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Oncology

First case of synchronous Leydig cell tumor and spermatocytic tumor in the unilateral testis

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A B S T R A C T

Both Leydig cell tumor (LCT), which is a sex cord-stromal tumor, and spermatocytic tumor (ST), which is a germ cell tumor, are rare testicular tumors. Synchronous LCT and ST in the unilateral testis are extremely rare because of their different origins. Herein, we report the case of an 84-year-old male patient with right scrotal swelling due to a testicular tumor. His age was out of the onset peak age of LCT but within ST. To the best of our knowledge, this is the first case with synchronous LCT and ST in the unilateral testis.

1. Introduction

Testicular tumors are relatively rare, accounting for only 1%–2% of worldwide male cancer diagnoses.[1] Leydig cell tumor (LCT) is the most common among the sex cord-stromal tumors, comprising approximately 5 % of testicular tumors in adults, but it accounts for <3 % of all testicular tumors.[1] LCT originates from Leydig cells which normally reside in the interstitium of testicles and can secret testosterone in response to luteinizing hormone. The onset peak of LCT is in the pre-pubertal age group and between the ages of 30–60 in adults.[1]

Seminoma is the most common germ cell tumor (GCT) originating from the germinal epithelium.[2] Seminoma accounts for 30%–40 % of all testicular tumors and it is the most common cancer in ages 15–35 years in males.[2] Spermatocytic tumor (ST), previously named spermatocytic seminoma, is a very rare GCT, accounting for approximately 1 % of all testicular tumors.[3] The age onset of ST has been approximately 52–56 years, with two-thirds of cases reported at >40 years.[4,5]

Mixture types of GCTs or non-germ cell tumors are frequently diagnosed in the unilateral testis when the tumor is removed by orchiectomy. However, synchronous LCT and GCT in the unilateral testis are extremely rare because of their different origins.[6,7] Here, we report the case of an 84-year-old male patient with right scrotal swelling due to a testicular tumor. His age was out of the onset peak age of LCT but within ST. To the best of our knowledge, this is the first case with synchronous LCT and ST in the unilateral testis.

2. Case presentation

An 84-year-old male patient with urinary retention presented to our urology department. Right-sided scrotal swelling was observed upon urothelial catheter insertion. He had noticed the swelling at least two years earlier but left it untreated because he felt no pain or changes in the scrotal swelling. A computed tomography (CT) scan revealed a right testicular tumor with rich blood flow and no metastasis (Fig. 1). Soluble interleukin-2 receptor, alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (β-HCG), and neuron-specific enolase serum levels were within the normal range. We planned an orchiectomy, but it was contraindicated due to severe heart failure with arrhythmia.

A scheduled CT scan performed six months after his first visit to our department indicated no metastasis and no changes in the testicular tumor. The above-described serum tumor marker levels remained within the normal range. Unfortunately, he passed away three weeks after the scan because of heart failure. We performed a right orchiectomy at his death after obtaining informed consent from his family and revealed a tumor within yellow necrotic tissue in the right testis (Fig. 2A). Two tumors were identified after formalin fixation (Fig. 2B). Tumor cells with abundant cytoplasm and a large nucleus and those non-uniform were positive and negative for calretinin immunostaining, respectively (Fig. 2C and D). Tumor cells with abundant cytoplasm and those non-uniform were diagnosed as LCT and ST, respectively (Fig. 3). The pathological results revealed the existence of synchronous LCT and ST in the unilateral testis.

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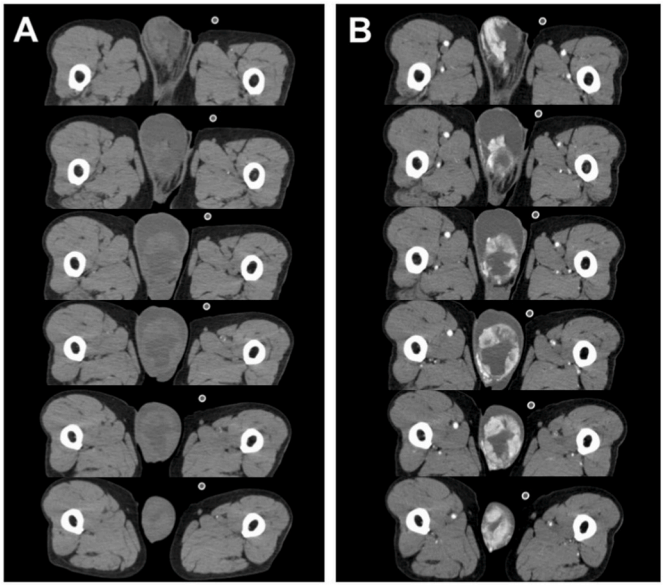

Fig. 1. Computed tomography (CT) scans.
(A) Pelvic plane CT scans. Horizontal view. (B) Pelvic-enhanced CT scans. Horizontal view. A right testicular tumor of 6 cm in size with rich blood flow was revealed. Fluid retention or necrosis inside of the tumor and a right-side hydrocele testis were presented. Calcification inside of the tumor and any metastasis were not observed.

