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Commentary

Congeneric and Consonant-Undifferentiated Pleomorphic Sarcoma Bone

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Undifferentiated pleomorphic sarcoma emerges as a malignant, pleomorphic neoplasm of bone devoid of definitive cellular differentiation. Tumour cells appear to lack a distinct lineage of cellular differentiation. Alternative nomenclature of malignant fibrous histiocytoma of bone or pleomorphic fibrosarcoma of bone is not recommended.

Initially scripted by Frieda Feldman and David Norman in 1972, the distinct entity of mesenchymal bone tumour is comprised of pleomorphic spindle shaped cells and epithelioid cells configuring a storiform or fascicular pattern. Neoplasm appears devoid of osteoid or production of cartilaginous matrix.

Thus, undifferentiated pleomorphic sarcoma of bone emerges as a diagnosis of exclusion. Appropriate tumour discernment mandates concurrence of clinical, radiological and histopathological features.

Undifferentiated pleomorphic sarcoma of bone is an extremely exceptional neoplasm configuring ~6% of primary malignant tumours of bone. A specific gender predilection is absent. Older adults > 40 years are commonly implicated [1,2].

Generally, uni-centric, undifferentiated pleomorphic sarcoma of bone implicates long tubular bones, especially circumscribing knee joint. Femur is commonly involved followed by tibia and humerus in decreasing order of frequency. Pelvic bones are commonly implicated within the appendicular skeleton [1,2].

Undifferentiated pleomorphic carcinoma of bone is associated with diverse genetic alterations and chromosomal structural aberrations wherein chromosomal gains are common observed, in contrast to chromosomal loss [1,2].

Losses within chromosome 8p, 9p, 10, 13q and 18q and gains within chromosome 4q, 5p, 6p, 7p, 8q, 12p, 14q, 17q, 19p, 20q, 22q and X may be exemplified.

Loss of heterozygosity within multiple genes as RB1, TB53, CDKN2A or ING1 is enunciated.

Genomic mutations within TP53 or chromatin remodelling genes as ATRX, DOT1L and H3F3A are frequently exemplified [2,3].

Of obscure aetiology, majority of undifferentiated pleomorphic sarcoma of bone emerge as primary or de novo neoplasms. An estimated 30% lesions appear as secondary tumefaction. Few tumours may emerge from pre-existing bone disease, bone infarct or Paget's disease of bone. Few lesions may concur with preceding irradiation to field of tumour emergence [2,3].

Exceptionally, neoplasm is associated with insertion of metallic prosthesis or hardware into the bone. Certain tumefaction may concur with hereditary diaphyseal medullary stenosis as encountered within Hardcastle syndrome [2,3].

Clinical symptoms appear contingent to tumour localization. Neoplasm may represent with swelling, tumour mass or pain within implicated joint as the knee. Pathological fracture may ensue.

Tumefaction is associated with distant metastases wherein metastasis within pulmonary parenchyma is commonly observed. Distant metastasis is encountered in up to 50% of undifferentiated pleomorphic sarcoma of bone [2,3].

Neoplasm may be appropriately categorized with tumour, node, metastasis (TNM) staging of bone tumours as denominated by American Joint Committee on Cancer (AJCC) guidelines [3,4].

Grossly, neoplasm appears to permeate and encircle pre-existing bony trabeculae. Neoplastic hue is variable and appears as grey/white, yellowish/tan or brownish/tan. Tumefaction is centred upon the medullary cavity. Destruction of cortical bone or implication of circumscribing soft tissue appears characteristic. Foci of tumour necrosis and haemorrhage are discernible [3,4].

Upon microscopy, the hyper-cellular neoplasm is comprised of spindle shaped, epithelioid or polygonal cells configuring a haphazard, storiform or fascicular pattern wherein storiform tumour articulations are commonly discerned. Cellular and nuclear pleomorphism is significant. Tumour cell component appears disseminated within a hyalinised stroma with scattered inflammatory cells. Foci of osteoid or cartilaginous matrix appear absent. Generally, atypical mitotic figures and tumour necrosis are encountered [3,4].

Undifferentiated pleomorphic sarcoma of bone emerges as a grade III sarcoma and depicts significant cellular and nuclear atypia with specific architectural configuration or distortion, in contrast to adult subtype of fibrosarcoma grade II [3,4].

