CASE REPORT

Large-cell calcifying Sertoli cell tumour with macrocalcification in partially resected testis of young adult patient

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Abstract

Introduction: There are less than 100 cases of Large-cell calcifying Sertoli cell tumour (LCCSCT) reported in English literature. Most of them are benign, bilateral and affect paediatric population. Malignant cases occur in older patients. LCCSCT is often associated with Carney complex or Peutz-Jaghers syndrome. We present the clinicopathological features of a young adult, with unilateral “stone-like” LCCSCT, without changes in hormonal status and no clinical characteristics of noted genetic disorders. Case Report: A 24-year-old male presented with painless hardening of the right testis. There was no gynaecomastia, and serum levels of human chorionic gonadotropin and α-fetoprotein were normal. Ultrasound depicted hyperechogenic, clearly demarcated intratesticular lesion. Partial orchiectomy was performed. Macroscopically, tumour appeared as almost entirely calcified round mass, measuring 10 mm. Histopathological evaluation showed well-circumscribed, unencapsulated tumour composed of massive calcified geographic formations, surrounded with tumour cells. Neoplastic cells were large, polygonal, with abundant eosinophilic cytoplasm, and formed irregular cords, pseudo tubular structures, and nests in a fibrous and myxoid stroma, surrounded with lymphocytes. Other forms of calcification were also present: Needle-like deposits and lamellar, mulberry-like structures. There was no necrosis, mitotic activity and nuclear pleomorphism. Immunohistochemical study was positive for inhibin α and negative for Melan A, EMA, synaptophysin, chromogranin and AFP. Discussion: LCCSCT needs to be differentiated from other, more frequent, sex cord stromal tumours. Clinical and genetical evaluation of these patients had to be performed, due to connection of LCCSCT with genetic abnormalities. In evidently benign cases, organ-sparing surgery should be considered for younger patients, followed by long term follow-up.

Keywords: Sertoli cell tumour, calcification, testis

INTRODUCTION

Sertoli cell tumours (SCT) are subset of sex cord stromal tumours, which account for less than 1% of all testicular tumours. Apart from most commonly diagnosed Sertoli cell tumour, not otherwise specified (NOS), there are 3 subtypes of STC: malignant Sertoli cell tumour, large cell calcifying (LCCSCT) and intratubular large cell hyalinising Sertoli cell neoplasia.¹ LCCSCT can be benign or malignant and it can affect one or both testicles multifocally causing microcalcifications. It is usually seen in boys and young adults. Forty percent of the cases are associated with Carney complex and Peutz-Jaghers syndrome (PJS). They are also accompanied by extragonadal endocrine symptoms such as sexual precocity, gynaecomastia, and acromegaly. There are less than 100 cases reported in English literature.²³ We present the clinicopathological features of a 24-year-old male, with unilateral LCCSCT, with one large calcified mass, without any changes in hormonal status and without any clinical characteristics related to genetic disorders.

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CASE REPORT

A 24-year-old male detected painless hard mass on his right testis. Physical examination of the scrotum revealed distinctively harder lower half of the right testis, with slight increase in the overall testicular volume. The examined testis appeared much heavier than the other. No clinical lymphadenopathy was palpable. A scrotal ultrasound depicted round, hyperechogenic, intratesticular lesion in the lower half of the right testis, clearly demarcated from surrounding testicular parenchyma. Further clinical examination revealed neither gynaecomastia nor distant metastases. Serum levels of human chorionic gonadotropin (HCG) and α-fetoprotein (AFP) were not elevated. There were no elements of Carney complex or PJS, including myxoma, pituitary tumour, adrenocortical hyperplasia, thyroid gland abnormalities, polyps in the gastrointestinal tract or skin pigmentation, especially on the lips and oral mucosa. Partial orchiectomy was performed. Gross examination showed fragments of normal appearing testicular tissue and completely calcified well circumscribed round mass, measuring 10 mm with gray-white cut surfaces. Calcified mass was first treated with formic acid. Tissue was then fixed in 4% neutral formaldehyde, embedded in paraffin, cut in 4-μm-thin sections, and stained with haematoxylin-eosin. An immunohistochemical study was performed using automatic immunostainer. The primary antibodies used were: inhibin α, Melan A, synaptophysin, chromogranin, α-fetoprotein (AFP), epithelial membrane antigen (EMA) and Ki-67.