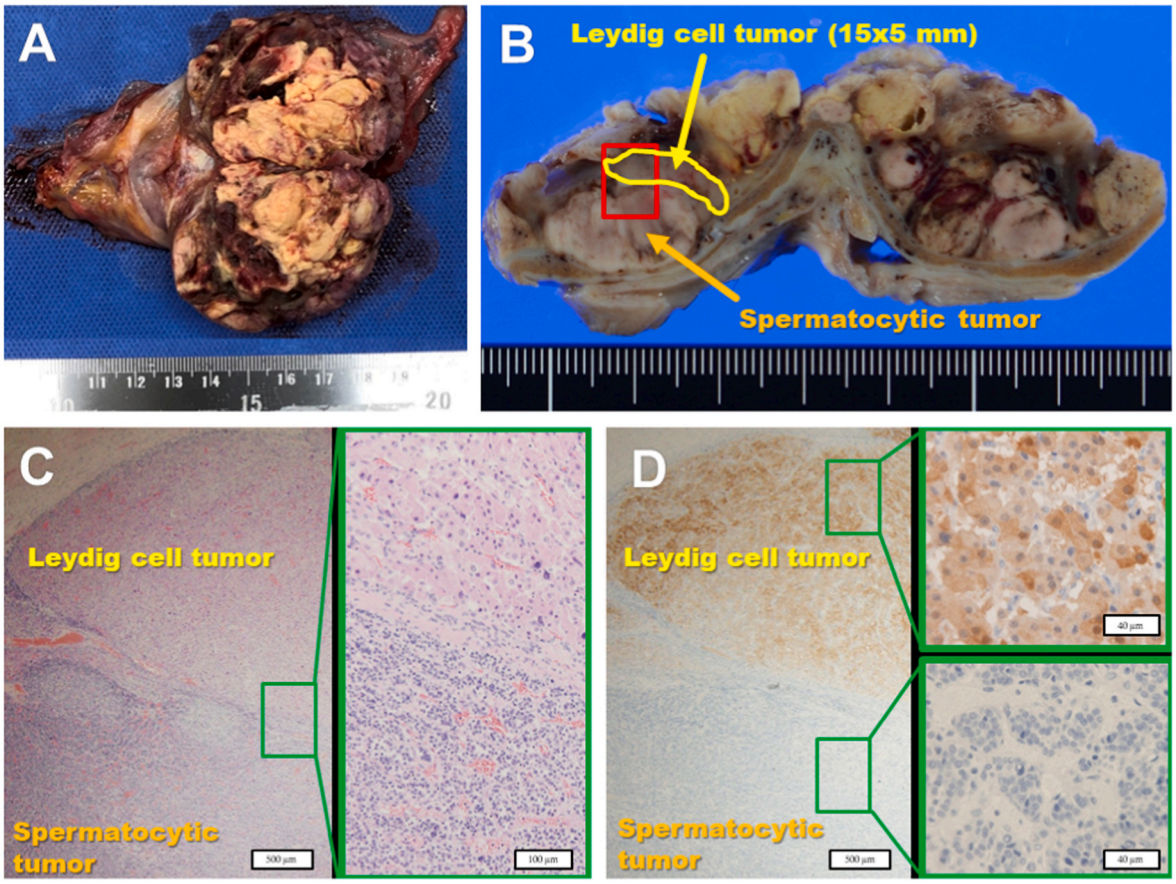

Fig. 2. Macroscopic and pathological findings of the testicular tumor.
Macroscopic findings of tumor section at orchiectomy (A) and after formalin fixation (B). Microscopic findings of the area marked with the red square in Figure B (C and D). Hematoxylin and eosin stain (C) and immunostaining of calretinin (D). The yellow tissue was necrosis (A). The mass of the Leydig cell tumor was 15 × 5 mm in size as indicated by the yellow area and adjacent to the mass of the spermatocytic tumor (B). The area of the Leydig cell tumor, which was positive for calretinin immunostaining, and the area of the spermatocytic tumor, which was negative for calretinin immunostaining, were adjacent to each other but those areas were not mixed (C and D). The spermatocytic tumor cells were multinodular or diffuse (C). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