FNCLCC stage	Description	Treatment
Stage I	Tumour ≤ 5 cm or ≤ 15 cm with absent lymph node involvement or metastasis OR grade I lesion	Wide local excision with ≥ 2 cm margins
Stage II	Tumour ≤ 5 cm with absent lymph node involvement or metastasis OR grade II/III lesion	Neoadjuvant/adjuvant radiation therapy and surgical resection
Stage III	Tumour > 5 cm with absent lymph node involvement or metastasis OR grade II/III lesion	Neoadjuvant/adjuvant chemotherapy with radiation therapy and surgical resection
Stage IV	Tumour of variable grade or magnitude with lymph node involvement and +/- metastasis	Neoadjuvant/adjuvant chemotherapy with radiation therapy and surgical resection

Table: *FNCLCC staging of undifferentiated pleomorphic sarcoma [1].*

FNCLCC: Fédération Nationale des Centres de Lutte Contre le Cancer.

Undifferentiated pleomorphic sarcoma of bone is immune reactive to vimentin.

Immune reactivity to CD34, SATB2 and high molecular weight cytokeratin (HMWCK) appears variable.

Tumour cells appear immune non reactive to diverse, distinct lineage markers. Myogenic markers as smooth muscle actin (SMA), desmin, h-caldesmon, myogenin or MyoD1 appear immune non reactive. Besides, immune non reactivity to cytokeratin, S100 protein, CD31, SOX10 and STAT6 is observed [5,6].

Undifferentiated pleomorphic sarcoma of bone requires segregation from various high grade sarcomas as osteosarcoma, leiomyosarcoma, rhabdomyosarcoma, synovial sarcoma, metastatic sarcomatoid carcinoma, metastatic carcinoma, distant metastasis from malignant melanoma, dedifferentiated chondrosarcoma or fibrous dysplasia [5,6].

Upon plain radiography, nonspecific features are exemplified. Neoplasm predominantly configures as an osteolytic, aggressive lesion with pathological fracture, inadequately defined perimeter, focal destruction of bony cortex or associated soft tissue tumefaction [6,7].

Upon T1 weighted and T2 weighted magnetic resonance imaging (MRI), a heterogeneous tumefaction is exemplified. Generally, tumefaction is centred upon meta-diaphyseal region of long bones and occasionally expands into the epiphysis [6,7].

Appropriate neoplastic discernment requires concordance of clinical, radiographic and histopathological features.

Cogent morphological features appear as aggregates of pleomorphic spindle shaped cells or epithelioid cells configuring a storiform or fascicular tumour pattern. Foci of osteoid or cartilaginous matrix appear absent. A distinctive lineage of cellular differentiation is absent, thus neoplasm is categorized as a diagnosis of exclusion [6,7].

Undifferentiated pleomorphic sarcoma of bone may be subjected to radical surgical extermination. Adjuvant chemotherapy may be beneficially employed. Radiotherapy may be appropriately adopted for eradicating neoplasms unamenable to surgical resection [6,7].

Prognostic outcomes are contingent to tumour staging. Neoplasm depicts overall 5 years survival at ~38% and 10 year proportionate survival at ~30%. Localized tumours are associated with superior prognostic outcomes.

Secondary undifferentiated pleomorphic sarcoma and metastatic tumefaction delineate unfavourable prognostic outcomes [6,7].

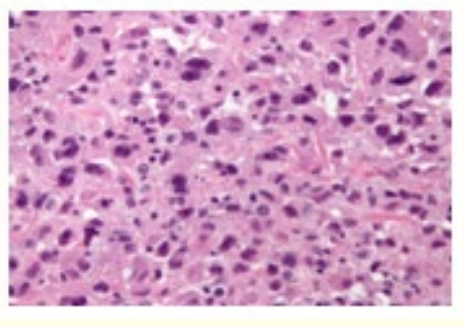

Figure 1: *Undifferentiated pleomorphic sarcoma depicting pleomorphic spindle shaped cells and epithelioid cells with significant cellular and nuclear pleomorphism configuring a storiform pattern. Surrounding stroma is hyalinised with scattered inflammatory cells. Mitotic figures are discernible [8].*

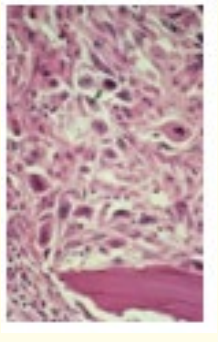

Figure 2: *Undifferentiated pleomorphic sarcoma delineating pleomorphic spindle shaped cells and epithelioid cells with significant cellular and nuclear pleomorphism configuring a storiform pattern. Circumscribing stroma is hyalinised with scattered inflammatory cells. Mitotic figures are observed [9].*

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8. Image 1 Courtesy: Wikipedia.

9. Image 2 Courtesy: Orthobullets.com.

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