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Well-differentiated and Dedifferentiated Giant Paratesticular Liposarcoma: A Report of Two Cases and a Review of the Literature

İyi Diferansiye ve Dediferansiye Paratestiküler Dev Liposarkomu: İki Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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Abstract

Paratesticular liposarcomas (PLSs) are mostly painless, slow-growing and extremely rare inguinal or scrotal masses. Reports of approximately 270 cases have been published in the literature so far, but only a few of them contain information about giant PLSs exceeding 10 cm in size. Correct diagnosis and treatment is important as PLSs tend to cause local relapses and distant metastases. Here, we aimed to present, and evaluate a dedifferentiated (24 cm), and a well-differentiated (12 cm) giant PLS in the light of the literature data.

Keywords: paratesticular, mass, liposarcoma, giant, sarcoma

Öz

Paratestiküler liposarkomlar (PLS) çoğunlukla ağrısız, yavaş büyüyen ve oldukça nadir görülen inguinal veya skrotal kitlelerdir. Literatürde şu ana kadar yaklaşık 270 vaka bildirilmiştir; ancak bunlardan sadece birkaçı 10 cm'yi aşan dev PLS hakkında bilgi içermektedir. PLS lokal relapslara ve uzak metastazlara neden olma eğiliminde olduğundan doğru tanı ve tedavi önemlidir. Burada 24 cm dediferansiye ve 12 cm iyi diferansiye dev PLS'si olan 2 olguyu sunmayı ve literatürü değerlendirmeyi amaçladık.

Anahtar kelimeler: paratestiküler, kitle, liposarkom, dev, sarkom

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Introduction

Liposarcomas, soft tissue malignancies originating from mesodermal tissues, account for around 20% of all sarcomas. They are generally seen in the retroperitoneal area and extremities [1]. Approximately 12% of liposarcomas originate from the spermatic cord, testicular tunica and epididymis and are called paratesticular liposarcomas (PLSs) [2]. When the tumor diameter exceeds 10 cm, the PLS is classified as "giant" [3]. According to a recent meta-analysis, there are 265 PLS cases in the literature, and only a few cases of giant PLS [4]. Due to its rarity, there is no standard guideline regarding the incidence, diagnosis, recurrence and treatment of PLS [5]. In this case report, we aimed to present our treatment approach for two cases of giant LPS.

