Case Report

Dedifferentiated liposarcoma of thigh: Tumor with monster cells

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ABSTRACT

Sarcomas are malignant soft tissue tumors that constitute <1% of malignancies and liposarcoma (LS) is the most common sarcoma with about 20%. Majority of LSs are well-differentiated (40%). About 5–10% of them will further progress and develop abrupt shift into dedifferentiated neoplastic tissue and contain nonlipogenic component that are labeled as dedifferentiated LSs. LSs commonly affect age group of 50–70 years and commonly occur over extremities and in retroperitoneum. Prognosis of LS depends on various parameters such as histological grade, type, size, location, and presence, or absence of metastasis. We hereby, report a case in 30 years adult male patient with clinical and radiological diagnoses as "intramuscular lipoma" over the thigh. Cytological examination revealed malignant nature of the soft tissue lesion. Histopathology revealed dedifferentiated LS containing highly bizarre tumor giant cells. This case report reemphasizes the cytology findings of this rare entity and reviews the literature on a dedifferentiated variant of LS.

Key words: Cytology, dedifferentiated, histopathology, liposarcoma

INTRODUCTION

Liposarcoma (LS) is most common malignant soft tissue tumor. Dedifferentiated LS (DDLPS) is the term refers to well-differentiated LS, which develops abrupt transformation to nonlipogenic high-grade sarcoma.[1] Malignant fibrous histiocytoma (MFH) such as histological features are most commonly observed phenotype, although other sarcomatous changes have been described less frequently.[2] The tumor occurs most commonly in 5th to 7th decade of life, predominantly involves retroperitoneal region and lower extremities. Surgical treatment is the mainstay of treatment. The dedifferentiated variant is known to be associated with a local recurrence rate of 41% to 52%, the metastatic rate of 15%, and about 30% disease related mortality rate.[3] In this case report, we describe DDLPS arising at the very young age group of 30 years. Clinically and radiologically, the tumor was diagnosed as an intramuscular lipoma. We offered a diagnosis of "malignant soft tissue tumor probably LS" on cytology and thereby alerting surgeon for wide surgical excision. Histopathology revealed tumor ranging from well-differentiated LS to highly pleomorphic MFH with "monster cell" component. We reemphasize the cytology findings of this rare entity and review the literature on a dedifferentiated variant of LS.

CASE REPORT

A 30-year-old male patient presented to the General Surgery Outpatient Department with complaints of swelling over the left thigh of 6 months duration. The onset of swelling was insidious, and it was rapidly increased in size for the past 1 month. He denied the history of trauma or other swellings anywhere in the body. He also complained associated dragging type of pain. The pain was increased in severity from the past 1 month. Local examination revealed

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a single, diffuse, huge, and ill-defined swelling measuring around 15 cm × 13 cm. The swelling was extending from subcutaneous plane deep into the muscular planes. The swelling had smooth surface, firm consistency, and located 10 cm above left knee joint [Figure 1a]. The overlying skin was unremarkable. There was no local rise of temperature. There were mild restriction and associated tenderness on movement of thigh muscles. It was nonpulsatile swelling. There were no any inguinal palpable lymph nodes. Clinical diagnosis of intramuscular lipoma was made, and the patient was referred to us for fine needle aspiration cytology (FNAC). The cytology smears showed fragments of adipocytes admixed with clusters of the pleomorphic spindle to round cells [Figure 2] with high nuclear to cytoplasmic ratio, hyperchromatic nucleus, prominent nucleoli, and abundant vacuolated cytoplasm. Many multinucleated tumor giant cells [Figure 2, upper inset] were seen in the background. Bizarre appearing lipoblasts displaying scalloped nucleus having multiple cytoplasmic vacuolations were also seen [Figure 2, lower inset]. The impression of malignant soft tissue tumor possibly LS was issued and advised histomorphological study for further confirmation.

