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Original Article

Morphological Spectrum of Liposarcoma of Extremities: A Series of 13 Cases from A Tertiary Care Centre of North-East India

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Abstract

Introduction: Liposarcoma is the most common soft tissue sarcoma in adults. Liposarcoma normally presents as slowly enlarging, painless mass in middle-aged person; but some lesions grow rapidly and become ulcerated. They most frequently arise from deep-seated stroma, dermal lesions being rare. The anatomical distribution of liposarcoma appears to be partly related to the histologic type. Both anatomical location and histologic subtypes are partly responsible for outcome and prognosis in liposarcoma patients. Although, the tumor can occur in almost any part of the body, more than half of cases involve the thigh.

Materials and Methods: This is a retrospective study whereby, all liposarcoma of extremities diagnosed in the Department of Pathology, Gauhati Medical College, Assam, over a period of 6 years (January 2010 to December 2015) were retrieved from the archives and reviewed. Each case was analyzed with respect to age, sex, tumor location, size, histologic subtype, the presence of necrosis, and mitotic activity. Immunohistochemistry wherever available was recorded.

Results: A total of 13 cases of liposarcoma of extremities were diagnosed during the study period. The age ranged from 37 to 76 years with median age of 56.7 years. Out of the 13 cases, 9 were male and 4 female with male:female ratio being 2.3:1. Myxoid and/or round cell liposarcoma accounted for 8 cases (61.5%), atypical lipomatous tumor/well-differentiated liposarcoma (WDLS) accounted for 2 cases (15.3%), dedifferentiated liposarcoma 1 case (7.6%), and pleomorphic liposarcoma 2 cases (15.3%). The lower extremity was more commonly involved (10/13 cases).

Conclusion: Because liposarcoma is rare, commonly recurs, it cannot be overemphasised that patients require a multidisciplinary approach involving pathology for accurate diagnosis as histologic grade and subtype determines therapy, follow-up and prognosis.

Key words: Extremity, Liposarcoma, Soft tissue sarcoma

INTRODUCTION

Liposarcoma is a soft tissue sarcoma of adipocytic origin with various clinicopathologic subtypes characterised by distinct molecular/cytogenetic abnormalities. Liposarcoma, although rare, represents one of the most common types of soft tissue sarcoma of the extremities, second only to malignant fibrous histiocytoma and followed by synovial Sarcoma.[1,2] Liposarcoma of the extremity typically presents in the 5th to 7th decades of life with incidence decreasing in young and extremely rare in children.[3] The anatomic distribution of liposarcoma appears to be closely related to histologic subtype. Myxoid/round cell liposarcoma and pleomorphic liposarcoma have a predilection for the extremities, whereas well-differentiated liposarcoma (WDLS) occurs predominantly in the retroperitoneum.

Tumor site, size, grade, and histologic subtype are significant in dictating patient prognosis. Limb tumors carry a better prognosis than retroperitoneal tumors.

Four main forms of liposarcoma are recognised - atypical lipomatous tumor/WDLS, dedifferentiated liposarcoma,

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myxoid/round cell liposarcoma, and pleomorphic liposarcoma.[4] The subclassification of liposarcoma has a dramatic prognostic significance, while tumors in the spectrum of atypical lipomatous tumor/WDLS only carry a risk of a local recurrence and possible dedifferentiation, the pleomorphic liposarcomas are high-grade malignancies with a very high risk of metastatic disease.[4]

MATERIALS AND METHODS

The study is a hospital-based retrospective study conducted in the Department of Pathology, Gauhati Medical College, Assam. All cases of liposarcoma of extremities with available formalin fixed, paraffin embedded tissue were selected from surgical pathology records between January 2010 and December 2015. The tumors were classified as upper extremity if it was beyond shoulder joint and lower extremity if it was beyond hip joint. All retroperitoneal, abdominal, groin, and pelvic liposarcomas were excluded from the study. Nature of the specimen was excisional/incisional biopsy (12 cases) and outside slides and blocks for review (1 case). Out of these, 12 were primary tumors and one was a recurrence. The patient characteristics (age and sex), tumor characteristics (site, size, histologic subtype, necrosis, and mitotic activity) were analyzed in these cases. Tissues were received in 10% formalin, processed routinely with hematoxylin and eosin staining and diagnosis based on the histopathologic examination. Immunohistochemistry for S-100, viamentin and MDM2 were performed for confirmation of diagnosis wherever required.

