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Mini Review

Flaky and Lardy-Atypical Lipomatous Tumour/ Well Differentiated Liposarcoma

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Introduction

Atypical lipomatous tumour or well differentiated liposarcoma is a low grade, lipogenic mesenchymal neoplasm comprised of mature adipocytes admixed with stromal cells. Tumour demonstrates minimal, focal cytological atypia and localized tumour aggression. Adipocytic components appear intermingled with variable quantities of stromal cellular components with consequent emergence of diverse morphological variants delineating significant histological variability. Characteristic ring or giant marker or rod chromosomes constituted of chromosome 12q13-15 engender localized amplification of several adjacent genes as MDM2. Adopted terminology and biological behaviour of the neoplasm is contingent to tumour location wherein deep seated tumefaction may dedifferentiate and subsequently exhibit localized or distant metastasis. Neoplasm may appropriately be alleviated with surgical eradication with a broad perimeter of tumour free surgical margin. Atypical lipomatous tumour or well differentiated liposarcoma incorporates a terminology contingent to tumour location and possible resectability.

The neoplasms emerge as true sarcomas and appear morphologically and genetically identical. Tumours occurring within peripheral location are devoid of possible distant metastasis and are preferably designated as atypical lipomatous tumour wherein comprehensive surgical resection appears curative. Deep seated tumours confined to retroperitoneum, mediastinum or spermatic cord are accompanied by possible localized reoccurrence, dedifferentiation and tumour associated mortality wherein a tumour free surgical margin may be challenging to obtain. The frequently encountered, adipocytic, malignant atypical lipomatous tumour or well differentiated liposarcoma configures an estimated 45% of liposarcomas [1,2]. Adult population is commonly incriminated with peak age of disease emergence between 40 years to 60 years. Neoplasm is exceptionally discerned in paediatric population although an association with Li-Fraumeni syndrome may be observed [1,2].

Majority (~100%) of atypical lipomatous tumour or well differentiated liposarcoma demonstrate ring or giant marker chromosomes or rod chromosomes derived from chromosome 12q13-15. Genomic amplification of chromosome 12q12-21 and amplification of carboxypeptidase M may ensue. Additionally, genetic rearrangements with amplification of chromosome 10p11-14 and complex genetic rearrangements within chromosomes 8 and chromosome 12 may be encountered [1,2]. Fluorescent in situ hybridization (FISH) or polymerase chain reaction (PCR) can be optimally employed to detect MDM2 or CDK4 genetic amplification, a feature which segregates the neoplasm from diverse soft tissue sarcomas [1,2]. Atypical lipomatous tumour or well-differentiated liposarcoma is commonly confined to deep seated soft tissues and especially incriminates proximal extremities or trunk. Frequent site of disease emergence is deep seated soft tissue of thigh followed by retroperitoneum, trunk, head and neck region or spermatic cord. Additionally, gluteal region, shoulder, torso or paratesticular area is frequently implicated [1,2]. Exceptionally, atypical lipomatous tumour or well differentiated liposarcoma may incriminate head and neck, mediastinum, distal extremities, subcutaneous tissue or diverse cutaneous surfaces. Atypical lipomatous tumour or well differentiated liposarcoma is categorized into ~lipoma-like liposarcoma ~sclerosing liposarcoma ~inflammatory liposarcoma [1,2]. Characteristically, a multi-lobulated, well circumscribed neoplasm is encountered upon macroscopic examination. Gross tumour infiltration is exceptionally discerned. Cut surface of lipoma-like lesion appears as marbled yellow. Tumours with minimal adipocytic differentiation occur as firm, fibrotic and greyish white. Enlarged lesions may depict peripheral foci of fat necrosis. Meticulous tissue sampling is optimal for detecting dedifferentiated component appearing as nonlipogenic, firm nodules or neoplastic foci diffusely admixed with low grade tumour areas. Grossly, atypical

lipomatous tumor or well differentiated liposarcoma manifests as an enlarged, well circumscribed, yellowish white, lobulated tumour mass of variable consistency. Foci of necrosis or miniature punctate haemorrhages may be detected [2,3].

