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Large Cell Calcifying Sertoli Cell Tumor of the Testis

Case Report with Ultrastructural Study

Jeong Hae Kie, MD,* Young Nyun Park, MD, PhD,* Sang Won Han, MD, PhD,† Nam Hoon Cho, MD, PhD,* and Jae Yoon Ro, MD, PhD‡

Large cell calcifying Sertoli cell tumor (LCCST) is a rare testicular tumor, usually occurring in young men before the age of 20. Ultrastructural study has been performed rarely demonstrating Sertoli cell features. We report a case of LCCST in a 7-year-old boy. A well-circumscribed yellowish-tan, 1.5-cm-sized mass was located within the left testicular parenchyma. The cut surface was somewhat resilient with multiple calcifications. On microscopic examination, the tumor was composed of large eosinophilic polygonal cells with abundant eosinophilic cytoplasm arranging in solid tubular and trabecular patterns, superficially mimicking Leydig cell tumor. However, there were multiple calcifications and the tumor cell nests were surrounded by PAS-positive basement membrane. Ultrastructural examination revealed the features of the Sertoli cell with Spangaro's crystals. The right testis showed a normal appearance by ultrasonogram and there were no other clinical features associated with Carney syndrome. *Int J Surg Pathol 7(2):109–114, 1999*

Key words: large cell calcifying sertoli cell tumor, electron microscopy, Carney syndrome, calcifications, Leydig cell tumor.

Large cell calcifying Sertoli cell tumor (LCCST) of the testis is a rare variant of Sertoli cell tumor, which has unique clinical findings [1–6]. This neoplasm occurs primarily during the first two decades of life. More than half of the cases show bilaterality and multifocality, and it may be associated with Carney syndrome. The characteristic features of the LCCST are large cells with abundant cytoplasm and calcifications.

LCCST is frequently misinterpreted as Leydig cell tumor because of its histologic resemblance including large cells with abundant eosinophilic cytoplasms and prominent nucleoli [7]. The correct diagnosis must be made on the basis of ultrastructural findings as well as the characteristic histologic findings including laminated calcifications and intratubular growth. We report a case of large cell calcifying Sertoli cell tumor in a 7-year-old boy with ultrastructural study.

Case Report

A 7-year-old boy was admitted because of an incidentally found palpable nontender left testicular mass. Ultrasonography revealed a 2.3-cm-sized hyperechoic mass with multiple calcifications in the

From the Departments of *Pathology and †Urology, Yonsei University College of Medicine, Seoul, and ‡Department of Pathology, Asan Medical Center, Seoul, Korea.

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Reprint requests: Young Nyun Park, MD, Department of Pathology, Yonsei University College of Medicine, #134, Shinchon-Dong, Seodaemun-Gu, Seoul, 120-752, Korea.

left testis while the right testis showed no abnormality. Physical examination revealed no other abnormal findings. Serum alpha-fetoprotein and human chorionic gonadotropin were within normal limits. The patient underwent left orchiectomy under the impression of Leydig cell tumor. During the operation, frozen section examination was performed in the biopsied tissue from the mass and the diagnosis of Leydig cell tumor was rendered. The postoperative course was uneventful. The patient is alive and well 11 months after operation.

Materials and Methods

The left radical orchiectomized testis was examined grossly and representative tissue sections were taken for microscopic examination. They were routinely processed and stained with hematoxylin and eosin and periodic acid-Schiff stains. Immunohistochemistry was performed on paraffin-embedded tissue sections by use of a peroxidase antiperoxidase method. Antibodies used for this study included Ki-67 (Dako, Carpinteria, CA) diluted at 1:50, PCNA (Dako) diluted at 1:100, S-100 (Dako) diluted at 1:20, vimentin (Dako) diluted at 1:300, AE1/AE3 (ZYMED, San Francisco, USA) diluted at 1:50, EMA (Dako) diluted at 1:200, and P53 (Novocastra, Newcastle, United Kingdom) diluted at 1:50. Quantification of Ki-67 and proliferating cell nuclear antigen (PCNA) staining was done by the method of Kratzer et al. [8]. Electron microscopic study was performed on the formalin-fixed tissue, which was postfixed in 3% glutaraldehyde with 0.2 mole/L sodium cacodylate buffer at pH 7.4, postfixed with 1% osmium tetroxide, dehydrated in graded steps of ethanol, cleared with propylene oxide, and embedded in epon resin. A 1-micron section was cut and stained with methylene blue and azure II to identify representative areas for ultrathin sectioning. Ultrathin sections were cut and stained with uranyl acetate and lead citrate and were examined under a Philips 300 electron microscope.