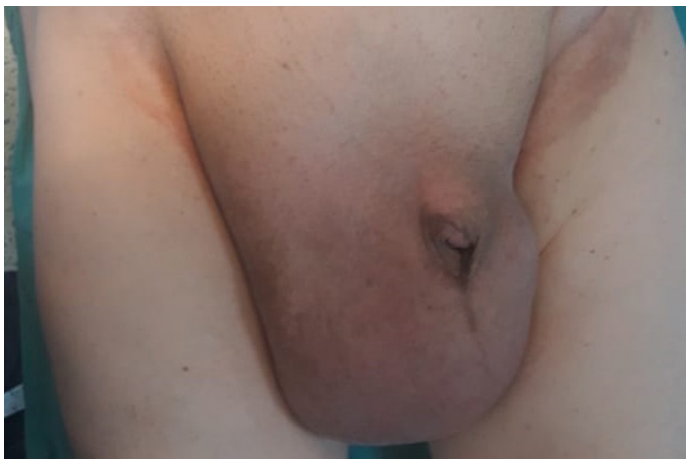

Figure 1. Preoperative view of the giant mass

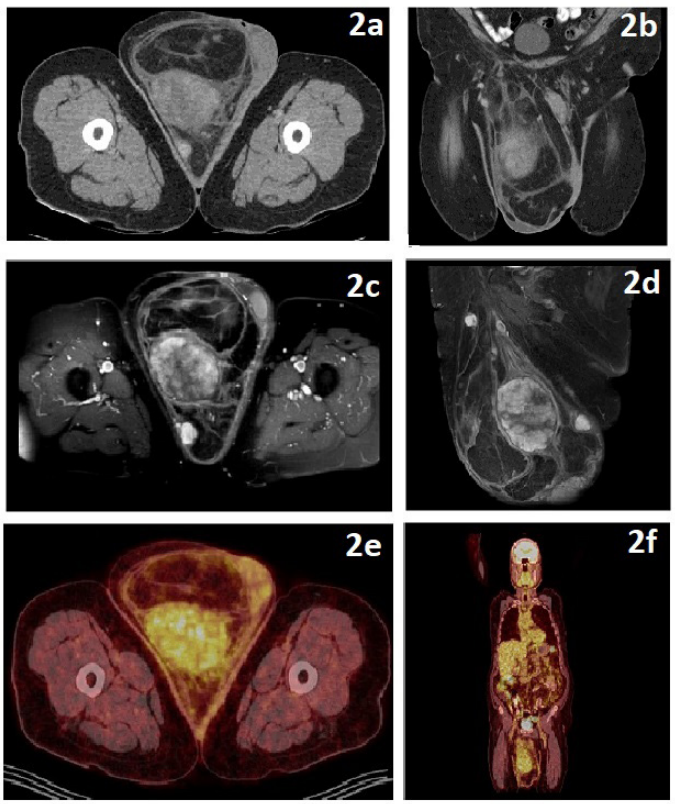

Figure 2. 2ab: Axial and coronal CT images; 2cd: Axial and sagittal MRI images; 2ef: Axial and coronal PET scan images

Case 1

A 63-year-old male patient presented to our outpatient clinic with a painless slowly growing scrotal mass that has been present for about 7 months (**Figure 1**). Physical examination revealed a giant solid mass in the right hemiscrotum. The mass lacked normal testicular tissue as detected during palpitation. The patient's preoperative levels of alpha-fetoprotein (AFP) (1.87 ng/mL), beta-human chorionic gonadotropin (β-hCG) (<1.20 ng/mL), and lactate dehydrogenase (LDH) (173 ng/mL) were as indicated. The contrast-enhanced computed tomography showed a solid mass of approximately 13.5x18.5x23.5 cm in size with heterogeneous fatty tissue containing septa and heterogeneous opacification extending from the right inguinal canal towards the right hemiscrotum (**Figures 2a, and b**). There were no signs of metastases in other organs. On examination, other soft tissues were normal. Magnetic resonance imaging (MRI) showed a solid mass of approximately 13.5x18.5x23.5 cm in size containing septa and heterogeneous fatty tissues herniated from the right inguinal canal towards the right hemiscrotum (**Figures 2c, and d**). Nodular heterogeneous opacifications in different sizes were observed in the superior (1.5x1.5 cm), in the middle (6.5x8.5 cm) and in the immediate inferior (2.5x2 cm) part of the mass. The positron emission tomography (PET) scan (F-18 FDG) imaging of the patient indicated increased 18fluorine-fluorodeoxyglucose (18F-FDG) uptake in the 9.0x6.5 and 3.0x2.2 cm solid components of the 18.0x12.5x24.0 cm fat- density septated mass lesion extending from the right inguinal canal into the scrotum (SUVmax: 8.0) (**Figures 2e, and f**). Thereupon, radical orchiectomy and hemiscrotectomy were performed through a right inguinal incision (**Figures 3a, and b**). A tumor weighing 2590 g with dimensions of 22x18x10 cm, and a negative surgical margin was sent to pathology and reported as dedifferentiated liposarcoma. The dedifferentiated component had the characteristics of myxofibrosarcoma which positively stained with immunohistochemically applied CDK4 (cyclin-dependent kinase-4) for the oncoprotein MDM2 (mouse double minute 2) and negatively with musicarmine stain (**Figures 4a, and b**).

The patient was administered 4 cycles of doxorubicin (50 mg) and ifosfamide (4 g) chemotherapy in the second postoperative month. In order to increase local control following chemotherapy, radiotherapy with a total of 28 fractions (50.4 Gy) and fractional doses of 1.8 Gy was applied using a Siemens Artiste Linear Accelerator Device (Siemens Medical Solutions,

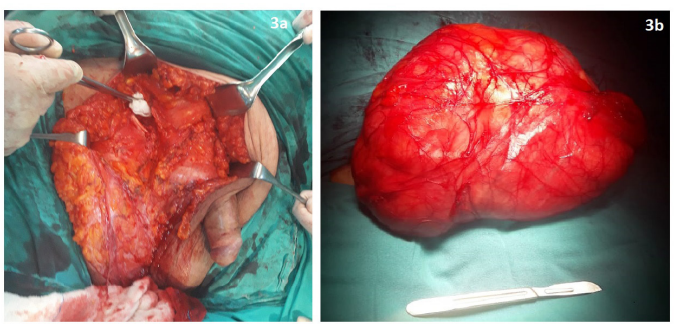

Figure 3. 3a: Surgical area after removal of the mass; 3b: Postoperative view of the giant mass

