) with no residual normal ovarian tissue. Hormonal studies are listed in Table 1. On day ten of life, she underwent left salpingo-oophorectomy and right ovarian biopsy with peritoneal washings. It was impossible to dissect the left Fallopian tube free from the mass. Right ovary pathology demonstrated JGCT as well, but peritoneal fluid was negative for neoplastic cells. After consultation with oncology, we elected to continue observation with surgery at a later date, to allow the possibility of ovary-sparing surgery.

She was discharged from the hospital at 5 weeks of age.
follow-up, her clitoromegaly had slightly improved, and her right ovary was smaller at 4.2 cm. At follow-up, her clitoromegaly had slightly improved, and her right ovary was smaller at 4.2 cm. Her right ovary had cystic areas of JGCT. Pathology demonstrated very small fragments of ovary with multiple nodules and cystic areas of JGCT. Peritoneal washings were again negative. Therefore, the tumor had been limited to the bilateral ovaries, corresponding to FIGO stage Iib, for which no chemotherapy is indicated. By Children’s Oncology Group (COG) staging, it would be stage II.

She was lost to follow-up after discharge for 2 years and seen again at the age of 2.5 years, fortunately without evidence of recurrence. Tumor markers were normal with Inhibin B less than 10 pg/mL and AMH less than 0.1 ng/mL, and ultrasound demonstrated no evidence of recurrent or residual tumor. She will continue long-term surveillance and will require hormone replacement therapy.

2. Discussion

Juvenile granulosa cell tumors (JGCT) are the most common sex cord-stromal tumor (SCST) in the pediatric population. Gynecologic tumors make up less than 5% of pediatric neoplasms, and SCSTs are rare within this group (10%), with germ cell tumors being far more common (60–70%). SCST most commonly presents between four and nine years of age and JGCT are exceedingly rare in infancy and early childhood. Peritoneal washings and biopsy of the contralateral ovary should always be performed [1,2,9].

Chemotherapy is recommended only if the tumor has spread beyond the ovaries. It is uncommon for patients to present with advanced disease. In one study from 2002, seven patients were identified with tumors stage II or higher. Adjuvant cisplatin-based chemotherapy was used with all patients achieving complete clinical remission. Radiotherapy was used in one patient with diffuse peritoneal metastases [10]. Schneider et al., in 2005 described long-term survival and remission in four of six patients with stages II and III JGCT following surgery and adjuvant chemotherapy with cisplatin-based therapy. The two patients that died described long-term survival and remission in four of six patients beyond the ovaries. It is uncommon for patients to present with advanced disease. In one study from 2002, seven patients were identified with tumors stage II or higher. Adjuvant cisplatin-based chemotherapy was used with all patients achieving complete clinical remission. 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evidence of spontaneous regression of JGCT after an infant’s parents refused bilateral oophorectomy. Two months after diagnosis of JGCT, the patient had normal hormone levels and this persisted over two years of follow-up [12].

Ovarian sex-cord stromal tumors (SCST), which includes JGCT as a subtype, have also been associated with familial pleuropulmonary blastoma (PPB) and the DICER1 gene mutation. The ovarian SCST may be the initial clinical presentation of DICER1 mutations within some families, so genetic testing should be considered in these patients, especially if they have any signs of leprechaunism or if they develop a PPB [13,14]. These families should also be counseled about registering with the PPB Registry at http://www.ppbregistry.org.

This is a rare case of congenital bilateral JGCT in a patient with no other genetic abnormalities. Initial surgical management was left salpingo-oophorectomy with delay of right salpingo-oophorectomy in hopes that the tumor would regress and allow ovariectomy surgery in the future. Especially with bilateral pathology, an ovarian sparing operation should be performed when possible. At her second operation for small bowel obstruction, the tumor remained concerning with no residual normal ovary and right salpingo-oophorectomy was performed. She will continue to follow-up with routine imaging and tumor markers for surveillance of late recurrence.

3. Conclusion

Congenital bilateral JGCT is exceedingly rare. Ovary-sparing surgery should be the primary goal, particularly in infants with bilateral disease, but often this cannot be achieved. With early diagnosis and treatment, outcomes are favorable, but long-term follow-up is imperative to detect any late recurrences.

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