Results

Gross Findings

The left testis measured 4.5 × 3 cm. A well-circumscribed, yellowish-tan 1.5-cm-sized mass was located within the parenchyma of the testis. Its surface was somewhat resilient with multiple calcifications (Fig. 1). There was no necrosis or hemorrhage. The epididymis and spermatic cord were unremarkable.

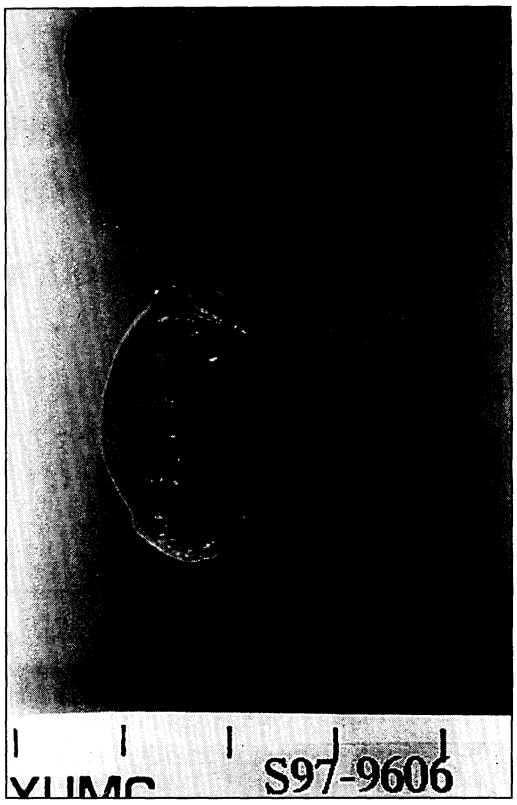

Fig. 1. Cut surface of the left testis shows a well-circumscribed tumor within the testicular parenchyma. The testicular appendage is unremarkable.

Light Microscopic Findings

On histologic examination, the tumor was well demarcated from the surrounding testicular tissue and was associated with slight lymphocytic infiltration at the periphery of the tumor. The tumor cells formed solid tubules, trabeculae, cords, and small nests. The stroma was loose and myxoid or somewhat hyalinized. Multiple laminated calcifications were seen within the tumor nests and stroma (Fig. 2). The neoplastic cells were large and round to polygonal with abundant eosinophilic cytoplasms. The nuclei were eccentric with relatively distinct nuclear membrane, fine chromatins, and prominent nucleoli (Fig. 3). Neither Reinke crystalloids nor Charcot-Bottcher crystals were found. The tumor cell nests as well as individual cells were surrounded by PAS-positive, diastase-resistant, basement-membrane-like material. Necrosis, mitosis, or vascular invasion of the tumor cells was not observed.

Fig. 2. Low magnification of LCCST shows tumor cells arranging solid tubules, traberculae, and cords within the myxoid loose stroma. Multiple calcifications are seen (H&E, ×40).

Fig. 3. The neoplastic cells are large, round to polygonal, with eccentrically located nucleoli (H&E, ×200).

Immunohistochemical Findings

This case showed diffuse strong reactivity for vimentin and focal strong reactivity for S-100. The immunohistochemical stains for EMA, p53, and AE1/AE3 were negative. Ki-67 expression value was 0.9% and PCNA expression value was 2.9%.