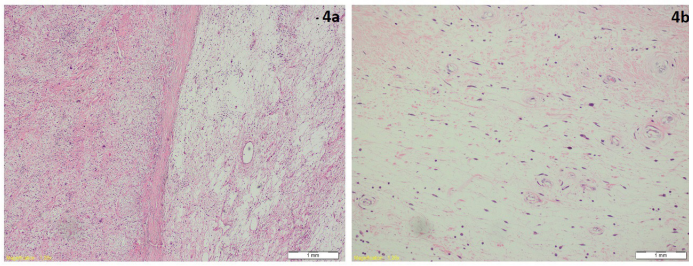

Figure 4. 4a: Sharp transition between dedifferentiated and well-differentiated components in hematoxylin-eosin staining at 4x magnification; 4b: Atypical spindle cells between mature lipocytes in connective tissu

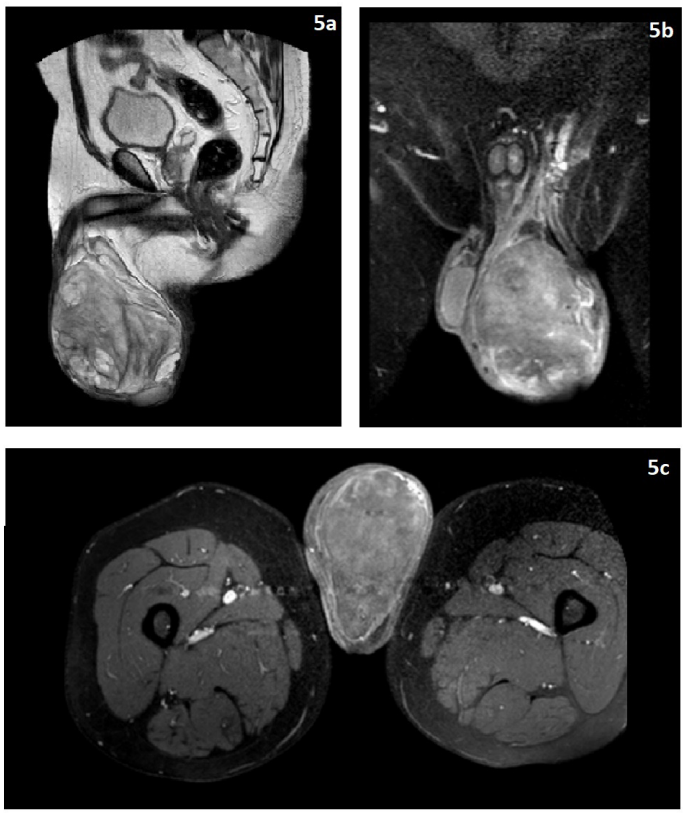

Figure 5. 5abc: Sagittal, coronal and axial section view of the giant scrotal mass in MRI

