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Conceptual Paper

The Ropy Ossein-Chondromyxoid Fibroma

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Preface

Chondromyxoid fibroma is an exceptional, benign, gradually progressive cartilaginous neoplasm initially scripted by Jaffe and Lichtenstein in 1948 [1]. World Health Organization defines chondromyxoid fibroma as a "benign tumour characterized by lobules of spindle-shaped or stellate cells that proliferate within an abundant intercellular matrix that can be myxoid, chondroid or fibrous in nature". Classically, the benign chondromyxoid fibroma displays incomplete cartilaginous differentiation.

Although plain radiography is characteristic, cogent histological concordance is essential for diagnosis. Adequate concurrence and interpretation of radiological and histopathological features is required. Chondromyxoid fibroma can be challenging to ascertain upon cytology, miniature tissue specimens or core needle biopsy.

Differentiation between chondromyxoid fibroma and chondrosarcoma is critical, challenging and necessitated on account of diversity in therapeutic management and prognostic outcomes. An estimated 22% of chondromyxoid fibromas may be misinterpreted as chondrosarcomas [2].

Disease characteristics

Chondromyxoid fibroma is an uncommon neoplasm configuring an estimated < 0.5% of bone tumours. Tumefaction commonly emerges within the metaphysis of long bones wherein the knee joint or proximal tibia is a frequent site of tumour occurrence. Miniature, tubular bones of the hand, feet, toes, pelvis, sacrum, vertebral column or craniofacial bones are infrequently incriminated in nearly < 5% instances. Isolated involvement of temporal bone is extremely exceptional [2,3].

Tumefaction depicts a slight male preponderance and is usually discerned within second to third decade. Lesions within short, tubular bones commonly arise within the third decade. Chondromyxoid fibroma is a potentially aggressive neoplasm [2,3].

Disease pathogenesis

Although of obscure origin, the neoplasm may depict a genetic origin. The neoplasm depicts an upregulation of glutamate receptor gene (GRM1) encoded upon chromosome 6. Majority (90%) of neoplasms depict a recombination with diverse partner genes. Repetitive cytogenetic aberrations of chromosome 6 are discerned in association with reoccurring genomic rearrangements of chromosomal bands 6p23–25, 6q12–15 and 6q23–27. Contributory predisposing factors are usually absent [2,3].

Chondromyxoid fibroma of the skull is posited to arise from embryonic cell rests entrapped within suture lines and is engendered during endochondral ossification [2,3].

Clinical elucidation

Clinical representation of the neoplasm is variable and pertains to tumour magnitude, site and extension of lesion. Lesions confined to the long bones manifest pain, usually of extended duration. Neoplasms arising within flat or miniature bones generally depict swelling and are occasionally accompanied by pain [2,3].

Tumefaction occurring within the skull manifests a bony lump with headache, neuralgia, facial pain, hearing loss, otalgia, convulsions, diplopia, exophthalmos and facial nerve palsy [2,3].

Histological elucidation

On macroscopic examination, a lobulated, irregular neoplasm with intact periosteum is exemplified. Upon curettage, multiple, firm, irregular, grey/white or pale brown tissue fragments are obtained. Cut surface is firm, glistening and demonstrates variably myxoid areas. Focal calcification may not be discernible with naked eye examination [4,5].

Upon cytological examination, moderately cellular smears depict fragments of metachromatic, fibrillary myxochondroid tissue. Aggregates of spindle-shaped cells and several osteoclast-like giant cells are observed. Nuclear atypia and foci of calcification are variable [4,5].

On microscopy, neoplasm depicts a distinctive, lobular architecture along with peripherally disseminated, cellular foci of chondrocytes and stellate cells alternating with centric, minimally cellular myxoid areas and foci of cystic degeneration [4,5].

Tumour cells are spindle-shaped or stellate with spherical to elliptical nuclei and indistinct, eosinophilic cytoplasm. Foci of necrosis or mitotic activity are absent. Foci of coarse calcification are variable [4,5].

Tumour lobules are segregated by cellular areas composed of innumerable spindle-shaped or spherical cells admixed with varying quantities and magnitude of multinucleated giant cells [4,5].