Electron Microscopic Findings

Electron microscopic study revealed neoplastic cells forming mostly solid nests, or tubule-like structures with surrounding basal lamina. The tumor cells were connected laterally by easily discernible junctions, and in some areas, their plasmalemmas

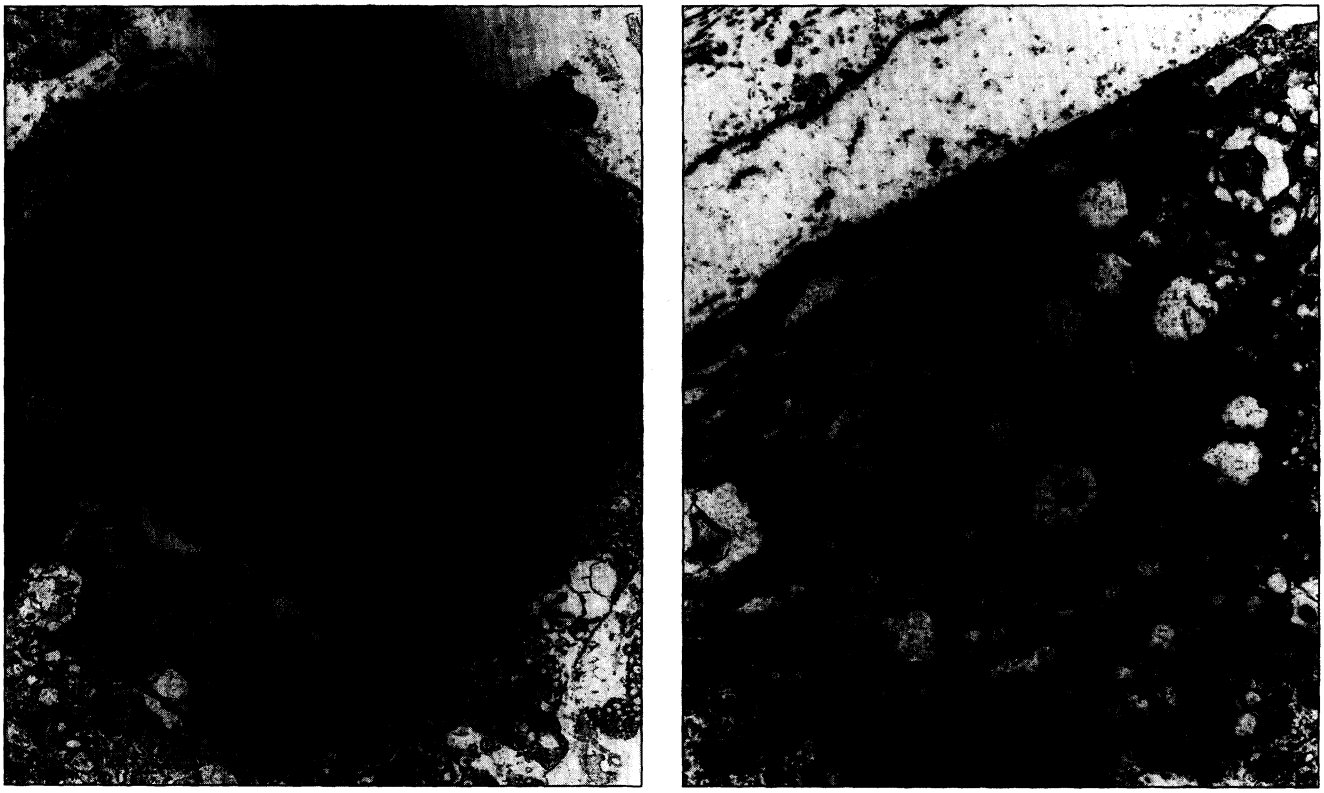

Fig. 4. (A) Neoplastic cells with irregular nuclei and prominent nucleoli form a solid nest surrounded by basal lamina. There are abundant organelles including smooth and rough endoplasmic reticulae, mitochondria, and lipid droplets in the cytoplasm (uranyl acetate and lead citrate, ×7,800). (B) High-power magnification details the surrounding basal lamina and abundant cytopasmic organelles (uranyl acetate and lead citrate, ×17,800).