Contrast enhanced computed tomography (CT) scan was done which showed a well-defined, lobulated hypodense (−90 to −40 HZ) lesion of size 16.6 cm × 9.0 cm × 5.3 cm seen along the muscular plane of the left thigh along the anterior aspect. Multiple enhancing septae noted within with no calcifications [Figure 1b and c]. No obvious capsular penetration and no involvement of underlying bone were noted. Enhancing solid component measuring 2.0 cm × 1.0 cm was noted in the inferior aspect of the lesion. There was no significant inguinal lymphadenopathy. The lesion appeared to be supplied by an artery arising from the left femoral artery just proximal to its bifurcation. CT scan of the chest was also done, and it was within normal limits with no evidence of any metastatic deposits. The radiological opinion was issued as complex intramuscular lipoma with probable malignant changes and requested for histopathological correlation.

With preoperative clinical diagnosis as malignant soft tissue tumor, the patient was posted for wide excision of the tumor under general anesthesia. C-shaped incision was made on a lateral aspect of mid-thigh extending to inguinal region. Intraoperatively, the tumor was found well-encapsulated and situated in between the thigh muscles. It was excised in total, and all adjacent structures around tumor were dissected, separated, and later refixed to their anatomical position. The tumor was sent for histopathological examination. Postoperatively, the patient received local radiation therapy and 6 months course is uneventful. Patient has been advised for long-term follow-up.

At pathology department, we received a well-circumscribed soft tumor measuring 17 cm × 9 cm × 6 cm. Outer surface covered by a fibrous capsule with congested blood vessels [Figure 3a]. Cut surface showed well-encapsulated yellowish, greasy solid tumor with lobulated appearance [Figure 3b]. There were no areas of hemorrhage or necrosis. Multiple histopathology sections studied showed well-circumscribed soft tissue tumor of lipogenic origin. The tumor was composed of lobules of adipose tissue with myxoid areas containing lipoblasts suggesting well-differentiated LS [Figure 4]. Highly pleomorphic lipoblasts [Figure 4, inset] were also seen. The tumor showed a mosaic pattern with well-differentiated LS islands abruptly transforming into nonlipogenic sarcomatous component with high-grade anaplasia features [Figure 5]. There were foci of sclerosis resembling diffuse fibromatosis and areas with intersecting fascicles with storiform appearance resembling well-differentiated fibrosarcoma. Areas containing pleomorphic MFH component [Figure 6] revealed "monster

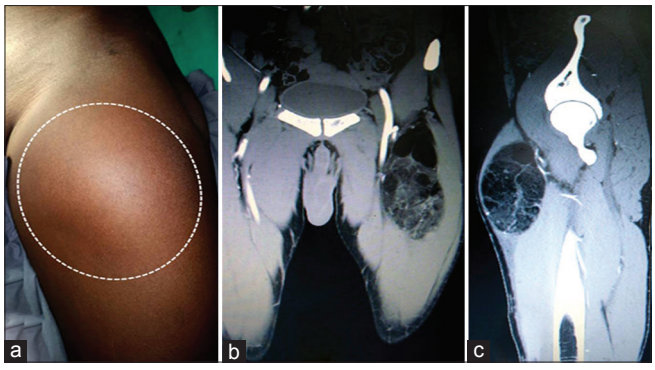

Figure 1: Diffuse, huge, ill-defined soft tissue swelling. (a) Contrast enhanced computed tomography scan showing a well-defined, lobulated, hypodense seen along the muscular plane of left thigh. Multiple enhancing septae noted within with no calcifications. (b and c) Anterior and lateral view

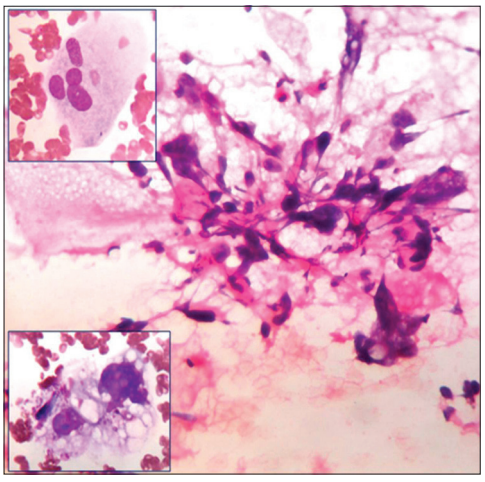

Figure 2: Cytology smears showing clusters of pleomorphic spindle to round cells. Many multinucleated tumor giant cells (upper inset); bizarre appearing lipoblasts displaying scalloped nucleus having multiple cytoplasmic vacuolations (lower inset) (H and E, ×20 and ×40)