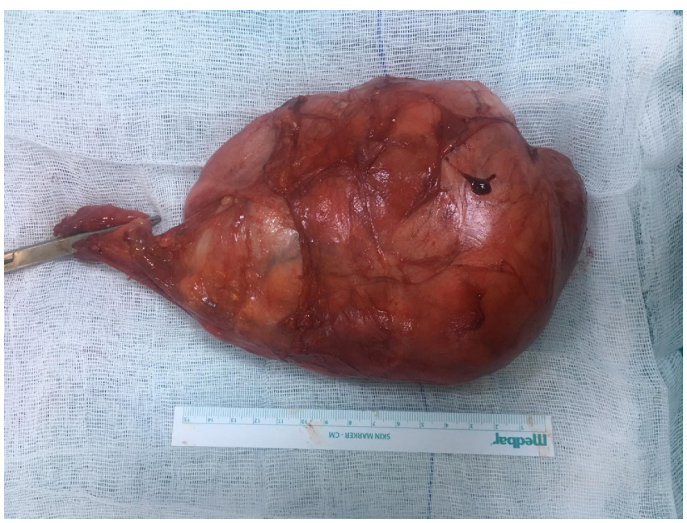

Figure 6. Postoperative view of the giant mass

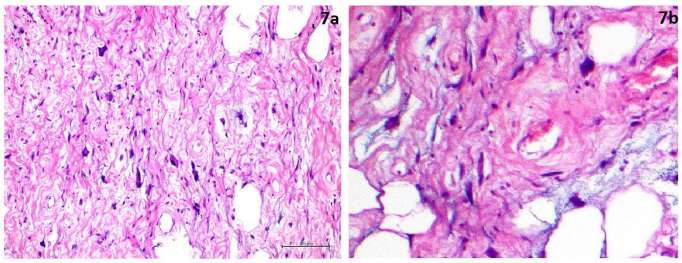

Figure 7. 7ab: In hematoxylin eosin staining at 40x magnification, prominent pleomorphic atypical cells with lipoblasts in eosinophilic background and myxoid changes in the background

Concord, CA, USA) with 6 MV photon energy. No recurrence was detected in the follow-up PET scan (F-18 FDG) obtained at the postoperative 18th month.

Case-2

A 58-year-old male patient was admitted to our outpatient clinic with a painless left hemiscrotal mass that has been growing for about a year. On physical examination, a 12 cm-mass filling the left hemiscrotum was palpated and normal testicular tissue could be partially palpated next to the mass. The patient's preoperative levels of AFP (2.82 ng/mL), β-hCG (<1.20 ng/mL), and LDH (250 ng/mL) were as indicated. MRI revealed a mass in the left hemiscrotum that completely filled the scrotum (**Figures 5a,b, and c**). It has widest dimensions of 12x7.7x7.6 cm and demonstrated heterogeneous necrotic areas in T1 hypo T2-weighted series. Heterogeneous opacifications in post-contrast series, increased diffusion and diffusion restriction in some places were observed. No signs of metastasis were observed. Radical orchiectomy was performed through a right inguinal incision (**Figure 6**). Pathological examination revealed a solid lesion weighing 1440 g and having dimensions of a 14x13x6.5 cm adjacent to but not involving the testicle. The capsule of the lesion was enveloped with typical testicular tissue. Negative surgical margins were obtained. Pathology report suggested a well differentiated liposarcoma. Focal positive nuclear staining was observed with immunohistochemically applied CDK4, but not with MDM2. It also stained positively for S100 protein (**Figures 7a, and b**). The patient was also evaluated by medical oncology due to the possibility of need for additional postoperative treatment. No additional treatment was recommended. No residual tumor or metastases were detected in the patient's postoperative 3rd month follow-up with PET scan (F-18 FDG).

Discussion

PLSs are mostly painless, slow-growing and extremely rare inguinal or scrotal masses [5]. Their origins are difficult to determine due to the complex anatomical structure of the scrotum and inguinal region, but presumably they originate most frequently (76%) from the spermatic cord [6]. In 2002, World Health Organization (WHO) classified liposarcomas based on their histology as well- differentiated, dedifferentiated, myxoid, round cell, and pleomorphic liposarcomas [7]. PLSs are mostly seen in adult patient groups aged between 50 and 60 years

[8]. Compared to well-differentiated low-grade liposarcomas, dedifferentiated liposarcomas have a more aggressive course and tend to have higher local recurrence rates, potential for distant metastasis, and a higher risk of death [9]. In metastatic cases, lung, bone, abdomen, and paraspinal soft tissue metastases are more common [10]. Therefore, application of imaging modalities that examine the thoracic, abdominal, and scrotal surgical regions would be appropriate for metastasis screening. For metastasis screening, we preferred to use PET scan, which is currently used primarily in many metastatic cancer types.

When the tumor diameter exceeds 10 cm, it is called a giant PLS [3]. They manifest as large scrotal mass lesions appearing just below the superficial inguinal ring [7]. Generally, these masses are misdiagnosed as hydrocele, epididymal cyst, inguinal hernia, hematocele or lipoma [9]. On ultrasonography (US), PLSs appear as heterogeneous, solid, hypoechoic lesions with relatively low vascularity, and sometimes liquefaction may accompany if necrosis is present [5,7]. However, US cannot always distinguish PLS from lipomas if the tumor is small or if it is a well-differentiated PLS with a homogeneous fat pattern [11]. Paratesticular liposarcomas are usually seen as heterogeneous mass lesions compatible with fat density in contrast-enhanced CT images. Contrast-enhanced CT can also provide important information regarding staging and follow-up [6]. Another useful imaging technique is MRI, which is the gold standard in the staging of soft tissue tumors. It does not only provide precise information about tumor foci, but also characterizes and defines the extent of local tumor spread [12].

