CASE REPORT

Paratesticular liposarcoma of the spermatic cord: a case report and review of the literature

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Abstract
Spermatic cord liposarcoma is a rare medical condition and liposarcomas are most commonly found in the retroperitoneum, in the extremities and less often in the head and the neck area. The spermatic cord is a rare site of origin, accounting for about 3–7% of all liposarcomas. We report a case of liposarcoma of spermatic cord. A 62-year-old male patient presented with a painless right inguinal mass. MRI (magnetic resonance imaging) showed a fatty mass in the right inguinoscrotal region, and was interpreted as an inguinal hernia containing omentum protruding into scrotum. The mass was removed with right testis and spermatic cord. The surgical margins were negative. Histopathological examination and immunohistochemistry revealed a well-differentiated liposarcoma. In this article, we discuss the clinical behavior of the spermatic cord liposarcoma and currently recommended treatment of the spermatic cord liposarcoma by reviewing the literature. In conclusion, spermatic cord liposarcoma are rare neoplasm that present as firm, slow-growing palpable paratesticular masses and the surgical treatment should include a wide resection around the inguinal canal, with removal of the spermatic cord and the surrounding soft tissue deep to the internal inguinal ring.

Keywords: spermatic cord liposarcoma, paratesticular masses, internal inguinal ring.

Introduction
Sarcomas of genitourinary region represent approximately 2% of soft tissue sarcomas [1, 2]. Almost 3% of malignant lesions of the spermatic cord are liposarcomas [3, 4]. Histological subtypes of malignant tumors are the paratesticular liposarcoma (20–56%), leiomyosarcoma (19–32%) and rhabdomyosarcoma (11–24%) [1, 5, 6]. These tumors are frequently misdiagnosed as benign tumors (most commonly being interpreted as lipomas of the spermatic cord). Regarding histology, paratesticular liposarcomas are divided into four subtypes: well-differentiated, myxoid or round cell, pleomorphic and dedifferentiated [3]. Paratesticular liposarcomas originate in mesenchymal tissue, and because of the slow growth have a low incidence and therefore clinical trials have not yet established proper treatment so far. Previous retrospective studies have suggested that adjuvant radiation therapy improves local control [7–9].

The objective of this case report and literature review, with a focus on a treatment and diagnosis, is that this pathology must be part of differential diagnosis of scrotal mass.

Case report
M.G., a 62-year-old male patient was admitted in the Department of Urology, Emergency County Hospital of Craiova, Romania, in May 2013, with right scrotal mass. There were no histories of local trauma, infection, weight loss or hereditary disease. All preoperative laboratory tests including complete blood count, biochemistry, a chest X-ray, were normal. Physical examination (Figure 1) showed a large, non-tender, mobile right scrotal mass, measuring 7/8 cm, slightly higher consistency, it seems delineate the right testicle, but that was common the right spermatic cord.

An ultrasound scan carried out at the time had suggested an inguinal hernia to be the cause. Clinically, however, the swelling was not typical of an inguinal hernia so an MRI (magnetic resonance imaging) scan was performed (Figure 2). The findings were interpreted as an inguinal hernia containing omentum protruding into the scrotum. There was no suspicion of malignancy to be the cause at the time. The patient underwent exploratory surgery via right inguinal approach (Figure 3) during which a well-defined round mass located above right testis was discovered; the vas deferens was involved. A complete radical right orchidectomy was performed with wide...
excision and high ligation of the spermatic cord, with removal the surrounding soft tissue deep to the internal inguinal ring.

Figure 2 – MRI scan showed bilateral testes with a heterogeneous mass in the right hemiscrotum (red arrow – tumor tissue).

The gross appearance was a solid mass of the adipose tissue (Figure 4), encapsulated and attached to the spermatic cord, a yellowish lipoma-like texture of the cut-surface (Figure 5). Histological examination, confirmed a well-differentiated liposarcoma (Figure 6). The surgical margins were free of tumors. Immunohistochemistry displays vimentin reactivity and negativity for keratins, S100 protein was negative in tumoral cell, CD34 was positive in endothelial cell, α-SMA (alpha-smooth muscle actin) was positive in stromal cell, p16 was positive and Ki67 was >10% in tumoral cell (Figure 7). The patient had a good postoperative clinical course without complications and was discharged on eighth postoperative day.