RESULTS

A total of 13 cases of liposarcoma of extremities were reported during the 6-year study period. The age range of the patients was 37-76 years with a median age of 56.7 years. Out of 13 cases, 9 cases were male and 4 cases were female with a male:female ratio of 2.3:1.

Regarding the site, the lower extremity was involved in 10 cases and upper extremity in 3 cases. In the case of lower extremity, 8 were in the thigh, 1 in popliteal fossa, and 1 in foot. In the case of upper extremity, 2 cases were located in arm and in thumb presenting as a recurrent mass (Table 1). The tumor size ranged from 8 cm to 27.5 cm with a mean size of 15.6 cm. The most common histologic type was myxoid and/or round cell liposarcoma (8 cases) followed by atypical lipomatous tumor/WDLS (2 cases), pleomorphic liposarcoma (2 cases), and dedifferentiated liposarcoma (1 case) (Table 1).

DISCUSSION

Liposarcoma, first described by Virchow in 1860s, is one of the most common soft tissue sarcomas of adult life, the relative incidence among other sarcomas ranging from 9.8% to 16%.[5] Its principal histologic subtypes are entirely separate disease entities with different morphology, genetics, and natural history.[6]

The recent WHO classification of soft tissue tumors recognises the following categories of liposarcoma: (1) Atypical lipomatous tumor/WDLS, (2) dedifferentiated liposarcoma, (3) myxoid/round cell liposarcoma, and (4) pleomorphic liposarcoma. The concept of round cell liposarcoma represents the high-grade counterpart of myxoid liposarcoma is generally accepted. The advent of cytogenetics and molecular investigations has contributed to better categorisation of this subset of mesenchymal neoplasms. Not only have they provided new insights into the histology of these tumors but they have also validated current classification schemes based on conventional morphologic observations.[7,8] Although liposarcoma can occur almost anywhere in the body, the extremities are a favoured site, especially the thigh region. This study was, therefore, conducted to study the morphologic spectrum of liposarcoma in the extremities.

Atypical lipomatous tumor/WDLS are synonyms describing tumors that are identical morphologically, karyotypically and in terms of histologic behavior but determined by tumor location and resectibility.[6] It occurs most frequently in the deep soft tissues of the limbs, especially the thigh. They occur in middle-aged adults with a peak incidence in 6th decade.[6] We found 2 cases of atypical lipomatous tumor/WDLS, one each in the 6th and 7th decade. Male and females are equally affected. In our study, both cases were females and were located in the thigh. Grossly, they were 21 cm and 18.6 cm in size, yellow with whitish areas. Microscopically, tumor consisted of mature fat separated by fibrous septa. Variably sized adipocytes with spindle cells having hyperchromatic nuclei and scattered multivaculated lipoblasts were noted. The recognition of lipoblasts is key to the diagnosis of liposarcoma. The characteristic morphologic features are well-demarcated cytoplasmic lipid that causes indentations in an irregular hyperchromatic nucleus and creates a scalloping of the nuclear membrane.[5] Small floret-like cells was noted in 1 case. Immunohistochemistry plays a very minor role in the differential diagnosis of atypical lipomatous tumor/WDLS.[6] The defining genetic features of atypical lipomatous tumor/WDLS cells are supernumerary ring and rod chromosomes that contain amplification of 12q14 - 15 region including the MDM2

Table 1: The complete data of 13 cases

Number	Age (years)	Sex	Site	Specimen	IHC[$]	Diagnosis
1	66	Male	Lower extremity (thigh)	Excision biopsy	Not done	WDLS*
2	53	Female	Lower extremity (thigh)	Excision biopsy	Not done	Myxoid LS**
3	45	Male	Lower extremity (thigh)	Excision biopsy	Not done	Myxoid LS
4	59	Male	Lower extremity (thigh)	Excision biopsy	Not done	Pleomorphic LS
5	52	Female	Upper extremity (arm)	Incision biopsy	Not done	Myxoid LS
6	60	Male	Lower extremity (thigh)	Excision biopsy	Not done	Myxoid/round cell LS
7	76	Female	Lower Extremity (thigh)	Excision biopsy	Not done	WDLS*
8	61	Fale	Upper extremity (arm)	Excision biopsy	Not done	Myxoid LS
9	67	Male	Lower extremity (thigh)	Slide and block review	S-100 (+) Viamentin (+)	Pleomorphic LS
10	49	Male	Lower extremity (popliteal fossa)	Excision biopsy	Not done	Myxoid/round cell LS
11	55	Male	Upper extremity (thumb)	Amputed thumb	S-100 (+) Viamentin (+) MDM2 (+)	Dedifferentiated LS
12	37	Male	Lower extremity (foot)	Excision biopsy	S-100 (+) Viamentin (+)	Myxoid LS
13	57	Male	Lower extremity (thigh)	Excision biopsy	Not done	Myxoid LS

