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Testicular Thecoma in an 11-year-old Boy with Nevoid Basal-Cell Carcinoma Syndrome (Gorlin Syndrome)

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Abstract We report a case of testicular thecoma in an 11-year-old Japanese boy with nevoid basal-cell carcinoma syndrome (Gorlin syndrome). He presented with left testicular swelling and underwent a radical orchiectomy on suspicion of a malignant paratesticular tumor. The tumor arose from the testis exophytically, and was diagnosed as a thecoma histopathologically. Ovarian thecoma-fibroma group tumors are closely associated with Gorlin syndrome, or with abnormalities in PTCH, a candidate gene for the syndrome. The occurrence of an extremely rare testicular thecoma in this case (the second in the literature) suggests that such an etiological association may also exist in pathogenesis of testicular tumors.

Keywords: thecoma; Gorlin syndrome; testis

A thecoma is a benign stromal tumor typically seen in the ovary, and characterized by spindle-shaped cells forming luteinization.¹ The pathogeneses of ovarian thecoma and fibroma are closely associated with a tumorigenic syndrome called nevoid basal-cell carcinoma syndrome (Gorlin syndrome) or abnormalities in its candidate gene, PTCH.² Herein, we report the first case of a testicular thecoma in a boy with Gorlin syndrome.

1. Case report

An 11-year-old boy was referred to us for painful scrotal swelling. His uncle had died of a cerebellar tumor. The boy had previously been diagnosed with a cerebellar medulloblastoma at 7 months of age, and received a series of surgeries, adjuvant multidrug chemotherapies, and radiation therapy. Since the age of 7 years, he had been administered leuprolide as a treatment for premature elevation of testosterone. Concurrently, the boy was diagnosed

with Gorlin syndrome, based on the presence of skin lesions and odontogenic keratocysts, but without detectable PTCH gene mutations.

At presentation, his external genitalia were at the prepubertal stage. He had palpably normal bilateral testes but swelling in the left paratesticular area. He was diagnosed with epididymitis based on magnetic resonance imaging (MRI, Fig.A), and spontaneous resolution of the pain. Seven months later, however, the paratesticular lesion increased in size and formed a firm non-tender mass. MRI revealed a heterogeneous 21-mm mass adjacent to the left testis (Fig.B). Germ cell tumor markers were negative. Testosterone was 29.9 ng/dL (normal range: 18-150 ng/dL), estradiol was 11.3 pg/mL (normal range: 5-16 pg/mL), luteinizing hormone was 0.9 mIU/mL (normal range: <1-5 mIU/ml), and follicular stimulating hormone was 1.4 mIU/mL (normal range: 2-7 mIU/ml). There were no signs of metastasis on radiography. An inguinal exploration revealed a well-circumscribed tumor located at the caudal end of the testis (Fig.C). Since the intraoperative pathological examination could not exclude a malignant mesenchymal tumor, a left radical orchiectomy was performed. Histopathologically, the tumor arose from the tunica albuginea of the testis. Spindle cells were predominant, with occasional luteinization (Fig.D). The luteinized tumor cells were positive for inhibin alpha and calretinin and negative for MyoD and desmin. Consequently, the diagnosis of thecoma was established. The patient has remained free from recurrence for 2 years.

2. Discussion

Thecoma is an extremely rare tumor in the testis, with just one previously reported case.³ Typically, thecomas are benign stromal tumors arising from ovarian theca cells, and constitute 1% of all ovarian tumors.¹ Ovarian stromal

tumors are classified into either thecoma or fibroma, and occasionally clumped together as a thecoma-fibroma group.

Gorlin syndrome is a disorder characterized by malformations of the skin, nerves, eyes, and bone,⁴ with frequent loss of heterozygosity at 9q22.3 or abnormalities in the PTCH gene, a homolog of the *patched* gene in *Drosophila*.⁵ Gorlin syndrome patients without detectable PTCH mutations, as in the present case, are believed to have germinal mosaicism.⁶ The syndrome are associated with basal cell carcinoma, ovarian tumor and medulloblastoma (as found in the present case). Many women with this syndrome develop ovarian thecoma or fibroma at a mean age of 30 years.^{2,7} In parallel with these findings, loss of heterozygosity at 9q22.3 is observed in 40% of sporadic ovarian thecoma-fibroma cases,⁸ suggesting a strong pathogenic association between PTCH abnormalities and thecoma-fibroma development.

A possible explanation for the occurrence of testicular thecoma is one analogous to the association between Gorlin syndrome and ovarian thecoma-fibroma, although the absence of a genetic linkage in the present case precludes a definitive conclusion. The cytotoxic chemotherapy against the prior cerebellar tumor may have enhanced a genetic predisposition to thecoma. Thus, thecoma-fibroma should be taken into the differential diagnosis for male patients with Gorlin syndrome presenting with an intrascrotal mass. Since bilateral lesions are seen in the ovary, testis-sparing surgery and contralateral surveillance should be recommended.⁷

3. Conclusion

The present case may suggest the existence of an unreported tumorigenic mechanism in the male gonads.

References

1. Roth LM: Recent advances in the pathology and classification of ovarian sex cord-stromal tumors: *Int J Gynecol Pathol* 2006; 25: 199-215.
2. Kimonis VE, Goldstein AM, Pastakia B, et al: Clinical manifestations in 105 persons with nevoid basal cell carcinoma syndrome. *Am J Med Genet* 1997; 69: 299-308.
3. Schenkman NS, Moul JW, Nicely ER, et al: Synchronous bilateral testis tumor: mixed germ cell and theca cell tumor. *Urology* 1993; 42: 593-5.
4. Gorlin RJ: Nevoid basal-cell carcinoma syndrome. *Medicine (Baltimore)* 1987; 66: 98-113.
5. Johnson RL, Rothman AL, Xie J, et al: Human homolog of patched, a candidate gene for the basal cell nevus syndrome. *Science* 1996; 272: 1668-71.
6. Wicking C, Shanley S, Smyth I, et al: Most germ-line mutations in the nevoid basal cell carcinoma syndrome lead to a premature termination of the PATCHED protein, and no genotype-phenotype correlations are evident. *Am J Hum Genet* 1997; 60: 21-26.
7. Evans DG, Ladusans EJ, Rimmer S, et al: Complications of the naevoid basal cell carcinoma syndrome: results of a population based study. *J Med Genet* 1993; 30: 460-4.
8. Tsuji T, Catusus L, Prat J: Is loss of heterozygosity at 9q22.3 (PTCH gene) and 19p13.3 (STK11 gene) involved in the pathogenesis of ovarian stromal tumors? *Hum Pathol* 2005; 36: 792-6.

Figure Legends

(A) and (B) Magnetic resonance imaging of the left intrascrotal mass (T2-weighted) at first (A) and second referral (B). (C) Gross appearance of the tumor. Th: Thecoma. T: Testis. E: Epididymis. (D) Microscopically, the tumor consisted of spindle cells, with occasional lutenized cells that are immunoreactive for inhibin alpha (figure not shown).