Congenital Juvenile Granulosa Cell Tumor of the Testis in Newborns

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Abstract. *Background: Granulosa cell tumor of the testis is a rare intermediate stromal cell tumor that can be distinguished in the adult and juvenile type. The juvenile type is the most common reason for scrotal swelling in newborns under the age of six months. Less than fifty cases of this disease entity have been reported in the literature. Patients and Methods: In the following article, two newborn patients with scrotal swelling and a histological confirmation of juvenile granulosa cell tumor of the testis will be presented. Results: Case 1: A newborn patient presented with massive scrotal swelling. Sonography of the testicle exhibited a multiple septic and cystic enlargement of the testicle without distinction of the testicular parenchyma being possible. The laboratory findings demonstrated normal testosterone levels, β-HCG and inhibin-B levels as well as an increased alpha-fetoprotein level of 35.350 ng/dl. Due to clinical and sonographic findings, an inguinal exploration and later, due to the impossibility of distinction of the testicular parenchyma, an inguinal orchiectomy of the right testicle was performed. Case 2: The clinical and sonographic examination of a newborn patient demonstrated a suspicious process of the left testicle. Sonography exhibited an enlarged testicle with cystic formations with the distinction of the testicular parenchyma not being possible. The laboratory findings demonstrated normal testosterone levels, β-HCG and inhibin-B levels as well as an increased alpha-fetoprotein level of 9.038 ng/dl and LDH of 768 U/I. An inguinal orchiectomy of the left testicle was performed. In both cases, a histological diagnosis of juvenile granulosa cell tumor of the testis was made. Conclusion: These two aforementioned cases demonstrate that juvenile granulosa cell tumor of the testis is a benign disease encountered in newborns, which exhibits an excellent prognosis. Inguinal orchiectomy is the therapy of choice. After surgical removal of the involved testicle is performed no further management is required.*

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Granulosa cell tumor of the testis is a rare intermediate stromal cell tumor that can be distinguished in the adult and juvenile type. Although the juvenile type accounts for only 1.2% of all prepubertal testis tumors entered into the Prepubertal Testis Tumor Registry, it is the most common stromal cord neoplasm of the testis in infancy (1-2). Juvenile granulosa cell tumor (JGCT) of the testis has only been clearly delineated as a distinct entity since 1985 (2) and has been named so due to its histological similarity to the ovarian granulosa cell tumor (3). To date, fewer than 50 cases have been reported in the literature. We report on two additional cases of newborn male infants presenting with JGCT.

Patients and Methods

Case 1. A newborn patient was reported to appear unremarkable during fetal ultrasound. He was born by normal spontaneous vaginal delivery and with no prenatal or postpartum medical problems. During an initial physical examination, the infant was found to have enlargement of the right hemiscrotum (Figure 1). A testicular ultrasound was performed revealing a normal left testicle in the scrotum. However, in the right hemiscrotum, testicular ultrasonography revealed a 6×6×4 cm multiple septic cystic enlargement of the testicle, "Swiss-cheese"-appearing without any distinction of the testicular parenchyma (Figure 2). The rim of this cystic mass was extremely hypervascular on color Doppler examination. Laboratory findings demonstrated normal testosterone, β-HCG and inhibin-B levels and an increased alpha-fetoprotein level of 35.350 ng/dl. Following clinical and sonographic findings, an

inguinal exploration and later due to the inability to distinguish the testicular parenchyma, an inguinal orchiectomy of the right testicle was performed without complications.

The specimen was tan with a mixture of solid and cystic areas. Gross examination revealed a 6×6×4 cm well circumscribed tumor. The cut surface showed a white-gray, glistening, spongy lesion (Figure 3). Microscopically, the tumor had a prominent solid pattern with focal follicles. The follicles were small and irregular and contained a basophilic fluid. The cells were spindle to round-shaped with nongrooved nuclei, a moderate amount of pale cytoplasm, and an indistinct border (Figure 4). Immunohistochemical stains were positive for CD99, inhibin, and calretinin, all of which are markers for gonadal stromal tumors. It was negative for desmin, smooth muscle actin, epithelial membrane antigen, S100 protein, and alpha-fetoprotein. His convalescence was uneventful. Up to the present day and after 24 months of follow-up, there is no evidence of disease recurrence.