*WDLS: Well differentiated liposarcoma, **LS: Liposarcoma, [$]IHC: Immunohistochemistry

gene. The most important prognostic factor in this subtype is an anatomic location with overall mortality ranging from 0% for atypical lipomatous tumor of extremities to more than 80% for WDLS of retroperitoneum.[9]

Dedifferentiated liposarcoma: Dedifferentiation or histologic progression to a higher grade, less well-differentiated neoplasm was first described by Dahlin.[10-12] Dedifferentiated liposarcoma develops in the same age group as atypical lipomatous tumor/WDLS reaching a peak during the early 7th decade. The retroperitoneal location is a favoured site of this subtype. <01% occur in subcutaneous site.[5] We retrieved 1 case of dedifferentiated liposarcoma of the thumb. The patient was 55 years, male with recurrent thumb mass. Grossly, specimen consisted of amputed thumb (Figure 1). Cut section was fleshy, whitish - yellow with destruction of underlying bone. Microscopic examination showed features of WDLS juxtaposed to areas of a high grade pleomorphic undifferentiated sarcoma (Figure 2). Immunohistochemistry for S - 100 was positive in well-differentiated areas and MDM2 was positive in dedifferentiated areas (Figure 3). An extensive review of literature shows that dedifferentiated liposarcoma of the thumb is very rare with only one reported case of de - novo subungual right thumb liposarcoma with brain metastasis.[13] Dedifferentiated areas may be high grade or low grade and are generally non lipogenic. Dedifferentiated liposarcoma, despite its high-grade morphology, exhibits a less aggressive clinical course than other subtypes of high-grade pleomorphic sarcoma.[12,14,15] Recent studies have shown that some dedifferentiated liposarcoma can show lipoblastic differentiation in the dedifferentiated, high-grade component, resulting in areas indistinguishable from pleomorphic liposarcoma, leading to consideration of revision of initial criteria for its diagnosis.[16,17]

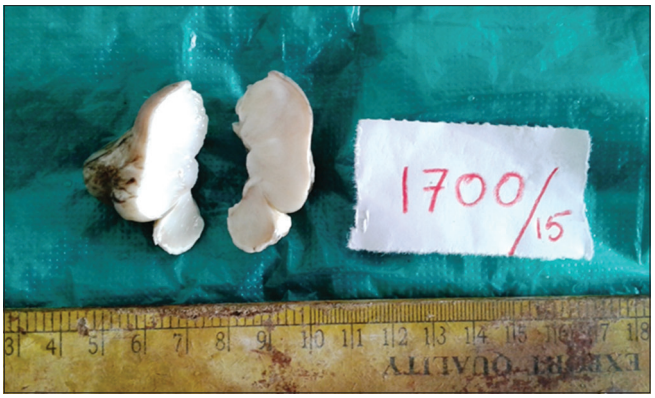

Figure 1: Specimen of amputed thumb showing fleshy, whitish - yellow cut surface (Dedifferentiated LS case)

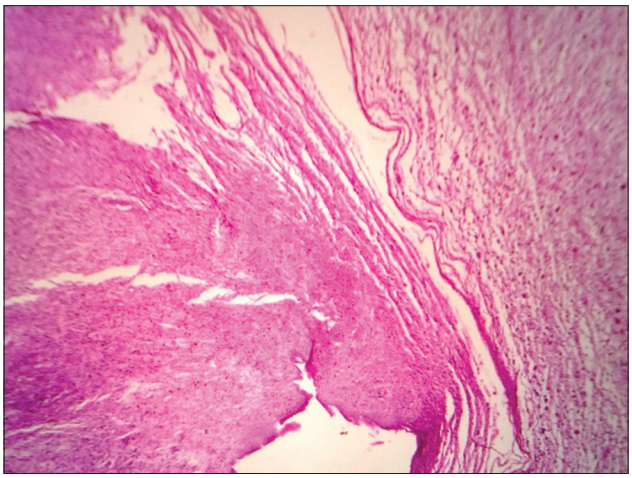

Figure 2: Low power view of dedifferentiated liposarcoma showing the pleomorphic undifferentiated component in the left side and the WDLS component in the right

