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LETTER TO THE EDITOR

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Recurrent paratesticular dedifferentiated liposarcoma after contralateral radical orchiectomy

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Dear Editor,

The concept of dedifferentiated liposarcoma (DDL) was first proposed by Evans in 1979.[1] Liposarcomas, including DDL and well-differentiated liposarcoma (WDL), occur most frequently in 50- to 70-year-old men within the retroperitoneum or extremities. DDL has a propensity for local recurrence, but distant metastasis is rare. Retroperitoneal DDL has a significantly worse prognosis than disease at other locations.[2] As paratesticular DDL is a rare entity, clinicians need to differentiate it from other common scrotal neoplasms or swelling diseases. Herein, we describe a case of recurrent paratesticular DDL after contralateral radical orchiectomy to improve understanding of this disease. Informed consent is obtained from the patient and this study is adherence to Declaration of Helsinki. The protocol of this manuscript was approved by the Human Research Ethics Committee in the First Hospital of Jilin University, Changchun, China.

A 53-year-old man felt distending pain around his right testicle for 20 days. Palpation revealed the absence of the left testis, a well-defined solid mass in the right scrotum, and a larger tough mass in the suprapubic region. A transillumination test of the scrotum was negative, and other physical examinations were normal. A left orchiectomy and regional lymph node dissection was performed due to the patient having "testicular cancer" 2 years ago. His previous pathological report documented a left testicular malignant tumor that was considered as a high-grade sarcoma, but without immunohistochemistry (IHC). Ultrasound (GE LOGIQ E9; GE Healthcare, Wauwatosa, WI, USA) revealed two partially fused hypoechoic nodules above the right epididymis (1.4 cm × 1.1 cm and 1.3 cm × 0.8 cm) and one suprapubic hypoechoic nodule (2.0 cm × 1.3 cm). Bilateral inguinal lymph nodes (range: 0.4–1.0 cm) could be seen by ultrasonography. Abdominal computed tomography (CT; PHILIPS Brilliance 64 CT Scanner; PHILIPS, Best, the Netherlands) scanning revealed subcutaneous fat gap turbidity and a high-density mass (0.5–1.6 cm) above the pubic symphysis (**Figure 1**). Additional pulmonary CT and whole-body bone scans (GE Discovery NM/CT 670; GE Healthcare) suggested no distant metastasis. Laboratory results including tumor markers (carcinoembryonic antigen [CEA], CA-242, alpha fetoprotein [AFP], free prostate-specific antigen [fPSA], total prostate-specific antigen [tPSA], CA125, cytokeratin 19 fragment [CYFRA21-1], neuron-specific enolase [NSE], CA-199, human chorionic gonadotropin [HCG], squamous cell carcinoma antigen [SCCA], and CA-724) and other routine serological tests were normal.

To clarify the diagnosis, the patient underwent ultrasound-guided percutaneous puncture (GE LOGIQ S8; GE Healthcare) on the suprapubic and paratesticular masses. Pathological results of both sites suggested malignant tumors that originated from mesenchymal tissue. Combining his medical history and IHC results, diagnoses of paratesticular DDL and suprapubic undifferentiated sarcoma were made. IHC of patient samples showed positive Vimentin and CD34 staining, suspected positive S-100 (several cells at the suprapubic site) and Ki-67 (>20%) staining, and negative Desmin, smooth muscle (SMA), CD117, Dog-1, and CK-pan staining (**Figure 1**).