Case 2. Clinical and testicular ultrasound examination of a newborn patient demonstrated a suspicious process of the left testicle. As for the aforementioned patient, this patient was also reported to appear unremarkable during fetal ultrasound, was born by normal spontaneous vaginal delivery and no prenatal or postpartum medical problems were noted. Testicular ultrasound of the left testis exhibited a 5×6×3 cm multiple septic cystic enlargement, "Swiss-cheese"-appearing with the distinction of the testicular parenchyma not being possible. The rim of this cystic mass was, as in the previous case, extremely hypervascular on color Doppler examination. Laboratory findings demonstrated normal testosterone, β-HCG and inhibin-B levels, an increased alpha-fetoprotein level of 9.038 ng/dl, as well as an LDH of 768 U/I. Due to clinical and sonographic findings, an inguinal exploration and later due to the inability to distinguish the testicular parenchyma, an inguinal orchiectomy of the left testicle was performed without complications. Gross examination, microscopical examination and immunohistochemical stains were compatible with the aforementioned first patient and revealed a JGCT as well. Up to the present day and after 9 months of follow-up, there is no evidence of disease recurrence.

Discussion

Stromal testicular tumors account for 8% of testicular neoplasms (4). JGCT is a rare testicular tumor that is thought to arise from a specialized gonadal stroma of the testicle and only a scant number of cases have been reported (5–7). This type of tumor is very similar in appearance histologically to a JGCT of the ovary. The ovarian counterpart of this tumor has been described on magnetic resonance imaging in the past (8). JGCT was a term first used by Crump in 1983 to describe a sex-cord stromal tumor occurring in an intra-abdominal testis in a 30-week-old fetus (5). Two years later, Lawrence *et al*. (2) reported 14 cases and firmly established this tumor as a distinct clinicopathological entity. The age at diagnosis ranges from neonates to 21 months and the distribution is equal in terms of right *versus* left side (2, 4, 6, 9). The presentation is that of a testicular mass without endocrinological abnormalities. In fact the detection of endocrine changes in patients with testicular lesions should exclude the diagnosis of JGCT (10).

Tumor markers such as alpha-fetoprotein and β-HCG are within the normal range for this age. A total of 20% of the cases reported are in children with chromosomal abnormalities affecting the Y chromosome (11, 12). Grossly the tumor appears as a tan to yellow mass with a mixture of solid and cystic regions without necrosis or hemorrhage. These cysts are thin walled, vary in size from 0.8 to 6.5 cm, and contain mucoid material (13, 14). Microscopically, the cysts are lined with single or multiple layers of granulosa cells with or without solid nodules of granulosa cells. The granulosa cells stain positive for cytokeratin and vimentin (14).

The differential diagnosis includes teratoma, cystic dysplasia of the testicle, Sertoli cell tumor and yolk sac tumor. Paratesticular masses such as paratesticular sarcomas should also be considered. Teratomas, yolk sac tumors, and paratesticular sarcomas have all been described as having cystic and solid components on ultrasound. Teratomas can be excluded due to the age of the patients. Yolk sac tumors originate in the testicle and spread locally to involve the epididymis. Paratesticular sarcomas usually originate in the spermatic cord and spread locally to involve the epididymis. All these tumors can grow to a large size and can involve all scrotal structures (15). Cystic dysplasia of the testicle is a rare condition that can originate during childhood and can persist into adulthood. Pathologically this reflects a cystic dilatation of the rete testis and additionally does not have a solid component and thus should not be hypervascular (16).

Although JGCT is universally benign and carries an excellent prognosis, the diagnosis of this disease is usually based on pathological assessment, most commonly made after surgery. Thus, inguinal orchiectomy still remains the cornerstone in the treatment of this relative uncommon entity. In recent years however, thanks to the increased sensitivity of radiological investigations and in combination with clinical suspicion, the pre-operative diagnosis of this tumor is now possible. Therefore, due to its benign nature, it is possible, with a high index of suspicion and a definitive frozen section diagnosis, to enucleate these tumors, leaving the remainder of the testis (17).

As seen in these two cases, JGCT of the testis is a benign disease with an excellent prognosis. Inguinal orchiectomy is the therapy of choice and after surgical removal of the involved testicle has been performed no further management is required.