Myxoid/round cell liposarcoma: Although myxoid liposarcoma typically occurs in middle-aged people, it is the most common type of liposarcoma in adolescents and young

adults. Myxoid liposarcoma has a predilection for the lower extremity and most frequently manifests as a multinodular, gelatinous mass.[5] In our study, 8 cases of myxoid and/or round cell liposarcoma were identified of which 6 cases were in lower extremity and 2 cases in upper extremity (Table 1). 2 patients were female and 6 male. Grossly, tumor size ranged from 11 cm to 21.5 cm (Figure 4). Microscopic examination showed lobules of bland, relatively uniform, spindled to ovoid cells in an abundant myxoid matrix with a prominent, delicate plexiform capillary network (Figure 5). Univacuolated and multivacuolated lipoblasts were seen. Mitotic activity was scant and areas of necrosis noted in 3 cases. 2 tumors showed significant areas of increased cellularity formed by cells having large, relatively uniform hyperchromatic nuclei, and scant eosinophilic cytoplasm (Figure 6) indicative of round cell differentiation.

Round cell liposarcoma is a poorly differentiated form of myxoid liposarcoma. Studies have shown that a round cell component of >5%, portends a higher risk of metastasis or death from disease.[18]

Pleomorphic liposarcoma: Pleomorphic liposarcoma is uncommon and rarely occurs in skin and subcutis.[19] They are most often located on an extremity, trunk and head and neck region. It may be evident as a painless, pedunculated, pink papulonodule.[20] Pleomorphic liposarcoma is the rarest subtypes of liposarcoma and is discriminated from the other high-grade sarcomas by the presence of pleomorphic lipoblasts.[5] In our study, 2 cases of pleomorphic liposarcoma located in the lower extremity, both elderly males were seen. Grossly, tumor size was 15.7 cm and 19.6 cm. Tumors were firm, nodular masses with white to yellow cut surface. Histologically, they were composed of sheets of predominantly pleomorphic spindled cells with variable numbers of pleomorphic lipoblasts (Figure 7). Necrosis was seen and mitotic count ranged from 3 to 6/10 hpf. The majority of pleomorphic liposarcomas resemble other high-grade pleomorphic sarcomas. As emphasised by Fletcher,[21] recognition of this subtype requires careful attention to light microscopic detail. The recognition of pleomorphic lipoblasts is the sine

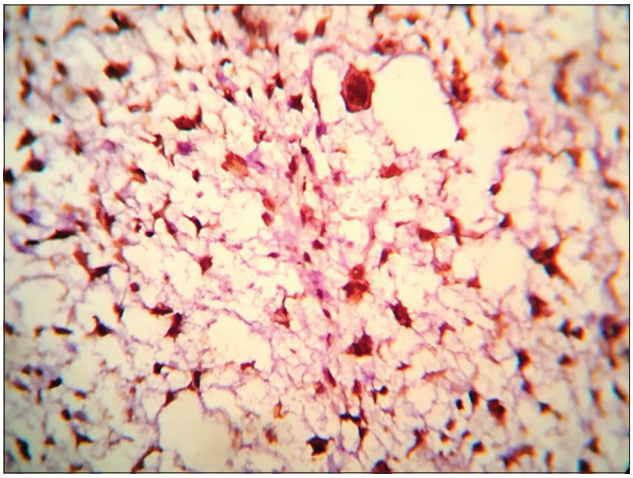

Figure 3: High power view of IHC showing nuclear positivity of MDM2 in the case of dedifferentiated liposarcoma