Afterward, the right paratesticular tumors and suprapubic abdominal wall tumor were resected. Resection of the right paratesticular tumors (7 cm × 3.5 cm × 2 cm) was done using the inguinal canal approach. During resection of the suprapubic tumor (7.5 cm × 6.5 cm × 4.5 cm), hard nodules located adjacent to the tumor (3 cm × 2 cm × 1.5 cm) and beneath the previous incision site (4 cm × 2.5 cm × 1.5 cm) were simultaneously removed (**Figure 1**). Both the surgery and the postoperative recovery were favorable. The final pathological results after surgery suggested DDL at four sites (**Figure 1**). At a 9-month telephone follow-up, he had gone through three cycles of doxorubicin (ADRIAMYCIN®; Pfizer, New York, NY, USA) and ifosfamide (HOLOXAN®; Baxter Oncology GmbH, Halle, Germany) (A/I) chemotherapy regime (doxorubicin 75 mg m^{-2} per day for day 1–3, plus ifosfamide 2.5 g m^{-2} per day for day 1–4), and no signs of recurrence or metastasis had been found.

Paratesticular masses are common clinical scenarios for urologists and andrologists. A recent study analyzed 138 orchiectomy specimens for paratesticular soft-tissue masses over 17 years. The most common malignancies were rhabdomyosarcoma, liposarcoma, and leiomyosarcoma. The most common benign neoplasm was spermatic cord lipoma, followed by leiomyoma and hemangioma. In young patients, paratesticular malignancies are frequently rhabdomyosarcomas, while in older patients, they are liposarcomas. Most benign lesions were incidental, while malignancies were not.[3]

Preoperative biopsy should be performed if malignancy cannot be excluded. DDL presents as a heterogeneous mass containing both atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDL) components and nonlipogenic high-grade

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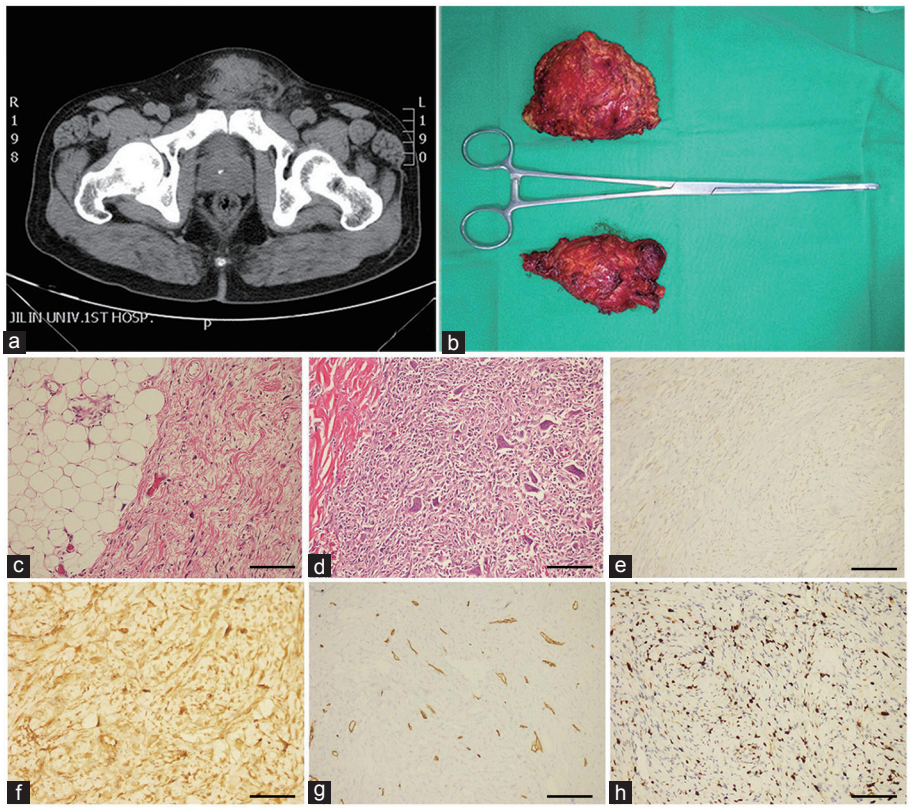