Neoplastic lobules are demarcated by a population of mononuclear, spindle-shaped cells admixed with multinucleated giant cells. Tumour lobules depict hypo-cellular centric zones surrounded by hyper-cellular peripheral segment. The intervening stroma is variably myxoid to chondroid, depicting diverse stages of cartilaginous development [5].

Tumour lobules are composed of stellate cells disseminated within a myxoid background. Cells may accumulate within the lacunae of chondroid areas. Tumour cells delineate a variable, eosinophilic cytoplasm, bipolar to multipolar cytoplasmic processes and elliptical to spindle-shaped nuclei. Significant nuclear pleomorphism and prominent nucleoli may be discerned in certain instances [4,5].

Lobular tumour pattern comprises of a myxomatous stroma admixed with immature cartilaginous cells confined to chondroid lacunae. Spindle-shaped cells with hyperchromatic nuclei are scattered within the myxoid matrix. Tumour lobules are hypo-cellular and subdivided by hyper-cellular fibrous tissue septa. Stellate tumour cells depict a lobular arrangement and an encompassing myxoid and chondroid stroma [5]. Osteoclast- like multinucleated giant cells are disseminated within the tumour periphery [4,5].

Perimeter of tumour lobules are imbued with spindle- shaped, fibroblast-like cells and scattered multinucleated, osteoclast-like giant cells. Mitotic activity is minimal [4,5].

Foci of coarse calcification may be observed within the stroma, particularly in neoplasms discerned within elderly population or arising upon unusual sites. Hemosiderin pigment deposition and infiltration with lymphocytes may be exemplified [4,5].

Foci of necrosis, cystic change or degenerative modifications are exceptional. Few (10%) instances are associated with areas of aneurysmal bone cyst-like appearance [4,5].

The neoplasm demonstrates upregulation of GRM1 gene. On ultrastructural examination, tumour cells depict cytoplasmic processes, intracytoplasmic accumulation of glycogen and thickening of nuclear membrane [4,5].

Immune histochemical elucidation

Tumour cells within the chondroid lobules are immune reactive to S100 protein and SOX9. Peripherally disseminated spindle-shaped cells are variably immune reactive to smooth muscle actin (SMA). Tumour cells are immune non reactive to CD34, RUNX2 and cytokeratin [2,3].

Differential diagnosis

Chondromyxoid fibroma requires a segregation from diverse cartilaginous neoplasms such as chondroblastoma, enchondroma, chondrosarcoma, chordoma, giant cell tumour and fibrous dysplasia [2,3]:

- Chondroblastoma is a benign, cartilaginous neoplasm which commonly arises within young, skeletally mature individuals. Characteristically, tumefaction arises within the epiphyseal region and is composed of islands of mononuclear cells or disseminated epithelioid along with an absence of stellate cells. Tumour cells demonstrate distinct cell borders and classic, grooved nuclei. Typical, chicken wire-like foci

of calcification are exemplified. Genomic mutations of H3.3 (H3F3B gene), situated on chromosome 17 are observed. Tumour cells are immune reactive to vimentin and S100 protein [2,3].