Histopathological evaluation showed well-circumscribed, unencapsulated tumour composed of massively calcified areas, surrounded with tumour cells (Fig. 1). Neoplastic cells were large, oval to polygonal, and had abundant eosinophilic granulated or clear cytoplasm (Fig. 2). The cells formed relatively solid sheets, irregular cords, tubular structures, and nests in a fibrous and myxoid stroma. Lymphocytic infiltration was present at the periphery of the tumour. Apart from amorphous large calcium deposits, other forms of calcification were noted: sharp, needle-like deposits of different size, round concentric, lamellar structures, that appeared as mulberry-like when small or as complex geographic formations, when large (Fig. 3-4). There was no necrosis, mitotic activity and nuclear pleomorphism. Residual testicular parenchyma

FIG. 1: Well circumscribed nests of tumour cells surrounding calcified mass (H&E, pre-treated with formic acid, x100).
FIG. 2: Neoplastic cells have round nuclei and pale voluminous cytoplasm. They are arranged in sheets and pseudo tubular structures (H&E, x200.)

FIG. 3: Various forms of calcium deposits. Tumour cells are surrounded by lymphocytes. (H&E, x100.)
showed atrophic changes with spermatogenesis reduction.

Immunohistochemical study expressed strong and diffuse immunoreactivity for inhibin α (Fig. 5). There was no reactivity for Melan A, EMA, synaptophysin, chromogranin or AFP. The proliferation index was low (0.5%).

DISCUSSION

LCCSCT was first described in 1980 by Proppe and Scully, who examined 10 cases. Since then, sporadic cases have been reported in English literature. Most of the patients are adolescents, and the average age is 16 years. They clinically present as slowly enlarging testicular mass. LCCSCTs are frequently bilateral and multifocal. However, in our case, tumour was unilateral and appeared in just one part of the testis, without its significant enlargement.

About 40% of LCCSCTs may be associated with genetic anomalies like Carney complex and PJS, and in those instances tend to have higher incidence of bilateral disease. PJS is an autosomal-dominant syndrome that predisposes patients to the development of different types of tumours. The characteristics of PJS are multiple hamartomatous polyps of gastrointestinal tract and hyperpigmented macules of the lips, palms, around the eyes, and in oral or bowel mucosa. Patients are at higher risk to develop colorectal cancer, as well as breast, small bowel, gastric, pancreatic ovarian and testicular cancers. Annual testicular palpation is recommended in boys with PJS for earlier detection of testicular Sertoli cell tumours. The Sertoli cell tumours of patients with PJS frequently do not have extensive calcifications. Carney complex is an autosomal-dominant multiple neoplasia syndrome that includes at least 2 of the various clinical manifestations: spotty skin pigmentation (lips, conjunctiva, vaginal and penile mucosa); cardiac myxoma that can cause sudden death; acromegaly, primary pigmented nodular adrenocortical disease, thyroid carcinoma, psammomatous melanotic schwannomas; blue nevus and LCCSCTs (or calcification on testicular ultrasound). LCCSCTs are estimated to occur in about 50% of men with this complex. Diagnosis of LCCSCT in our patient was followed with thorough examination in the search of other components of this complex. Since there were no indications, genetic tests were not performed.