Paraffin-embedded blocks and cross-sections were prepared in the conventional manner and stained with Hematoxylin–Eosin (HE).

Microscopic examination of HE-stained slides showed variation in cell size, nuclear atypia of adipocytes stromal cells and variable number of lipoblasts (Figure 6, a and b). There was a hyperchromatic stromal cells, multivacuolated lipoblasts set in collagenous background and foci of atypical lipomatous element (Figure 7a). Prominent aggregates of lymphoid cells and plasma cells were noted. Microscopically, there were mature adipocytes showing variation in cell size. Focally nuclear atypia was evident. In areas, individual nuclei were compressed to crescent shape (Figure 6c).

CD34 is a monomeric transmembrane glycoprotein that was shown to react with a variety of non-hemopoietic tissues and their tumors, including dendritic interstitial fibroblastic cells, vascular endothelium and endoneurial cells as well as with neoplastic cells in a variety of mesenchymal tumors such as dermatofibrosarcoma, epithelioid sarcoma, solitary fibrous cells and gastrointestinal stromal tumors. CD34 has a role as an adhesion molecule in the bone marrow, and it is postulated to have a role in presenting carbohydrate ligands to selectin and in regulating adhesion to stromal cells. Extensive membrane and cytoplasmic staining for CD34 is also consistent feature of spindle cell lipomas. In addition, CD34 immunoreactivity identifies a sparse network of dendritic spindle cells in a variety of lipomatous tumors including angiolipomas, myxoid liposarcomas and well-differentiated liposarcoma. In our case, CD34 was positive in endothelial cells (Figure 7c).

α-SMA, an isoform typical of smooth muscle cells and present in high amounts in vascular smooth muscle cells, was demonstrated in the cytoplasm of pericytes of various human organs by means of immunochemistry at the electron microscopic level. In smooth muscle cells and pericytes, α-SMA was localized in the microfilament bundles. Antibodies to intermediate filament proteins are useful tissue-specific markers because the protein composition of these structures markedly differs, depending on cell type. Other components exhibit more restricted tissue specificities. For example, different tissues contain actin isoforms that vary in amino acid sequence and isoelectric point. Skeletal, cardiac and vascular smooth muscles each contain unique α-actin. Non-muscle cells contain actins of β- and γ-mobility. These six different actin isoforms share >90% sequence homology throughout the entire molecule. In our case, α-SMA was positive in stromal cells (Figure 7d).

P16 is an important cell cycle regulator, also known as cyclin-dependent kinase inhibitor-2A, which is a product of the p16INK4a gene located on the short arm of chromosome 9 and is a marker to differentiate well-differentiated liposarcoma from deep-seated lipomas. P16 inhibits progression through the cell cycle by binding to CDK4/6 and preventing inactivation of retinoblastoma protein and appears to be more sensitive for well-differentiated liposarcoma than CDK4 or MDM2. In our case, p16 was positive in lipoblasts (Figure 7b).
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Figure 6 – (a) Lipoblasts with irregular shapes; (b) Stromal atypical cell; (c) Area with morphological aspect characteristic for well-differentiated sclerosing variant of liposarcoma. HE staining, ×200.

Figure 7 – Immunohistochemical pattern of studied tumor: (a) Lipoblasts with irregular shapes and stromal atypical cells, HE staining, ×200; (b) P16 positivity, ×200; (c) CD34 positive in endothelial cells, ×200; (d) α-SMA positive in stromal cells, ×200; (e) Ki67 >10% in tumoral cells, ×200; (f) S100 protein negative in tumoral cells, ×200.

Distinguishing atypical lipomatous tumor or well-differentiated liposarcoma from benign adipocytic neoplasms and dedifferentiated liposarcoma from pleomorphic or myxoid liposarcoma can be difficult. Well-differentiated liposarcoma and dedifferentiated liposarcoma characteristically harbor amplifications of the CDK4 and MDM2
cell cycle oncogenes with protein overexpression and can also overexpress the cell cycle regulator p16. The immunohistochemical trio of MDM2, CDK4 and p16 is a useful diagnostic tool in distinguishing well-differentiated liposarcoma and dedifferentiated liposarcoma from other adipocytic tumors. A tumor was regarded as positive for MDM2 or CDK4 when one or more nuclei were stained per individual high-power field. MDM2 typically showed scattered stained nuclei with increased numbers of positive cells in the most cellular areas.