- Central chondrosarcoma is composed of infiltrative, variably cellular cartilaginous lobules. Chondrosarcoma depicts an extensive, irregular destruction of bone cortex along with incrimination of abutting soft tissue. Histologically, a lobular tumour pattern, myxoid stroma, peripheral accumulation of tumour cells and nuclear atypia is observed. However, chondrosacrcoma is a monotonous neoplasm constituted of enlarged tumour lobules, abundant myxoid ground substance and minimal fibrosis. Foci of mature hyaline cartilage are evident. Mutations of IDH genes are characteristically exemplified. Upon plain radiography, destructive, osteolytic lesions with a "moth eaten" appearance and infiltration into adjacent bone or soft tissue are accompanied by foci of calcification. Chondrosarcoma is immune reactive to S100 protein and vimentin [2,3].
- Chondroid variant of chordoma simulates hyaline cartilage, a modification which may be focal or extensive. Chordoma is a midline tumour and is associated with significant bone destruction and extra-osseous extension. The lobulated tumefaction is composed of miniature cords, dense epithelioid sheets and singular cells disseminated within a myxoid matrix. A component of vacuolated "physaliferous" cells is imbued with abundant clear to eosinophilic cytoplasm, vesicular nuclei and heterogeneous nuclear pleomorphism. Mitotic figures may be observed. The neoplasm is immune reactive to cytokeratin and epithelial membrane antigen (EMA) [2,3].
- Fibrous dysplasia demonstrates characteristic radiological and histopathological features and is composed of branching and anastomosing irregular trabeculae of woven bone with an absence of osteoblastic rimming. Myxoid change and adipose tissue metaplasia of encompassing stroma is occasional. Secondary aneurysm bone cyst-like foci may be discerned [2,3].
- Chondromyxoma-like low-grade osteosarcoma demonstrates lobular arrangement of cartilaginous foci along with configuration of neoplastic osteoid appearing as thick, elongated bony trabeculae. Fascicles of spindle-shaped cells with mild nuclear atypia are embedded within a fibrosclerotic stroma. Tumefaction depicts an invasive growth pattern. Mitotic activity is minimal [2,3].
- Giant cell tumour lacks chondroid differentiation and appears within adult subjects. Giant cell tumour predominantly arises within epiphyses of long bones. Neoplasm depicts a uniform distribution of osteoclast-like, multinucleated giant cells scattered amidst mononuclear cells. Tumour cells are immune reactive to RUNX2, SATB2 or H3.3 (G34W). Neoplasm can be appropriately treated with denosumab, a RUNX ligand inhibitor [2,3].
- Enchondroma commonly appears within fingers and toes. On histology, a pauci-cellular cartilaginous component is observed along with foci of mottled and endochondral ossification. Lobules of hyaline cartilage are enveloped with bone and perichondrium. The hyper-cellular neoplasm depicts a component of bi-nucleate cells and is devoid of fibrous tissue septa segregating myxomatous and chondroid stroma. Foci of necrosis are common [2,3].
- Low-grade infections of the bone are associated with a periosteal reaction whereas chondromyxoid fibroma depicts a discontinuity of bone cortex. Bone infection demonstrates a preliminary neutrophilic infiltration with inflammation. Delayed stage depicts fibrosis of the marrow with infiltration of chronic inflammatory cells, several multinucleated giant cells and a preponderance of plasma cells. Fragments of necrotic bone are observed [2,3].
- Simple bone cyst is commonly encountered in children and adolescents. Grossly, the fluid- filled cyst is layered by an attenuated fibrous tissue membrane. The cyst is traversed by fibrous tissue imbued with osteoclast -like, multinucleated giant cells, foamy histiocytes, cholesterol clefts and hemosiderin-laden macrophages. Irregular bands of fibrin-like, calcified material may span the cyst [2,3].
- Aneurysmal bone cyst is composed of cystic, haemorrhagic spaces layered with osteoclast-like giant cells admixed with solid sheets of proliferating spindle-shaped cells and configuration of blue bone. Upon magnetic resonance imaging, the neoplasm manifests a lytic, expansible lesion with variable fluid levels. The cyst may be associated with several benign and malignant bone and cartilaginous neoplasms. Aneurysmal bone cyst depicts expansion of bone cortex with bubbly appearance on plain radiography, akin to chondromyxoid fibroma [2,3].

- Osteochondromyxoma is an extremely exceptional, benign, myxoid neoplasm configuring a chondroid and osteoid matrix. Tumefaction occurs in association with Carney's complex. The neoplasm commonly arises within diaphysis of radius, tibia or nasal bone. The variably cellular neoplasm is composed of sheets or lobules of polygonal, bipolar or stellate cells admixed with osteoid, chondroid and myxoid matrix. The neoplasm lacks upregulation of GRM1 gene or adjunctive aberrations of chromosome 6. Generally, genomic mutations of PRKAR1A gene, situated upon chromosome 17, are observed [2,3].

Investigative assay

Upon plain radiography, long bones depict an eccentric, lytic, radiolucent, metaphyseal lesion with well circumscribed, sclerosed and scalloped intramedullary edges. Epiphyseal growth plate is rarely breached. Secondary aneurysmal bone cyst-like areas may be observed [7,8].