Calcifications detected on testicular ultrasound
LARGE-CELL CALCIFYING SERTOLI CELL TUMOUR

are not specific to LCCSCTs, but characteristic “Christmas tree-like” appearance of multiple small lesions is almost pathognomonic for this tumour. In our case, instead of multiple small calcifications, ultrasound showed LCCSCTs as one round, smooth, hyperechogenic “stone-like” area. Calcifications in LCCSCTs need to be distinguished from those in teratoma, seminoma, embryonic carcinoma, and Leydig cell tumours, and from those in infectious or inflammatory lesions.6,7

LCCSCT has to be differentiated from other sex cord stromal tumours like Sertoli cell tumours NOS, or Leydig cell tumour, which are diagnosed more frequently. Sertoli cell tumours NOS are usually composed of cells with clear, often-vacuolated cytoplasm due to presence of lipids. Sometimes, part of the tumour can be composed of cells with eosinophilic cytoplasm. These cells do not have abundant cytoplasm, like the cells in LCCSCT. Typically, there are no stromal inflammatory cells. Minor dystrophic calcifications may be seen within the stroma, but laminated calcifications are absent, and multifocality is uncommon. In addition, there are no associated endocrine syndromes.12 There are some similarities between LCCSCT and Leydig cell tumour in their clinical features and histopathology. Both tumours can occur during childhood and occasionally cause gynaecomastia. Leydig tumour cells are also polygonal with eosinophilic cytoplasm, and may be accompanied by calcification or ossification. The appearance of extensive calcification and characteristic mulberry-like calcification well developed basal lamina which is highlighted by PAS or silver stain, variable tubular growth, more myxoid stroma and the presence of inflammatory infiltrate, favour the diagnosis of LCCSCT. LCCSCT also has no Reinke crystals, and unlike Leydig cell tumour it has patchy staining for Melan A and CD10, and more diffuse S100.13,14 An accurate diagnosis of LCCSCT is important due to its possible association with genetic disorders. Our case showed no staining for Melan A, neither synaptophysin nor chromogranin, which are positive in about 70-90% of Leydig cell tumors.14 Diagnosis was also facilitated by large geographic and mulberry-like calcifications.

Malignant LCCSCT have different clinicopathological features.5 They present at an older age, between 28 and 70 years. They are larger on gross examination, and they are always unilateral and solitary. Histologically, tumour should be diagnosed as malignant if it demonstrates more than 2 of the proposed criteria: Spread beyond testis (tunica albuginea, epididymis, spermatic cord), Size > 4 cm, Mitoses ≥ 3/10 high power fields, significant nuclear atypia, necrosis and lymphovascular invasion.15 Metastases are seen in retroperitoneal lymph nodes but haematogenous spreading to
bone, liver or lungs can occur. Because of his age and unilateral presentation, our patient could have fallen in the malignant category, however, Ki67 proliferating index was insignificant and there were no histological signs of invasiveness.

LCCSCTs in literature have been managed with partial orchiectomy in the prepubertal population, specifically when the patients also have PJS or Carney complex. This is due to the fact that these tumours, when occurring in patients with syndromes, are more likely to be benign. Based on limited evidence that exists with LCCSCT, patients under 17 years, with negative tumour markers and tumour size less than 2.5 cm, have low chance of malignancy. Some authors suggest partial orchiectomy in unilateral cases, in the setting of a normal contra lateral testis. That was the course clinicians took for our patient. Since there was no radiological evidence of malignancy, preserving a viable testis in the event of benign disease was worth risking a second procedure in case of a malignant pathological finding. Because of its rarity, natural course and possible recidivism of this tumour have not been established. Routine scrotal ultrasounds, and physical examinations, could be the adequate method of surveillance.

CONCLUSION
Our case adds to the reported literature on LCCSCT, with atypical macrocalcification. This is an extremely rare tumour, with low chance of malignancy. Clinical and genetical evaluation of these patients has to be performed, due to connection of LCCSCT with genetic abnormalities. In cases with evidently benign behaviour of this tumour, organ-sparing surgery should be considered for younger patients, followed by long term follow-up.

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REFERENCES