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Juvenile Granulosa Cell Tumor of the Testicle – Report of a Neonatal Case with Positive Alpha-fetoprotein Immunohistochemical Staining

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ABSTRACT

We report on a case of juvenile granulosa cell tumor of the testicle in a neonate, a rare testicular tumor in children. No genital ambiguity, anatomic abnormalities, nor sex chromosome aneuploidy was noted in this patient. In our case, despite positive staining for alpha-fetoprotein which is most consistent with yolk sac tumors, all clinical, gross anatomic, histologic, and other immunohistologic characteristics of the tumor remained consistent with the diagnosis of juvenile granulosa cell tumor. The alpha-fetoprotein positivity of the tumor remains unexplained.

Introduction

Testicular tumors in the pediatric population are majority yolk sac tumors, followed by stromal derived tumors, teratomas and seminomas. According to the Prepubertal Testis Tumor Registry of the Urologic Section of the American Academy of Pediatrics, of 395 total tumors registered, 244 (62%) were yolk sac tumors and 43 (11%) were stromal tumors—of the stromal tumors, 11 (26%) were juvenile granulosa cell tumors (JGCT) making up less than 3% of the total. Twenty-two of the tumors within this registry were from neonates, six each being JGCT or yolk sac tumors.

JGCT is the most common subtype of sex cord-stromal tumor diagnosed in the male neonatal population and is sometimes associated with intraabdominal testes, sex chromosome abnormalities, and/or ambiguous genitalia.[1] It usually presents as a painless scrotal mass, peaking in incidence during the first two years of life and then again in young adulthood, with ultrasound findings demonstrating a multicystic mass. These tumors generally have a complex cystic appearance on gross pathologic examination, histologically appear similar to ovarian granulosa cell tumors, and immunohistologically characteristically stain positive for inhibin and negative for alpha-fetoprotein (AFP).

Case description

The patient was a male born at 39 weeks gestational age to a G_1P_{1001} 22-year-old mother who received routine prenatal care, had no significant past medical, surgical or infectious history, via spontaneous vaginal delivery complicated by prolonged rupture of membranes and associated intrapartum elevated temperature.

The delivery itself was complicated by heavy meconium requiring tactile stimulation, nasal and oral suctioning of the neonate in the delivery room. He was subsequently observed for sepsis as per hospital protocol.

His birth weight, length, and head circumference were 3550 grams, 53 centimeters, and 35 centimeters, respectively, all within 50-90th percentiles. The only pertinent positive finding on physical exam was an enlarged descended left testis, smooth and firm to palpation and translucent upon light examination without any associated erythema or tenderness noted. The right testis was descended and palpable without enlargement, and his penis was normal.

Scrotal ultrasound revealed an enlarged left testicle measuring 2.7 × 1.7 × 2.7 centimeters that was completely replaced by a multicystic mass with internal vascular flow (Figs. 1 and 2). Differential diagnosis included teratoma, granulosa cell tumor, or less likely, yolk sac tumor. The right testicle was normal. Pre-surgical

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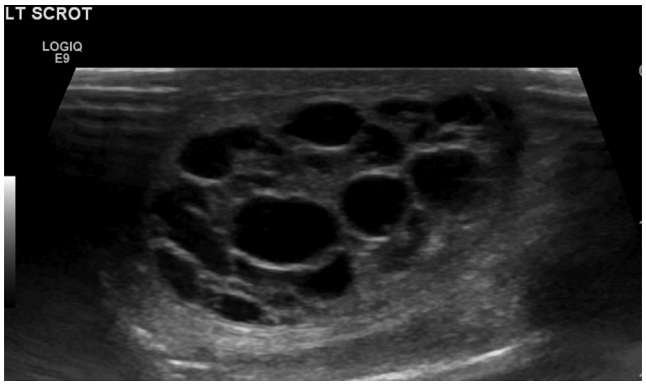

Figure 1. Sonogram of tumor showing complete cystic replacement of testes.

urology and hematology/oncology referrals were made in addition to laboratory testing that included lactate dehydrogenase (885 IU/L, normal 160-450 IU/L), beta- human chorionic gonadotropin (48.58 IU/L, normal ≤50 IU/L) and alpha-fetoprotein (113, 200 ng/ml, no reference range).

On day two of life, the patient underwent a left radical inguinal orchiectomy without complications. Gross pathologic examination revealed a 2.5 × 2.0 × 1.0 centimeter gray–white ovoid mass with multiple cysts containing light yellow glistening fluid which was basophilic/mucicarminophilic upon staining. The tumor was limited to the testis/epididymis without extension into the spermatic cord. Histologically there were variably shaped and sized follicles within a fibrous stroma containing foci of nests of tumor cells. The tumor cells were mostly small- to medium-sized with round to oval nuclei, inconspicuous nucleoli, and ranging from scant to abundant, pale to lightly eosinophilic, sometimes vacuolated cytoplasm. Immunohistochemical stains were positive for inhibin, calretinin, CD99, SF-4, FOXL2, and importantly, AFP, while negative for CD30, CD117, D2-40, PanCK, PLAP, glypican-3 and OCT3/4. The patient was discharged home with a diagnosis of JGCT with appropriate subspecialty follow-up.