Miniature, flat bones demonstrate expansible, loculated, lytic lesions associated with localized tissue destruction. Lesions confined to the ribs are fusiform with attenuated superimposed bony cortices. Tumours of sacrum and vertebral column delineate a breach within the bone cortex along with extension into adjacent soft tissue or spinal canal and may appear malignant upon radiography [7,8].

Upon plain radiography, an eccentric lesion within meta-diaphysis of long bones or a centric, width-spanning lesion within short tubular bones is exemplified. A well-defined, scalloped perimeter encompasses the tumefaction. Intra-lesional trabeculae, cortical thinning and expansion are visualized. However, periosteal reaction is exceptional [7,8].

Computerized tomography (CT) delineates a relatively homogenous, well-circumscribed, osteolytic lesion with a wavy perimeter and foci of calcification. Intra-tumoral calcification is discerned in lesions of craniofacial bones, in contrast to long bones. Bone matrix also exhibits calcification [7,8].

Computerized tomography (CT) demonstrates a soft tissue lesion infiltrating abutting bone. Destruction of bony septa is associated with partial bone erosion and attenuated, circumscribing bone cortex. Intrinsic tumour mineralization is well delineated upon CT. Enhanced uptake is observed upon fluoro-deoxy-glucose positron emission computerized tomography (PET-CT) [7,8].

Magnetic resonance imaging (MRI) displays an avascular, lobulated tumefaction of varying magnitude arising within specific sites. Magnetic resonance imaging (MRI) is beneficial in determining extension of lesion. Tumefaction delineates a diffuse, hypointense signal upon T1-weighted imaging and a heterogeneous, hyper-intense signal upon T2-weighted imaging. Significant, diffuse image enhancement is observed following administration of gadolinium contrast [7,8].

Therapeutic options

Chondromyxoid fibroma may be appropriately alleviated with curettage, curettage with bone grafting or cement, en bloc surgical excision or amputation [7,8].

Singular curettage of the neoplasm may be followed by localized tumour reoccurrence in around 20% to 80% tumours, possibly due to inadequate extraction of the tumour [7,8].

Curettage with bone grafting or cementation demonstrates tumour reoccurrence in nearly 7% subjects [7,8].

Surgical extermination of the neoplasm is an optimal therapeutic modality. En bloc surgical resection is the treatment of choice. Extent of surgery is contingent to tumour site, magnitude and extension. Post operative complications such as neurological deficit, loss of hearing, hoarseness, resection of abutting nerves and tumour reappearance may manifest. Localized tumour reoccurrence may necessitate revision surgery [7,8].

Radiation therapy may be advantageously employed in instances with incomplete surgical eradication of the neoplasm or tumour reoccurrence following surgical excision. Lesions of skull base may be particularly benefitted with radiotherapy [7,8].

Comprehensive disappearance of the neoplasm may occur following radiofrequency ablation [7,8].

Amputation is optimally adopted in instances with malignant metamorphosis and multiple tumour relapses [7,8].

Malignant transformation may occur following radiation therapy. Malignant metamorphoses of chondromyxoid fibroma is infrequent although exposure to radiotherapy for inoperable or recurrent lesions enhances possible malignant conversion [7,8].

Neoplasm	Histological similarities	Histological disparities
Chondrosarcoma	Highly cellular neoplasm with lobular growth pattern, myxoid areas. Immune reactive to vimentin and S100 protein.	Invasive pattern of tumour growth. Bony trabeculae, well-differentiated hyaline matrix and absence of fibrous tissue. Cords of tumour cells are surrounded by myxoid stroma. Ample mitosis
Chondroblastoma	Multinucleated giant cells are scattered in a chondroid matrix. Immune reactive to vimentin and S100 protein.	Characteristic spherical, immature chondroblasts depict a distinct cytoplasmic membrane with abundant cytoplasm. Nuclei are centric and spheroidal ("fried egg" appearance).
Chordoma	Chondroid variant of chordoma with a myxoid matrix	Infiltrative perimeter. Aggregates of physaliferous cells with vacuolated, eosinophilic, foamy cytoplasm are arranged along the bony trabeculae. Immune reactive to cytokeratin and EMA.
Giant cell tumour	Multinucleated giant cells	Spatial arrangement of osteoclastic giant cells with stromal fragments. Lack of chondroid differentiation.
Fibrous Dysplasia	Myxoid changes occurring in fibrous dysplasia	Irregular trabeculae with immature woven bone. Variably cellular background with loosely arranged fibrous stroma.
Enchondroma	Lobular growth pattern	Well differentiated hyaline cartilage.
Osteosarcoma	Chondromyxoma-like and chondroblastic variant of low grade osteosarcoma demonstrate vast chondromyxoid fibroma-like foci	Neoplastic osteoid with nuclear atypia and mitosis.