cells" with high-grade anaplasia [Figure 6, insets] displaying multinucleated tumor giant cells. The nonlipogenic sarcoma component constituted 50% of the tumor mass. Mitosis ranged from 3 to 5/10 HPF at MFH areas. In spite of high-grade, there was no evidence of necrosis or hemorrhage. The tumor was limited by fascia in all the resected margins. Impression of dedifferentiated LS French Federation of Cancer Centre System (FNCLCC) grade 2, histological grade 3, and stage T2aNxMx was issued. Further confirmation with genetic analysis for MDM2 amplification and immunohistochemistry for histiocytic markers (CD68) was advised, but not carried out due to financial constraints.

DISCUSSION

LS is most common malignant soft tissue tumor that constitutes 20% of sarcomas.[1] LS are further categorized into four subtypes according to the WHO classification: Well = differentiated LS also known as atypical lipomatous tumor (ALT) which constitutes 50% of LS and carries 5 years survival rate of 100%. Myxoid LS also known as round cell LS constitute 40% of LS and carries 88% of 5 years survival rate. Dedifferentiated and pleomorphic LS are rare and carry 56% and 39% of 5 years survival, respectively.[1]

The term DDLPS is applied when well-differentiated LSs/ALT show abrupt transformation into high-grade nonlipomatous sarcoma, which is known to occur in 10% of cases.[2]

LS are usually located in the deep soft tissues. ALT are most frequently located in the limbs, particularly the thighs while DDLPS are most frequent in the retroperitoneum. LS affect adults, the incidence peaks around 60 years. The well-differentiated LSs grow slowly but dedifferentiated sarcomas grow faster and have a higher ability to metastasize than well-differentiated LSs.[3]

Despite the misleading benign appearance of these malignant tumors clinically as well as radiologically, complete preoperative investigations should be performed.

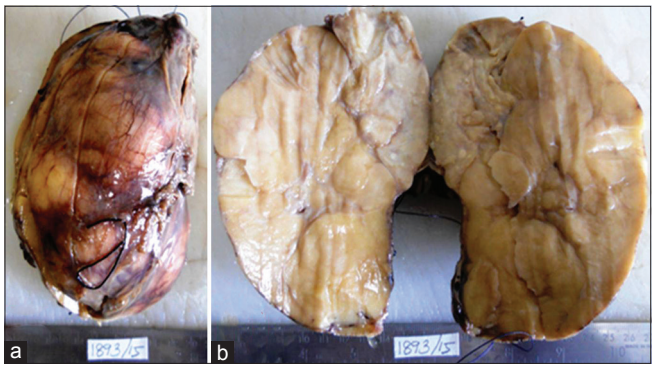

Figure 3: A well-circumscribed soft tumor with outer surface covered by fibrous capsule. (a) Cut section showing yellowish, greasy solid tumor with lobulated appearance (b)

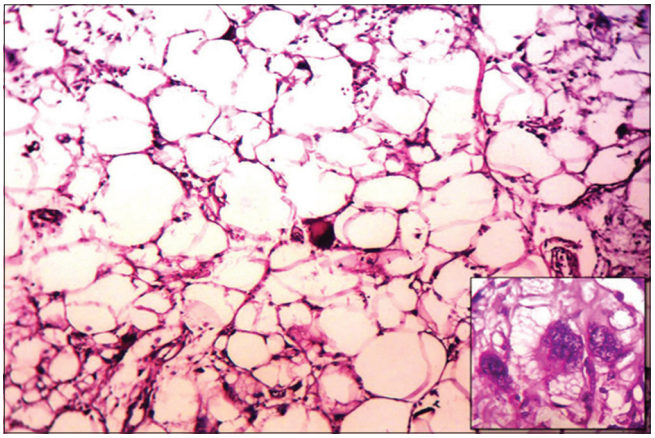

Figure 4: Tumor composed of lobules of adipose tissue containing lipoblasts suggesting well-differentiated liposarcoma. Highly pleomorphic lipoblasts (inset) were also seen (H and E, ×10 and ×40)