Since discharge the patient has clinically done well without any symptoms or signs of recurrence. He continues to have his tumor markers followed every three months, with his most recent results at 7 months of age being as follows: inhibin A antibody (1 pg/ml, normal <2 pg/ml), beta- HCG (<1 mIU/ml), and AFP (41.9 ng/ml).

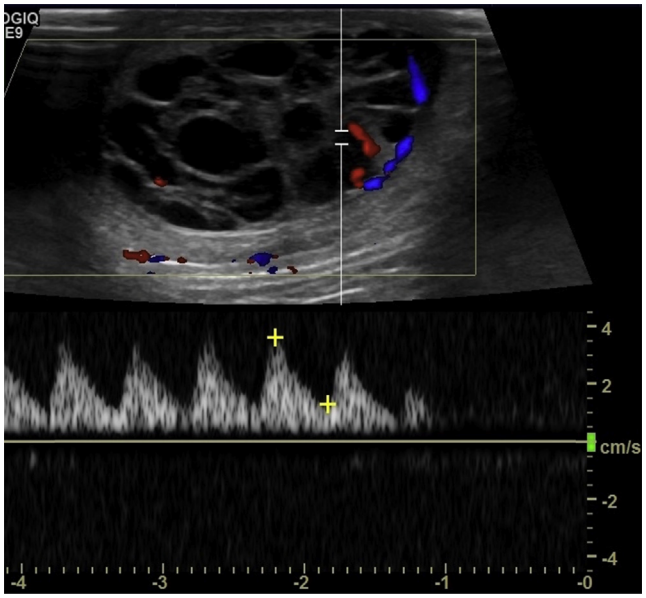

Figure 2. Sonogram with Doppler demonstrating minimal bloodflow to lesion.

Discussion

Usually JGCT has strong inhibin expression and negative AFP immunohistochemistry staining. However, its immunohistologic pattern is on occasion difficult to distinguish from that of yolk sac tumors. A clinicopathologic study of 70 cases of JGCT performed by Kao et al described 79% of cases with mixed follicular and solid patterns staining positive for inhibin, calretinin, WT1 and FOXL2. AFP staining was uniformly negative except for one case that showed focal reactivity.[2] Our case would be the second one reporting the same AFP positivity in this type of tumor.

Since JGCT is a subtype of stromal tumors which is hormonally inactive, serum AFP and BHCG levels are obtained postoperatively, with the former effectively ruling in yolk sac tumor if remaining persistently elevated.

In cases such as ours where immunohistochemical stains fail to be absolutely diagnostic for JGCT, nonroutine tests on the tumor tissue could be done. For example, findings on electron microscopy such as dual epithelial-smooth muscle differentiation, similarity to primitive Sertoli cells and pre-ovulatory granulosa cells, granulosa cells with continuous basal lamina, and cytoplasmic filaments with evenly distributed dense bodies resembling smooth muscle, may be definitive.[3,4] Additionally, molecular markers such as cytoplasmic expression of SOX9 or dysregulated immunohistologic expression of GATA6 and CSF1R could also be helpful.[5,6]

Conclusion

JGCT occasionally manifest AFP positivity, a marker that argues a yolk sac origin of the tumor and betrays its stromal origin. In order to mete out this ambiguity, in addition to measurement of serum tumor markers post excision, electron microscopic examination and staining for additional immunohistologic markers GATA6 and CSF1R can be performed. Adding these modalities to the diagnostic search to definitively rule out possible yolk sac origin or admixture within a JGCT increases the prognostic certainty of a benign course post-excision of the tumor and should be performed routinely in these rare cases.

Conflicts of interest

None of the authors have any financial conflicts of interest in relation to this paper.

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References

1. Partalis N, Tzardi M, Barbagadakis S, Sakellaris G. Juvenile granulosa cell tumor arising from intra-abdominal testis in newborn: Case report and review of the literature. *Urology*. 2012;79:1152–1154.
2. Kao CS, Cornejo KM, Ulbright TM, Young RH. Juvenile granulosa cell tumors of the testis. A clinicopathologic study of 70 cases with emphasis on its wide morphologic spectrum. *Am J Surg Pathol*. 2015;39(9):1159–1169.
3. Ranu SU. *Testis and Epididymis: Sex-cord Stromal Tumors—Granulosa Cell Tumor*. Pathology; 2013. Outlines.com. http://www.pathologyoutlines.com/topic/testisgranulosa.html. Accessed 25 October 2016.
4. Perez-Atayde AR, Joste N, Mulhern H. Juvenile granulosa cell tumor of the infantile testis. Evidence of a dual epithelial-smooth differentiation. *Am J Surg Pathol*. 1996 Jan;20(1):72–79.
5. Kalfa N, Fellous M, Boizet-Bonhoure B, et al. Aberrant expression of ovary determining gene FOXL2 in the testis and juvenile granulosa cell tumor in children. *J Urol Oct*. 2008;180(4 Suppl):1810–1813.
6. Mould AW, Duncan R, Serewko-Auret M, et al. *Int J Cancer*. 2009 March 1;125(4):1122–1132.