were slightly interdigitated. The nuclei were often irregularly shaped with deep indentations and large nucleoli. The cytoplasm contained abundant organelles including smooth and rough endoplasmic reticula, mitochondria, and lipid droplets (Fig. 4). A few ribosome-lamella complexes with hollow cylindrical configuration or parallel pattern were seen. A bundle of intracytoplasmic filaments was found in a tumor cell, and it measured 1 μm long and 0.1 μm wide, which was consistent with Spangaro's crystal (Fig. 5).

Discussion

Large cell calcifying Sertoli cell tumor (LCCST) was first described in 1980 by Proppe and Scully [1]. To the present, about 47 cases have been reported [8]. The term *large cell calcifying Sertoli cell tumor* was selected for these neoplasms because there were two characteristic features, large cells with abundant cytoplasm and calcification, which were present to some extent in all cases.

The histogenesis of the LCCST still remains uncertain; however, most reports state that Sertoli cell is the origin of this tumor. One of the major differential diagnoses is Leydig cell tumor, and the current case was initially misinterpreted as Leydig cell tumor on frozen section because of large polygonal cells with relatively abundant eosinophilic cytoplasm. Later, we diagnosed it as LCCST on permanent section on the basis of several light microscopic features. First, multiple calcifications were seen in the tumor. Second, neoplastic cells formed the solid tubules, trabeculae, and cords, which are general characteristics of LCCST [9]. Third, many clusters of tumor cells as well as individual large cells were surrounded by PAS-positive basement membrane [3,6]. Fourth, Reinke crystalloids were not observed in the tumor [9]. Recently, Kratzer et al. reported a malignant form of this tumor, and the criteria included were a size more than 4 cm, extratesticular growth, gross or microscopic necrosis, high-grade cytologic atypia, and vascular invasion [8]. They claimed that the presence of at least two features