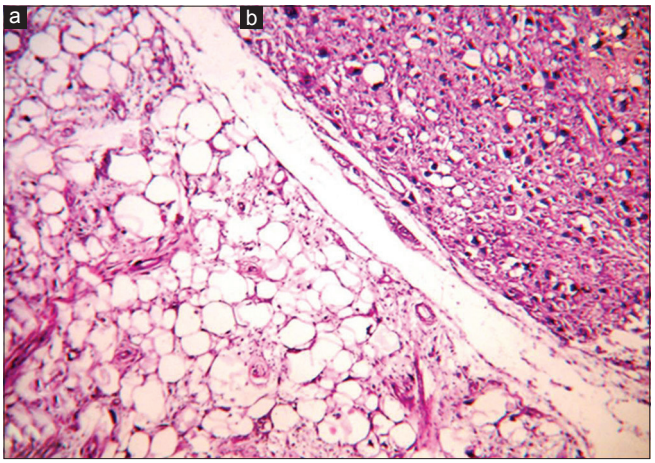

Figure 5: Tumor showing mosaic pattern with well-differentiated liposarcoma. (a) Abruptly transforming into nonlipogenic sarcomatous component. (b) (H and E, ×10)

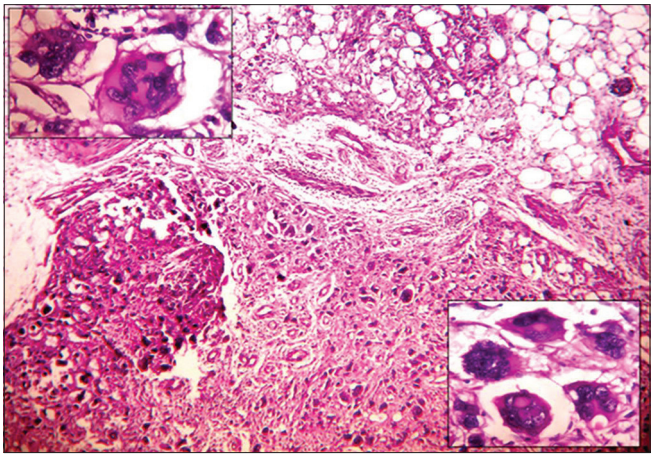

Figure 6: Tumor areas containing pleomorphic malignant fibrous histiocytoma component revealing "monster cells" with high-grade anaplasia and multinucleated tumor giant cells (insets) (H and E, ×4 and ×40)

Any deep-seated soft tissue tumor that exceeds 5 cm in size should be considered as "being suspect" and requires biopsy prior to any excision procedure. FNAC plays an important role at this juncture. It is easy to perform, cost-effective and most of the time provides an accurate diagnosis.[4] Diagnosis of sarcomas by FNA is challenging due to the cytomorphologic overlap in many soft tissue lesions, particularly in spindle cell lesions. Sarcomas usually show hemorrhage, necrosis, dense fibrosis or matrix material which may mask the morphology of viable tumor cells. The diagnosis can be challenging due to the scant cellularity of the aspirates. In these cases, concurrent cell block can help to obtain diagnostic material.[5] In our case, cytological examination by Papanicolaou and Leischman stained smears studied showed a hypercellular sample. The smears showed a mixed population of cells. There were multinucleated, pleomorphic giant cells with abundant vacuolated cytoplasm, smaller clusters of cells with a high nuclear/cytoplasmic ratio, and cells with spindled and elongated nuclear features. Fragments of adipose tissue were also seen. Lipoblasts are conceptually a precursor form of adipocytes and histologically defined as lipid-containing, multivacuolated cells possessing hyperchromatic, indented, or often scalloped nuclei. The "lipoblast-like cells" or "pseudolipoblasts" are seen in a variety of conditions such as fat necrosis, hibernomas, foreign body granulomas, pleomorphic lipoma, chondroid lipoma, plexiform neurofibroma, signet ring melanoma, carcinoma, and lymphoma.[1] Hence, we offered a diagnosis of "malignant soft tissue tumor, most probably LS" and requested further confirmation by histopathological study. This alerted surgeon for wide surgical excision of the tumor and thereby preventing limited excision, as wide surgical resection is the mainstay of treatment for the LSs. Biopsy plays a crucial role in accurate histopathological diagnosis, and proper staging would enable the oncology committee to implement the most appropriate therapeutic protocol.