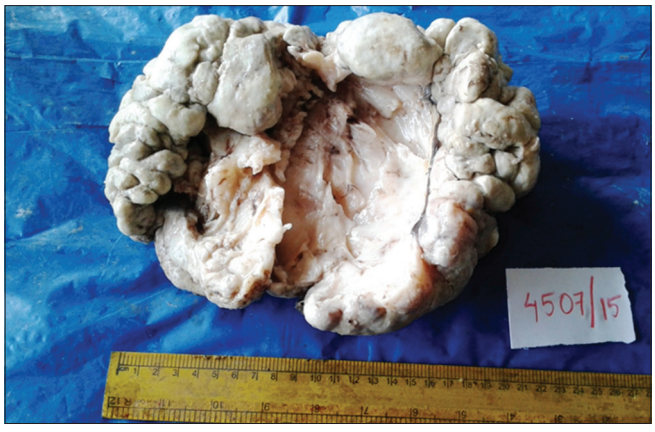

Figure 4: Showing the gross picture of myxoid liposarcoma

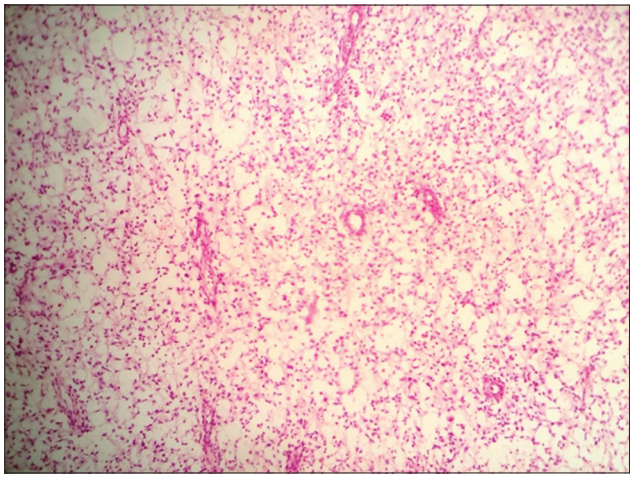

Figure 5: Low power view of myxoid liposarcoma showing the myxoid matrix and the prominent plexiform capillary network

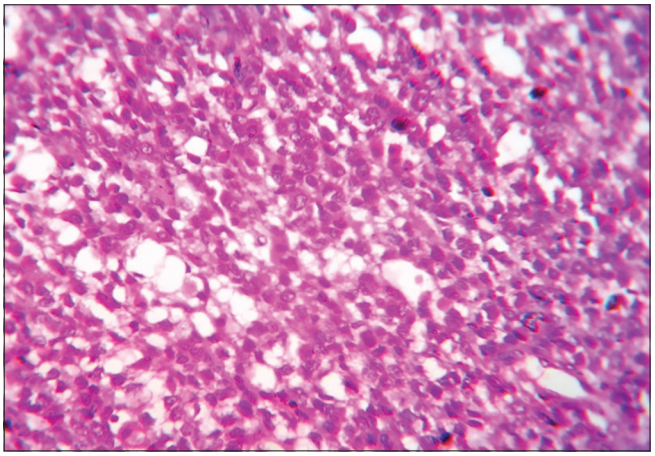

Figure 6: High power view of round cell liposarcoma showing the round cell morphology and the lipoblasts

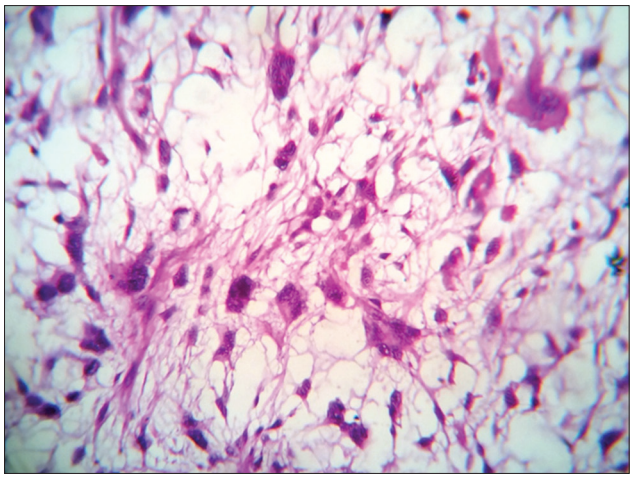

Figure 7: Low power view of pleomorphic liposarcoma showing pleomorphic lipoblasts and the pleomorphic spindled cells

qua non for identification of pleomorphic liposarcoma; immunohistochemical stains are more helpful in excluding other types of pleomorphic sarcomas than confirming a diagnosis of pleomorphic liposarcoma.[22]

CONCLUSION

The morphologic spectrum of liposarcoma and it's subtypes is broad and often underappreciated. Awareness of the diverse histologic appearance and anatomic localization of the various subtypes combined with a robust diagnostic approach are necessary to arrive at a correct diagnosis.

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