Figure 1: Abdominal CT, gross pathology, and histopathology results of the tumors. (**a**) Abdominal CT revealed a subcutaneous mass lesion above the pubic symphysis. (**b**) Gross pathologic examination revealed that the right intrascrotal dissection block contained two partially fused neoplasms, partial testicle, partial epididymis, and partial spermatic cord (below) and the suprapubic dissection block contained one complete neoplasm and its surrounding fat tissue (above). (**c**) Postoperative H and E ×200 staining showed WDL components. (**d**) Postoperative H and E ×100 staining showed DDL components. Preoperative bioptic immunohistochemistry findings ×200 with (**e**) S-100, (**f**) Vimentin, (**g**) CD34, and (**h**) Ki-67 antibody showed DDL characteristics for samples from both sites. Scale bars = 100 μm in **c**–**h**. S-100 and Vimentin are markers for lipoblast; CD34 is a marker for dedifferentiation degree. CT: computed tomography; DDL: dedifferentiated liposarcoma; H and E: hematoxylin and eosin; WDL: well-differentiated liposarcoma.

sarcoma components. Before IHC and fluorescence *in situ* hybridization (FISH) were widely used, retroperitoneal DDL was often misdiagnosed as either ALT/WDL or malignant fibrous histiocytoma. IHC and FISH detecting mouse double-minute 2 (MDM2) and cyclin-dependent kinase 4 (CDK4) are currently the standard criteria for DDL.[4] A recent report noted that using p16 in combination with MDM2 and CDK4 for IHC could increase diagnostic specificity by helping to discriminate ALT/WDL and DDL.[5] Therefore, preoperative biopsy is essential to reduce unnecessary orchiectomies, and IHC is critical for diagnosing uncommon paratesticular tumors such as DDL. If conditions permit, MDM2 and CDK4 staining should be performed.

En bloc resection of primary DDL is important for improving prognosis because of its propensity for local recurrence. In this case, we inferred that the hard nodule located beneath the previous incision was local recurrence; the suprapubic and inguinal masses were metastatic tumors either from the left intrascrotal tumor 2 years ago or from the right paratesticular DDL. Radiotherapy is required if complete resection fails. Chemotherapy is suggested for metastatic DDL. Laboratory studies have suggested that targeted therapy, such as fibroblast growth factor receptor (FGFR) inhibitors and tyrosine kinase inhibitors, might work for DDL.[6,7] Radiotherapy, chemotherapy, and targeted therapy are clinical options for DDL. Surgical resection remains the mainstay of DDL treatment, as medical options for patients with aggressive relapse or metastasis are limited.[2]

Approximately 8.9% of atypical lipomatous tumors recurred locally, of which 50% recurred after 60 months; in total, 17% of *de novo* DDLs recurred within 60 months of presentation.[8] In a study that reviewed 148 DDL patients, distant metastases were observed in 44 of 148 patients (29.7%), 9 of 44 (20.5%) at presentation, while 35 of 44 patients (79.5%) developed them later, with a median interval of 8 months. The median survival time was 28 months for patients with metastases and 38 months for patients without metastases.[9] Therefore, regular long-term follow-ups are necessary. Based on the current data, follow-up should last over 5 years, and the interval should be every 6 months within the first 5 years and every 12 months afterward. Magnetic resonance imaging (MRI) scanning is highly recommended for follow-up because it is sensitive enough to detect lipomatous lesions.

In conclusion, paratesticular DDL is an extreme rare entity. Preoperative biopsy is essential to confirm the diagnosis. Complete surgical resection is a *sine qua non* for DDL treatment, but chemotherapy, radiotherapy, and targeted therapy can also be considered. Finally, long-term follow-up is necessary to improve prognosis.

AUTHOR CONTRIBUTIONS

JW and YPD carried out the study concept, design, data gathering, and manuscript drafting. SXL carried out medical records and follow-up. JHH and CXW carried out surgery. CXW supervised the manuscript revision and took responsibility for the integrity and accuracy of the data. All authors read and approved the final manuscript.

COMPETING INTERESTS

All authors declared no competing interests.

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