Histomorphology of DDLPS usually shows remains of ALT with an abrupt shift to dedifferentiated neoplastic tissue. The dedifferentiated tissue is most commonly nonlipogenic and pleomorphic, reminiscent of undifferentiated pleomorphic sarcoma such as MFH.[6] In addition, heterologous differentiation occurs in about 10% of DDLPS and may present as rhabdomyosarcoma, fibrosarcoma, osteosarcoma, chondrosarcoma, or angiosarcoma.[7] Thus, DDLPS may mimic a broad spectrum of soft tissue tumors. The clinical prognosis of DDLPS is better than for other high-grade sarcoma and is not affected by the presence of heterologous differentiation.[7,8]

A hallmark of ALT and DDLPS is the genomic amplification of the MDM2 gene. This can be detected by fluorescence *in situ* hybridization and may facilitate diagnosis.[8]

The prognostic factors of LS include the site of origin, tumor size, depth, patient age, and comorbid associated conditions and most importantly histological type and stage of tumor. The current standard therapy of DDLPS is wide surgical excision.[2] No consensus exists about the minimal length of the resection margins, and the widest resection possible should be archived. This is particularly challenging in the retroperitoneum which may explain the high rates of local recurrences of DDLPS. It may spread to distant sites in 15–20% of cases while ALT does not metastasize. The clinical prognosis is better compared to other high-grade soft tissue sarcomas.[9]

CONCLUSION

DDLPS has pleomorphic histomorphology, and the diagnosis is facilitated by the demonstration of well-differentiated LS component. Deep-seated adipose tissue tumor of more than 5 cm size should be considered an LS until proved otherwise. Cytological examination is cost effective and provides an accurate diagnosis if sampling is done properly and evaluated using various stains such as Papanicolaou, Leischman, and hematoxylin and eosin, as each stain will have its own advantages. These rare tumors should be diagnosed correctly with a multidisciplinary team approach involving surgeon, radiologist, pathologist and oncologist. Prognosis is favorable when the tumor is completely excised, and there is no evidence of distant metastasis. However, long-term follow-up is advisable for any sarcoma patients.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Enzinger FM, Weiss SW. Liposarcoma. In: Soft Tissue Tumors. 3rd ed. St. Louis, MO: Mosby; 1995. p. 431-66.
2. Henricks WH, Chu YC, Goldblum JR, Weiss SW. Dedifferentiated liposarcoma: A clinicopathological analysis of 155 cases with a proposal for an expanded definition of dedifferentiation. Am J Surg Pathol 1997;21:271-81.
3. Coindre JM, Pédeutour F, Aurias A. Well-differentiated and dedifferentiated liposarcomas. Virchows Arch 2010;456:167-79.
4. Al-Maghraby HQ, Khalbuss WE, Rao UN, Cieply K, Dacic S, Monaco SE. Fine needle aspiration biopsy diagnosis of

dedifferentiated liposarcoma: Cytomorphology and MDM2 amplification by FISH. Cytojournal 2010;7:5.
5. Dodd LG. Update on liposarcoma: A review for cytopathologists. Diagn Cytopathol 2012;40:1122-31.
6. Sioletic S, Dal Cin P, Fletcher CD, Hornick JL. Well-differentiated and dedifferentiated liposarcomas with prominent myxoid stroma: Analysis of 56 cases. Histopathology 2013;62:287-93.
7. Thway K, Flora R, Shah C, Olmos D, Fisher C. Diagnostic utility of p16, CDK4, and MDM2 as an immunohistochemical panel in distinguishing well-differentiated and dedifferentiated liposarcomas from other adipocytic tumors. Am J Surg Pathol 2012;36:462-9.
8. Lucas DR, Shukla A, Thomas DG, Patel RM, Kubat AJ, McHugh JB. Dedifferentiated liposarcoma with inflammatory myofibroblastic tumor-like features. Am J Surg Pathol 2010;34:844-51.
9. Coindre JM, Hostein I, Maire G, Derré J, Guillou L, Leroux A, *et al*. Inflammatory malignant fibrous histiocytomas and dedifferentiated liposarcomas: Histological review, genomic profile, and MDM2 and CDK4 status favour a single entity. J Pathol 2004;203:822-30.