Discussion

Well-differentiated liposarcoma is a locally aggressive neoplasm and because well-differentiated liposarcoma shows no metastatic potential in absence of dedifferentiation, tumors that occur at surgically amenable sites, where curative surgical excision is possible, are designated atypical lipomatous tumor [10]. The definition of dedifferentiated liposarcoma as non-lipogenic has been somewhat revised with the recognition of cases that contain admixed lipoblasts within the spindle cell or pleomorphic sarcomatous component [11].

Sonography has a sensitivity of 95–100% for distinguishing extratesticular lesions from intratesticular lesions [12]. Para-testicular sarcomas usually have a heterogeneous pattern and are seen as hypervascular tumors on Doppler sonography [13, 14]. Liposarcomas are seen commonly as bulky, heterogeneous tumors that have variable amounts of fat with hyperechoic areas [13, 14]. Computed tomography (CT) scan may be helpful in establish tissue characteristics, morphologic features and tumor location [13] and determining the extent of the mass into the neighboring tissue [15], as well as is helpful in distinguishing primary spermatic cord tumors from a retroperitoneal process extending into the scrotum.

MRI characterizes and delineates the extension of the tumor, distinguishing extratesticular from testicular pathologic processes and cystic lesion from solid lesion [13].

The World Health Organization classification of soft tissue tumors recognize five categories of tumors: well differentiated, dedifferentiated, myxoid, round cell and pleomorphic. The well-differentiated liposarcomas are divided into sclerosing liposarcoma, adipocytic (lipoma-like) liposarcoma and inflammatory and spindle cell liposarcoma [16].

In our case, histopathological diagnosis was of well-differentiated liposarcoma sclerosing subtype. In well-differentiated liposarcomas, subtypes according to histopathological feature are adipocytic (lipoma-like), sclerosing, inflammatory, spindle cell.

In adipocytic subtype, microscopically there are mature adipocytes showing variation in cell size. In some areas, individual nuclei are compressed to crescent shape and focally nuclear atypia is evident. Lipoblasts may or may not be present but some hyperchromatic stromal cells are present. In sclerosing subtype, there are scattered hyperchromatic stromal cells, multivacuolated lipoblasts set in collagenous background and foci of atypical lipomatous element are noted. In inflammatory subtype, there is a dense chronic inflammatory infiltrate almost obscuring the lipogenic areas and prominent aggregates of lymphoid cells and plasma cells are noted. In spindle cell subtype, there is proliferation of bland spindle cell in a fibrous or myxoid background together with atypical lipomatous component including lipoblasts.

Immunohistochemically, the most useful markers for confirming a diagnosis of well-differentiated liposarcoma are MDM2 and CDK4, which show nuclear expression in both spindle cells and adipocytes. The intensity and extent of staining for these markers is greatest in dedifferentiated liposarcoma, reflecting a greater degree of MDM2 amplification [17]. The high-mobility group A2 (HMGA2) protein is another intranuclear architectural factor that is overexpressed in dedifferentiated liposarcoma, although benign lipomatous tumors are also often positive for this marker [18]. Dedifferentiated liposarcoma may express desmin regardless of the presence or absence of a component of heterologous rhabdomyosarcomatous differentiation [19]. Liposarcomas are immunoreactive for CDK4 and MDM2 markers, which can help differentiated the liposarcomas from benign lipomas [20]. In liposarcomas, the most specific immunohistochemical marker is the S100 protein, which is positive in 90% of cases; high-grade liposarcomas are often positive for desmin [21].

Keratin is typically negative in well-differentiated liposarcoma and recent studies have suggested that p16 expression may also be used to support the diagnosis of well-differentiated and dedifferentiated liposarcoma [22, 23].

Conclusions

Liposarcomas of spermatic cord are rare entities and they should be included in the differential diagnosis of scrotal mass. Radical orchectomy with free surgical margins should avoid recurrence and an extended period of follow-up is often required of patients with liposarcoma of spermatic cord because of late recurrence.

Conflict of interests

The authors declare that they have no conflict of interests.

References

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