Table: Differential diagnosis of chondromyxoid fibroma [2].

Figure 1: Chondromyxoid fibroma depicting a hypo-cellular neoplasm composed of spindle-shaped cells, osteoclast-like multinucleate giant cells subdivided by fibrous tissue septa [9].

Figure 2: Chondromyxoid fibroma delineating peripheral accumulation of osteoclast-like, multinucleated giant cells admixed with spindle-shaped cells and a myxoid and chondroid matrix [9].

Figure 3: Chondromyxoid fibroma exhibiting dissemination of spindle-shaped cells within a chondroid and myxoid stroma [10].

Figure 4: Chondromyxoid fibroma exhibiting spindle-shaped cells admixed with multinucleated giant cells and an enveloping chondroid and myxoid stroma [11].

Figure 5: Chondromyxoid fibroma enunciating spindle-shaped cells along with few multinucleated giant cells disseminated within a chondroid and myxoid matrix [12].

Figure 6: Chondromyxoid fibroma exemplifying spindle-shaped cells admixed with multinucleated giant cells and a circumscribing chondro-myxomatous stroma [13].

Figure 7: Chondromyxoid fibroma demonstrating a lobulated neoplasm composed of spindle-shaped cells scattered within a chondroid and myxoid background [14].

Figure 8: Chondromyxoid fibroma exemplifying a spindle-shaped cellular component intermingled with few multinucleated giant cells and a myxoid ground substance [15].

Bibliography

1. Jaffe HL and Lichtenstein L "Chondromyxoid fibroma of bone: a distinctive benign tumor likely to be mistaken especially for chondrosarcoma". *Archives of Pathology* 45 (1948): 541-551.
2. Elsamanody A., *et al*. "Chondromyxoid Fibroma of the Mastoid: A Rare Entity with Comprehensive Literature Review". *The Journal of International Advanced Otology* 16.1 (2020): 117-122.
3. Romeo S., *et al*. "Heterogeneous and complex rearrangements of chromosome arm 6q in chondromyxoid fibroma: delineation of breakpoints and analysis of candidate target genes". *The American Journal of Pathology* 177 (2010): 1365-1376.
4. Scheila MG., *et al*. "Chondromyxoid fibroma of the nasal bone". *International Archives of Otorhinolaryngology* 13 (2009): 117-120.
5. Oh N., *et al*. "Chondromyxoid fibroma of the mastoid portion of the temporal bone: MRI and PET/CT findings and their correlation with histology". *Ear, Nose and Throat Journal: SAGE Journals* 92 (2013): 201-203.
6. Wang J., *et al*. "Chondromyxoid fibroma of the petrous apex". *The Journal of Neuroradiology* 38 (2011): 255-256.
7. Hakan T and Vardar Aker F "Chondromyxoid fibroma of frontal bone: A case report and review of the literature". *Turkish Neurosurgery* 18 (2008): 249-253.
8. Thompson AL., *et al*. "Chondromyxoid fibroma of the mastoid facial nerve canal mimicking a facial nerve schwannoma". *Laryngoscope* 119 (2009): 1380-1383.
9. Image 1 and 2 Courtesy: Webpathology.com
10. Image 3 Courtesy: Pathology outlines.
11. Image 4 Courtesy: Libre Pathology.
12. Image 5 Courtesy: Journal of Scientific society.
13. Image 6 Courtesy: SM Journals.
14. Image 7 Courtesy: Atlas of genetics and cytogenetics in oncology.
15. Image 8 Courtesy: BMJ Case Reports.

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