Upon cytological examination, mature adipocytes appear intermingled with enlarged cells incorporated with multi-lobulated nuclei. Bizarre tumour cells may occur[2,3]. Upon microscopy, atypical lipomatous tumour or well differentiated liposarcoma demonstrates atypical, hyperchromatic stromal cells admixed with variably quantifiable lipoblasts. Enlarged or retroperitoneal tumours commonly exhibit an amalgamation of diverse morphological patterns within a singular lesion. Lipoma-like subtype enunciates tumour cells with variation of adipocyte magnitude and nuclear atypia. Inflammatory subtype exhibits an intense inflammatory infiltrate admixed with the lipogenic component. Sclerosing subtype exemplifies bizarre stromal cells intermixed within a fibrillary, sclerotic, collagenous stroma [3,4]. Contingent to subtype, tumour is minimally cellular and constituted of mature adipose tissue with adipocytes of variable magnitude. Significant cellular and nuclear atypia may be discerned. Bands of fibrotic tissue traverse neoplastic cellular aggregates. Stroma is composed of spindle shaped cells incorporated with enlarged, hyperchromatic nuclei. Atypical tumour cells appear aggregated within fibrous tissue septa or may delineate a perivascular distribution. Foci of heterologous differentiation are infrequent. Mitotic figures are uncommonly discerned [3,4].

Atypical lipomatous tumour or well differentiated liposarcoma exhibits distinct histologic subtypes designated as ~lipoma-like subtype is a frequently discerned variant comprised of disseminated atypical cells which may be diffuse, innumerable or extremely infrequent. Lipoblasts are frequently encountered. Macroscopically, tumour may simulate a lipoma [3,4] ~sclerosing subtype follows lipoma-like variant in frequency and exemplifies a predilection for retroperitoneal area or paratesticular region. Collagenous fibrous tissue appears admixed with scattered adipocytes and atypical, multinucleated stromal cells. Besides, the minimal lipogenic component may be challenging to ascertain within miniature tissue samples [3,4]. ~inflammatory subtype is an exceptional variant comprised of chronic inflammatory cells as mature small lymphocytes. B lymphocytes exceed T lymphocytes with configuration of occasional lymphoid follicle. Inflammatory cells appear disseminated within a cellular, fibrotic and collagenous stroma with sparsely dispersed, atypical, multinucleated cells. Chronic inflammatory exudate may obscure native adipocytes. Neoplasm is predominantly confined to retroperitoneum wherein distinction from nonlipogenic tumours may be challenging [3,4]. ~mixed subtype is comprised of an admixture of aforesaid variants and may be appropriately discerned with cogent tissue sampling. ~lipoleiomyosarcoma is an exceptionally discerned variant constituted of low grade liposarcoma exemplifying leiomyosarcomatous differentiation of minimal grade. Variable quantities of smooth muscle component may appear associated with enlarged vascular articulations. Disease pathogenesis is akin to atypical lipomatous tumour or well differentiated liposarcoma. Dedifferentiation may ensue [3,4]. ~atypical lipomatous tumour or well differentiated liposarcoma with low grade osteosarcoma-like areas represents a variant wherein foci reminiscent of parosteal osteosarcoma or low grade central osteosarcoma may configure the neoplasm. Characteristically, retroperitoneal well differentiated liposarcoma exhibits an anomalous adipose tissue component upon magnetic resonance imaging(MRI) and foci of 'stranding' appear indicative of thick fibrous bands. However, clinical significance of aforesaid subtypes is limited [3,4] (Figures 1 & 2).

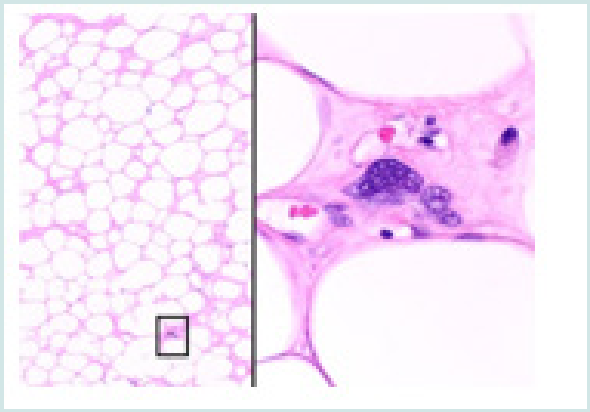

Figure 1: Atypical lipomatous tumour enunciating vacuolated mature adipose tissue cells imbued with hyperchromatic nuclei. Mild cellular and nuclear atypia and pleomorphism is seen. Multinucleated giant cells and traversing bands of fibrous tissue are observed [6].

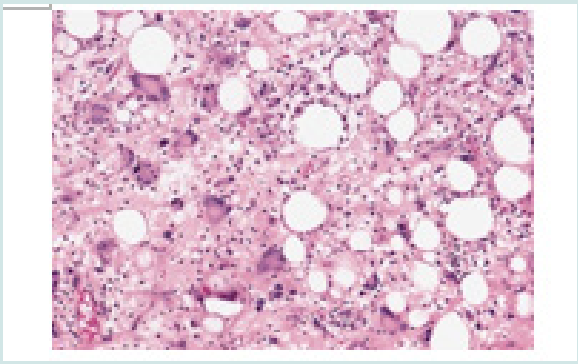

Figure 2: Atypical lipomatous tumour demonstrating aggregates of lipoblasts and mature adipocytes with minimal cytological and nuclear atypia, pleomorphism and hyperchromatic nuclei commingled with multinucleated giant cells and traversing bands of fibrous tissue septa [7].

