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Editorial

Flux and Upheaval-Bone Metastasis

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Bone metastasis emerges as a commonly discerned malignant bone tumour and is preponderantly derived from a distant primary, metastatic carcinoma. Contributing primary tumours are predominantly(~80%) confined to prostate, breast, thyroid and renal or pulmonary parenchyma. Generally, adult population denominates distant metastasis in aforesaid neoplasms. Bone metastasis from primary neoplasms as neuroblastoma, Wilm's tumour, osteosarcoma, Ewing's sarcoma, peripheral neuro-ectodermal tumour (PNET) or rhabdomyosarcoma appear to occur within paediatric population [1,2]. Bone metastasis may be associated with dissemination of tumour cells into intra-spinal region along the Batson's plexus of veins [1,2]. Individuals > 60 years inflicted with sarcomatoid carcinoma demonstrate bone metastasis predominantly comprised of malignant, plump spindle shaped cells invading the bone, in contrast to diverse bone sarcomas and associated carcinomas wherein renal cell carcinoma is a frequent and concurrent primary site [1,2]. Frequently, bone metastasis is encountered within sites as axial skeleton, proximal femur or bone marrow of proximal humerus. Exceptionally, lesions distal to elbow or knee are encountered. Solitary lesions of bone metastases may occur with primaries confined to renal parenchyma or thyroid gland [2,3]. Small bones of hands and feet expound primaries disseminated from carcinomas confined to colon, pulmonary or renal parenchyma.

Bone metastasis may demonstrate cogent clinical symptoms as blastic lesions, bone pain, nerve root or spinal cord compression, spinal cord compression with dorsal pain, para-paresis, sensory symptoms as paraesthesia and numbness upon and beneath the level of spinal cord compression [2,3]. Autonomic dysfunction with bowel and bladder incontinence or impotence emerge as delayed symptoms. Permanent neurological damage may induce paraplegia [2,3]. Hypercalcemia may occur on account of malignant metamorphosis wherein osteolytic bone metastases may concur with hypercalcemia in ~30% lesions and is associated with inferior prognostic outcomes [3,4]. Hypercalcemia may induce symptoms as nausea, anorexia, abdominal pain, constipation or altered mental state. Pathological fractures with bone destruction may ensue with fractures occurring within thoracic and lumbar spine. Pathological fractures are associated with significant morbidities with constant pain, radiculopathy as sciatica secondary to pelvic fracture, skeletal deformities and immobility [3,4]. Myelophthisis secondary to symptomatic anaemia appears secondary to infiltration of bone marrow due to metastatic tumour cells. Pancytopenia may emerge within the delayed phase [3,4].

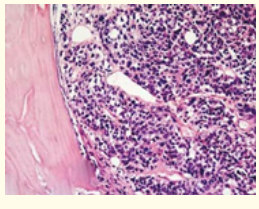

Figure 1: Bone metastasis from lung primaries depicting numerous glandular articulations layered by neoplastic cells imbued with abundant cytoplasm and prominent nucleoli surrounded by spindle shaped cellular stroma embedded within trabeculae of woven bone [7].

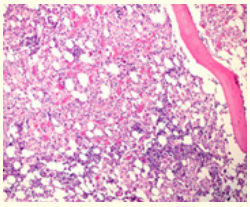

Figure 2: Bone metastasis from breast primaries delineating glandular articulations with open ended configuration circumscribed by plump spindle cellular stroma. Aforesaid malignant glandular articulations are enmeshed within trabeculae of woven bone [8].

Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system(3,4).

Tumour Differentiation

- **Score 1:** Sarcomas resembling normal tissue.
- **Score 2:** Sarcomas with defined histological differentiation.
- **Score 3:** Undifferentiated sarcomas or sarcomas of uncertain histologic differentiation.