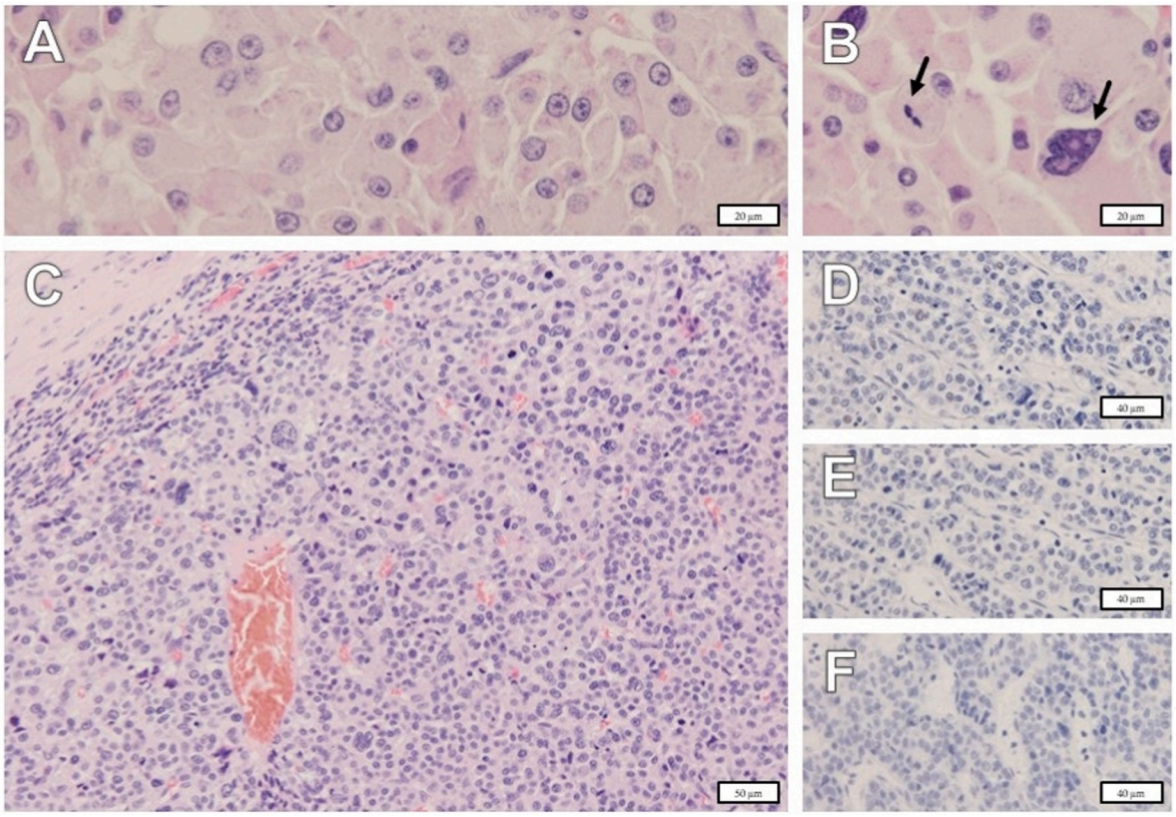

Fig. 3. Histopathological findings of Leydig cell tumor and spermatocytic tumor.
Histopathological findings were obtained from Leydig cell tumors (A and B) and spermatocytic tumors (C–F). Hematoxylin and eosin staining (A–C). Alpha-fetoprotein (AFP; D), human chorionic gonadotropin (HCG; E), and D2-40 immunostaining (F). Leydig cell tumor was presented as the cells with abundant cytoplasm and large nucleus (A). Few tumor cells with intra-nuclear mitosis or irregular and large cell nuclei, indicated by arrows, demonstrated a malignant potential (B). Three types of tumor cells: small cells with scant cytoplasm, intermediate cells with round nuclei, and giant cells with multiple nuclei (C). Immunostainings of AFP, HCG, and D2-40 were negative (D–F). These results were characteristic of spermatocytic tumors.

Table 1
Characteristics of immunostaining for three tumors
PLAP: placental alkaline phosphatase.

	Leydig cell tumor	Spermatocytic tumor	Seminoma
calretinin	+	−	−
Melan A	+	−	−
vimentin	+	−	−
CD117	−	+	+
D2-40	−	−	+
OCT3/4	−	−	+
PLAP	−	−	+

3. Discussion

Ifeyinwa et al. rarely reported and summarized cases of synchronous LCT and seminoma in the unilateral testis.[6,7] However, to the best of our knowledge, this is the first case with synchronous LCT and ST in the unilateral testis.