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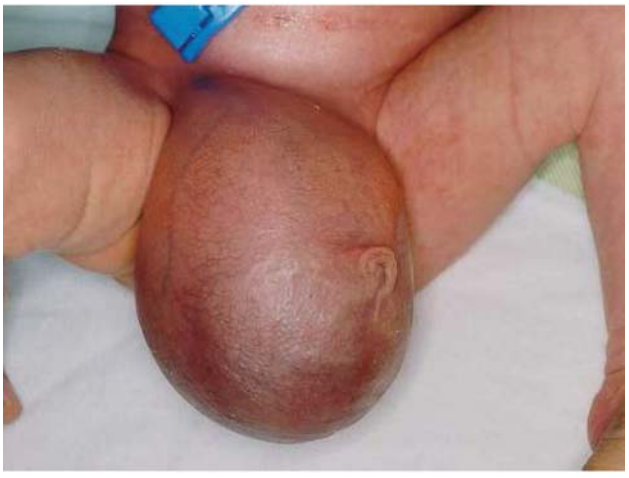

Figure 1. *Enlargement of the right hemiscrotum due to JGCT.*

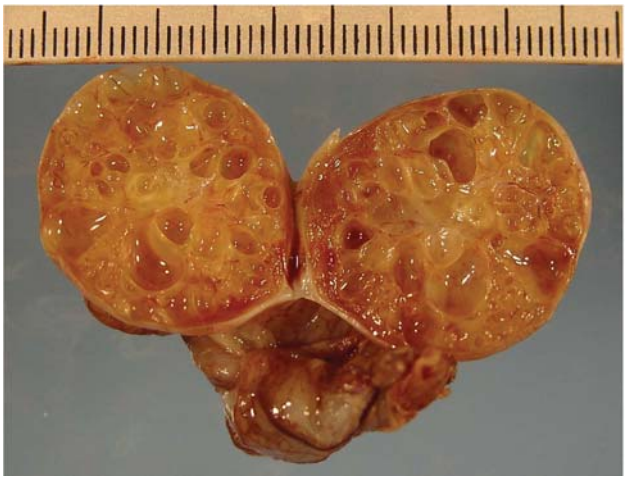

Figure 3. *Macroscopic finding of a JGCT exhibiting a white-gray, glistening, spongy lesion.*

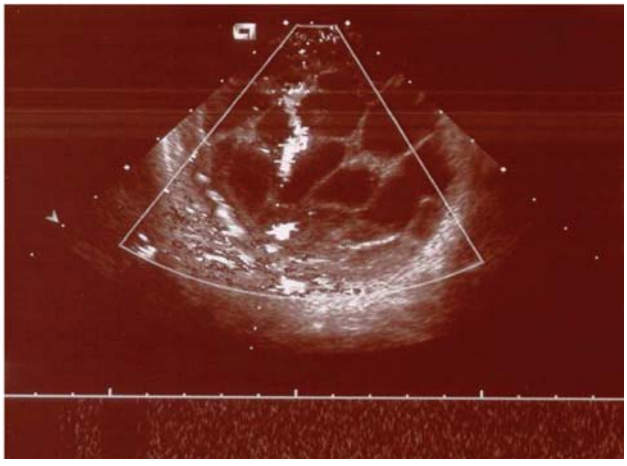

Figure 2. *A multiple septic cystic enlargement of the testicle, "Swiss-cheese"-appearing without any distinction of the testicular parenchyma.*

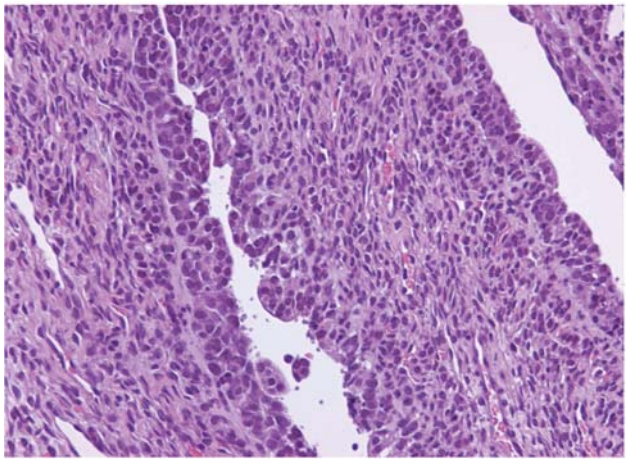

Figure 4. *Spindle- to round-shaped cells with non-grooved nuclei, a moderate amount of pale cytoplasm, and an indistinct border. (HE, original magnification ×100).*

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