Atypical lipomatous tumour or well differentiated liposarcoma can be graded as per Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading of adult sarcomas which is designated as •tumour differentiation score is 1 for atypical lipomatous tumor or well differentiated sarcoma pertaining to resemblance to normal tissue •mitotic index is categorized as ~score 1: 0 to 9 mitoses per 10 high power fields ~score 2: 10 to 19 mitoses per 10 high power fields ~score 3: >19 mitoses per 10 high power fields •tumour cell necrosis denominates ~score 0: absence of tumour necrosis while procuring one slide per 2 centimetre tumour diameter ~score 1: <50% of tumour appears necrotic upon morphological examination ~score 2: >50% of tumour appears necrotic upon morphological examination. Contingent to aforesaid parameters, atypical lipomatous tumour or well differentiated liposarcoma is graded as ~Grade 1: score 2 or 3 ~Grade 2: score 4 or 5 ~Grade 3: score ≥ 6 [3,4].

Atypical lipomatous tumour or well differentiated liposarcoma appears immune reactive to MDM2, CDK4 and p16. Focal fat necrosis may be immune reactive to MDM2 and CDK4. Tumour cells appear immune reactive to S100 protein, CD34 or desmin. Neoplastic cells are immune non-reactive to HMB45[4,5]. Inflammatory subtype of atypical lipomatous tumour or well differentiated liposarcoma requires segregation from conditions such as Castleman's disease, Hodgkin's lymphoma, inflammatory myofibroblastic tumor and sclerosing mesenteritis or idiopathic retroperitoneal fibrosis. Lipoma-like subtype of atypical lipomatous tumour or well differentiated liposarcoma necessitates demarcation from neoplasms as lipoblastoma, classic lipoma, lipomatous angiomyolipoma, massive localized lymphedema, myxoid liposarcoma, paraffinoma and spindle cell / pleomorphic lipoma [4,5]. Sclerosing subtype of atypical lipomatous tumour or well differentiated liposarcoma mandates distinction from neoplasms as atypical spindle cell lipomatous tumour, dedifferentiated liposarcoma or lipomatous hemangiopericytoma [4,5]. Besides, conditions such as intermuscular/intramuscular lipoma, lipomatosis, myolipoma, angiomyolipoma, fibrolipomatosis, hibernoma or fat necrosis may necessitate a distinction. Optimal, curative therapeutic strategy for treating atypical lipomatous tumour or well differentiated liposarcoma is comprehensive surgical resection [4,5].

The neoplasm appears insensitive to radiotherapy or chemotherapy. Tumour prognosis and possible distant metastases is contingent to probable dedifferentiation and tumour sites amenable to surgical excision. Aforesaid factors pertain to tumour localization and vary from >20% within retroperitoneal tumours to <2% within tumours confined to extremities. Atypical lipomatous tumour or well differentiated liposarcoma is devoid of distant metastasis which may ensue with dedifferentiation [4,5]. Comprehensive surgical extermination of the neoplasm with wide zone of tumour free surgical margin is an appropriate methodology for alleviating the neoplasm. Precise anatomic location is a significant factor contributing to prognostic outcomes. Tumour metastasis is accompanied with dedifferentiation and significantly decimated overall survival. Tumours confined to retroperitoneum or centric body sites may dedifferentiate, reoccur and induce tumour associated mortality. Cogent surgical eradication of the neoplasm with tumour free surgical margins of aforesaid neoplasms may be challenging [4,5].

Tumour confined to surgical margins and sclerosing subtype is associated with decimated localized recurrence free survival. Subcutaneous or intramuscular neoplasms may reappear although characteristically appear devoid of dedifferentiation or localized dissemination or distant metastasis. Possible tumour dedifferentiation is directly proportionate to site of tumour occurrence and duration of tumour evolution [4,5]. Tumours arising within mediastinum, retroperitoneum or spermatic cord demonstrate an adverse prognosis on account of tumour location and enhanced possible localized reoccurrence. Tumours implicating extremities demonstrate superior prognosis with >90% survival upon 10 years of monitoring. Thus, atypical lipomatous tumour confined to extremities may be subjected to active surveillance in order to circumvent excessive therapy [4,5].

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6. Image 1 Courtesy: Wikimedia commons
7. Image 2 Courtesy: Pathology outlines

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