Our Case 1 came with more than one screening examination (CT, MRI and PET) applied in another center before consulting to us. However, our Case 2 applied directly to us. We preferred MRI as preoperative imaging, primarily because of its superiority over the other imaging techniques in demonstrating the surgical site and surrounding soft tissues. On the same day, we made the surgical decision without wasting time in line with the accelerated reports submitted to us by the radiology physicians. In our opinion, it may be more appropriate to use other imaging methods (CT or PET scan) in the postoperative follow-up of metastases. Diagnosis of PLS is mainly made based on the histopathological, immunohistochemical and cytomorphological features of the mass lesion.

When a diagnosis of PLS is suspected, an urgent radical procedure must be performed to avoid the high risk of local recurrence and worsening of the prognosis. The gold standard in PLS treatment is radical orchiectomy with high ligation of the spermatic cord. Wide excision and hemiscrotectomy can also be performed in cases where the mass is larger and local invasion is suspected [13]. The issue of lymph node dissection is controversial. There is not enough data to show that superficial inguinal or retroperitoneal lymph node dissection has any therapeutic efficacy [6]. However, some studies have suggested the application of lymphadenectomy limited to the radiologically detected suspicious lymph nodes [14]. Surgical margin positivity is a risk factor for early recurrence and distant metastases [15]. A clinical study showed that 3-year local recurrence-free survival rates were 100%, and 29% in cases with negative, and positive surgical margins, respectively.

Generally, since liposarcomas are the most radiosensitive types of the sarcomas, radiotherapy is used for local control. In some cases of liposarcomas, remission has been achieved with radiotherapy alone, but the results in PLS are not yet clear. If surgical margin positivity is observed after surgical resection or if there is evidence of a tumor showing a high grade and aggressive behavior, adjuvant radiotherapy may be applied to the inguinal region and scrotum in addition to surgery to prevent local recurrence [16]. Recurrence may occur after radiotherapy in dedifferentiated aggressive tumors. Data on the effectiveness of chemotherapy in metastatic PLS are limited. However, some recent studies have recommended the use of doxorubicin, vincristine and cyclophosphamide [15]. Although the place and effectiveness of adjuvant therapies in the treatment of scrotal liposarcoma are controversial, our first case is one of the largest scrotal liposarcoma cases in the literature, which led us to apply adjuvant therapy more aggressively. However, further studies are needed to define a standard treatment in this regard. With the information we have, application of this type of specific treatment was decided for the patient.

It is important to inform young patients about sperm preservation before orchidectomy. The patient should be informed of the possibility of the presence of dysfunctional testicular tissue remaining after orchiectomy. Apart from this, the information that potential use of adjuvant chemotherapy, and radiotherapy in case of need may adversely affect fertilization, should be shared with the patient. Although long-term infertility after radiotherapy is rarely observed in studies on testicular tumors, it has been found that chemotherapy may cause long-term infertility in a dose-dependent manner. Therefore, the patients who cannot preoperatively preserve their sperms, should be informed about this adverse outcome of chemotherapy before application of adjuvant treatments [17].

In our study, two PLSs were successfully treated and the patients were cured. However, the short postoperative follow-up period of our patients stands out as a limitation of our study. In order to contribute more precise information to the literature, meta-analyses of the cases with longer follow-up periods cited in the literature should be conducted.

Conclusion

PLSs are extremely rare malignant soft tissue tumors. Contrast-enhanced CT and MRI are prominent methods in diagnosis, but the final diagnosis of PLS is made based on histopathological and immunohistochemical evaluation. The gold standard treatment method is radical orchiectomy, and when necessary, a multimodal approach including radiotherapy and chemotherapy is recommended. Long-term follow-up is required due to the risk of local recurrence and distant metastases.

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Informed Consent: An informed consent was obtained from the patient.
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Conflict of Interest: The authors declare that they have no conflict of interest.

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