LCT is generally benign, with <10 % being considered malignant. Radical inguinal orchiectomy is a sufficiently curative treatment for most stage 1 seminoma and benign LCT.[1,2] Three of the five previously reported synchronous LCT and seminoma cases received only orchiectomy, and the other two cases received adjuvant radiotherapy after orchiectomy.[7] These five cases demonstrated pathologically benign LCTs and their outcomes were not available or alive >10 years. These results revealed that synchronous LCT and seminoma in the unilateral testis did not worsen the patient's prognosis compared with solitary tumors of LCT or seminoma, although the physiological influences of the synchronous to each other remain unclear. Therefore, synchronous LCT and ST were expected to demonstrate a favorable prognosis because of the good prognosis for ST without the sarcomatous variant, as in our case.[3]

Conversely, the literature reported features favoring malignant behavior of LCT, such as metastatic disease, tumor of >5 cm in size, a high mitotic rate, tumor necrosis, angiolymphatic invasion, infiltrative margins, and extratesticular extension.[8] The overall median survival of the malignant LCT group was reported for 2.3 years (range: 0.02–17.3).[8] Malignant LCT may demonstrate a poor response to chemotherapy or radiation. Surgical resection, such as retroperitoneal lymph node dissection, will be considered if it metastasizes.[1]

Clinically and preoperatively diagnosing synchronous LCT and ST in the unilateral testis is difficult because their synchronicity contains no characteristic findings. Scrotal ultrasound, CT scans, or magnetic resonance imaging did not indicate a significant difference between LCT and ST. Serum tumor marker levels, such as AFP and β-HCG, did not necessarily increase in both LCT and ST, and the elevation of these markers indicated no synchronicity of LCT and ST.

One key finding for the pathological ST diagnosis by hematoxylin and eosin staining is tumor cell nonuniformity. There are three types of tumor cells: (a) small cells, 6–8 μm, with scant cytoplasm; (b) intermediate cells, 15–20 μm, with round nuclei and chromatin ranging from granular to spireme-type; and (c) giant cells, 50–100 μm, with multiple nuclei.[3,4] Initially, we diagnosed the tumors as composed of LCT and seminoma cells, but we changed our diagnosis of seminoma to ST due to nonuniformity and negativity for immunostaining of D2-40. Immunostaining is useful for differentiating tumors such as LCT, ST, and seminoma (Table 1).[1–3,8] LCT stains positively for calretinin, Melan A, and

vimentin and negatively for CD117, D2-40, OCT3/4, and placental alkaline phosphatase (PLAP). ST stains positively for CD117 and negatively for D2-40, OCT3/4, and PLAP. Seminoma stains positively for CD117, D2-40, OCT3/4, and PLAP. These immunostaining characteristics helped in the pathological diagnosis of LCT and ST to differentiate seminoma, and these immunostainings helped us correctly diagnose ST from the beginning.

4. Conclusion

We report a case with synchronous LCT and ST in the unilateral testis. The clinical characteristics and physiological influences of the synchronicity remain unclear due to their rarity.

Consent

Written informed consent was obtained from the patient's family for the publication of this case report.

Declaration of generative AI in scientific writing

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CRediT authorship contribution statement

Takashi Ando: Writing – original draft, Resources, Investigation, Data curation, Conceptualization. **Makoto Naito:** Writing – review & editing, Resources, Investigation.

Declarations of competing interest

None.

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References

1. Pomajzl AJ, Siref LE. Leydig cell cancer [Internet]. In: *StatPearls*. Treasure Island (FL: StatPearls Publishing; 2023. https://www.ncbi.nlm.nih.gov/books/NBK549800/. Accessed July 4, 2023.
2. Cedeno JD, Light DE, Leslie SW. Testicular seminoma [Internet]. In: *StatPearls*. Treasure Island (FL: StatPearls Publishing; 2023. https://www.ncbi.nlm.nih.gov/books/NBK448137/. Accessed May 30, 2023.
3. Secondino S, Viglio A, Neri G, et al. Spermatocytic tumor: a review. *Int J Mol Sci*. 2023;24:9529.
4. Carrière P, Baade P, Fritschi L. Population based incidence and age distribution of spermatocytic seminoma. *J Urol*. 2007;178:125–128.
5. Hu R, Ulbright TM, Young RH. Spermatocytic seminoma: a report of 85 cases emphasizing its morphologic spectrum including some aspects not widely known. *Am J Surg Pathol*. 2019;43:1–11.
6. Obiorah IE, Kyrillos A, Ozdemirli M. Synchronous Leydig cell tumor and seminoma in the ipsilateral testis. *Case Rep Urol*. 2018;2018, 8747131.
7. Mitchinson MJ, Salaman JR, Arno J. Seminoma and intestitial-cell tumour of the testis. *Br J Surg*. 1968;55:32–33.
8. Featherstone JM, Fernando HS, Theaker JM, Simmonds PD, Hayes MC, Mead GM. Sex cord stromal testicular tumors: a clinical series—uniformly Stage I disease. *J Urol*. 2009;181:2090–2096. ; discussion 2096.