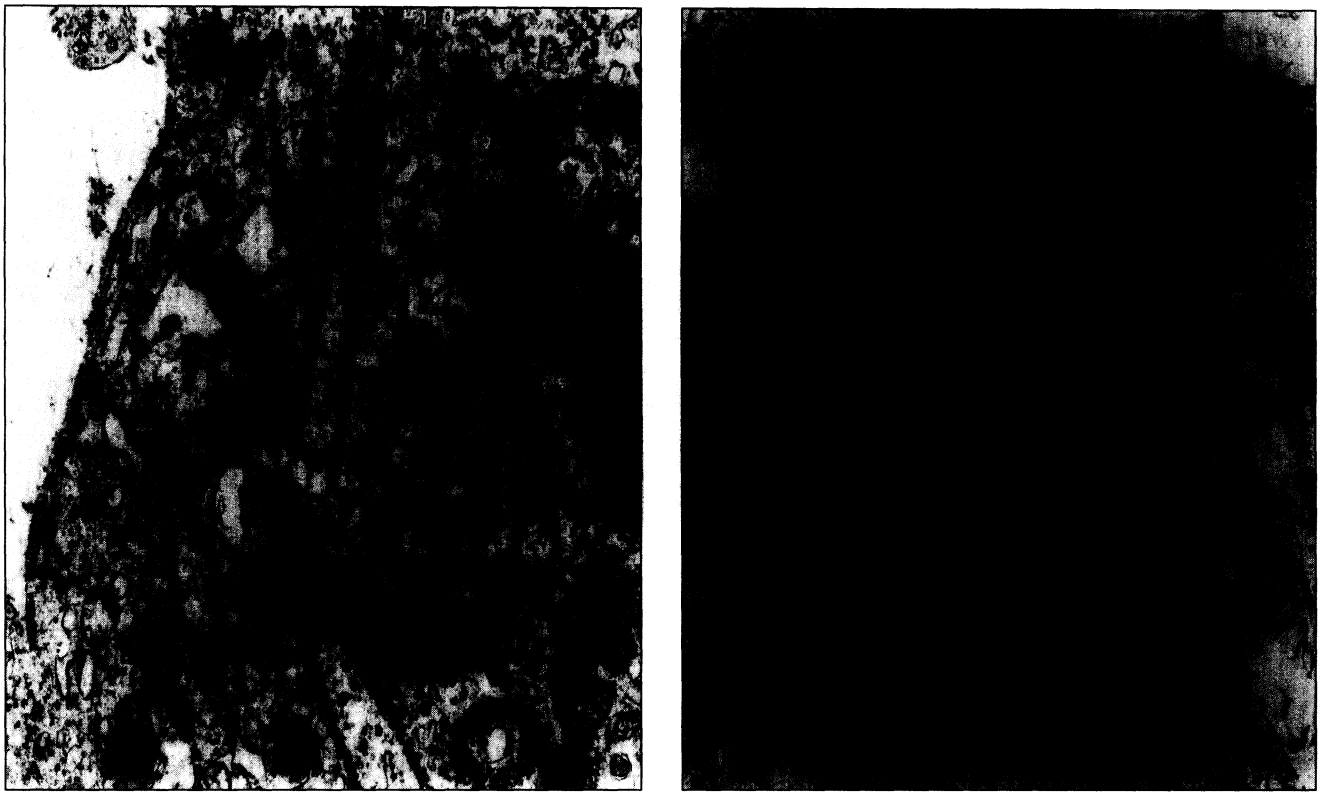

Fig. 5. Electron microscopic finding shows (A) ribosome-lamella complexes with hollow cylindrical configuration and parallel pattern (uranyl acetate and lead citrate, ×1,500) and (B) a bundle of intracytoplasmic filaments (Spangaro's crystal) (uranyl acetate and lead citrate, ×3,900).

among these criteria indicates malignancy, and the presence of any one of them, especially in a patient more than 25 years of age, should be suspicious of malignant behavior. This case had none of these features.

The ultrastructural feature of LCCST has been rarely described [2–4,6,9], and the features of the current case were consistent with Sertoli cell origin of this tumor. Most neoplastic cells were arranged in solid, tubule-like structures surrounded by basal lamina. The cytoplasm had abundant lipid droplets and smooth endoplasmic reticulum, which are the characteristics of Sertoli cells. Some tumor cells showed notched nuclei, which have also been described as a characteristic finding of normal as well as neoplastic Sertoli cells [10]. The diagnostic feature of Sertoli cells is the presence of Charcot-Bottcher crystals (10 to 25 μm long and 2 to 3 μm wide) [11]. This case showed aggregated intracytoplasmic filaments, measuring 1 μm long and 0.1 μm wide. It was consistent with Spangaro's crystals, which have been suggested as a precursor form of Charcot-Bottcher crystals [11,12]. The ribosome-lamella complexes were also found in our case. They have been described in cases of hairy cell leukemia, and less commonly in other hematopoietic disorders, as well as in steroid-producing cells and LCCST [3]. Annulate lamellae described in the Sertoli cells in normal testes were not found in this case.

LCCST occurs usually before the age of 20 with bilaterality and multifocality in many cases [5,9]. Also, it may be associated with Carney syndrome in which patients develop lentigines of the face; myxomas of the heart, skin, soft tissue, and elsewhere; myxoid fibroadenomas of the breast; blue nevi of the skin; pigmented nodules of the adrenal cortex associated with Cushing's syndrome; growth-hormone-producing adenomas of the pituitary gland; and psammomatous melanotic schwannomas. The presenting case did not show any other associated clinicopathologic manifestation. In view of the young age of the patient, the possibility of late onset of the clinical symptoms cannot be excluded, and therefore, careful clinical follow-up is warranted.

In conclusion, LCCST is a rare testicular neoplasm with typical histologic and ultrastuctural features of Sertoli cell origin, although there are some similarities of microscopic features with Leydig cell tumor.

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