Mitotic count as discerned within 10 successive high power fields (HPFs) within significantly mitotically active areas

- **Score 1:** 0 - 9 mitoses
- **Score 2:** 10 - 19 mitoses
- **Score 3:** ≥ 20 mitoses

Tumour necrosis

- **Score 0:** Absence of necrosis
- **Score 1:** < 50% necrosis
- **Score 2:** ≥ 50% necrosis

Tumour grade is comprised of total figures obtained with tumour differentiation, mitotic count and tumour necrosis and is denominated as

- **~Grade 1:** 2 to 3 points
- **~Grade 2:** 4 to 5 points
- **~Grade 3:** 6 to 8 points

Bone metastases requires segregation from neoplasms as primary bone sarcoma, multiple myeloma, primary malignant lymphoma of the bone, secondary or post-irradiation sarcoma or osteomyelitis. Acute osteoporotic fractures, fractures due to metastasis and osteoporosis necessitate distinction [4,5]. Bone metastasis may be appropriately discerned with plain X-rays or orthogonal radiographs. Upon imaging, bone metastases characteristically occurs as osteolytic, sclerotic, osteoblastic or mixed lesions [4,5]. Computerized tomography (CT) may be adopted for preoperative assessment of metastatic disease, especially for lesions arising within shoulder girdle or pelvic girdle [4,5]. Magnetic resonance imaging (MRI) may be employed for detection of bone metastasis or marrow involvement prior to development of osteoblastic lesions. Upon T1 weighted magnetic resonance imaging, signal intensity appears minimal whereas T2 weighted sequences of enhanced signal intensity may appear [4,5]. Nuclear medicine scans may be beneficial in discerning bone metastases with osteo-tropic radioisotopes employed for manoeuvers as skeletal scintigraphy, single photon emission computerized tomography (SPECT) and positron emission tomography (PET) scan [4,5]. Skeletal scintigraphy or bone scan is a commonly employed radionuclide imaging technique wherein 99mTc- methylene diphosphonate (MDP) bone scan appears appropriate for detection of skeletal metastases. Radioisotope imaging methods depict bone metastatic lesions as zones of enhanced tracer uptake. In contrast to multiple myeloma, isotope bone scans appear confirmatory of cogent bone metastasis [4,5]. Bone scan may appropriately scan the entire skeleton. The procedure depicts a sensitivity of ~78% with consequent preliminary neoplastic detection. Lesion detection is significant with the employment of radionuclide bone scanning for neoplasms with prominent osteoblastic activity. Bone scans depict minimal specificity for differentiating between benign and malignant bone lesions and evaluation of predominantly osteolytic lesions. Bone scans may be employed to monitor disease progression and response to therapy [4,5]. Single photon emission computerized tomography (SPECT) with 99mTc- methylene diphosphonate (MDP) bone scan may be advantageously adopted in order to discern bone lesions with a specificity of ~91% [4,5]. Positron emission tomography (PET) employs radiotracers 18 fluorine-fluorodeoxyglucose(F FDG) or 18F

sodium fluoride (NaF) for detection of skeletal metastases [4,5]. A combination of aforesaid imaging techniques and modalities engenders enhanced anatomic and functional visualization with ameliorated diagnostic precision [4,5]. Laboratory investigations as complete blood count and a comprehensive metabolic panel aid in discernment of bone metastasis. Complete blood count (CBC) may demonstrate anaemia, thrombocytopenia or pancytopenia within delayed disease stage. Serum calcium and alkaline phosphatase levels appear elevated due to persistent osteolytic activity [4,5]. Serum biomarkers of enhanced bone turnover may be employed as indicators of bone resorption. Tartrate-resistant acid phosphatase (TRAP) levels appear elevated in subjects with bone metastasis consequent to breast and prostate cancer [5,6]. Bone metastasis may be aptly subjected to localized radiation therapy, non steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, osteoclast inhibitors as bisphosphonates and denosumab, bone targeted radiopharmaceutical therapy as β emitting agents strontium-89 or α-emitting radium-223 [5,6]. Systemic chemotherapy and prophylactic surgical intervention may be adopted for treating impending or complete pathological fracture of long bones. Spinal decompression and stabilization may be adopted to relieve spinal cord compression. Limited or singular bone lesion may be suitably managed with en bloc resection of site of metastasis for achieving localized tumour control [5,6]. Localized tumour ablation through procedures as radiofrequency ablation (RFA), cryoablation or focused ultrasound (FUS) appears beneficial in subjects with reoccurring or persistent pain following radiation therapy [5,6]. Complications secondary to surgical intervention delineate clinical symptoms as pain, haemorrhage, infection, injury to nerves and vascular articulations with consequent numbness or paralysis or tumour reoccurrence. Additionally, neoplastic progression and mortality may ensue due to surgical complications or disease progression [5,6].

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7. Image 1 Courtesy: Pathology outlines.

8. Image 2 Courtesy: Science photo library.