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Conceptual Paper

The Bumpy Rachis-Benign Notochordal Cell Tumour

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Preface

Notochord associated neoplasms of the vertebral column are comprised of benign notochordal cell tumour, ecchordosis physaliphora and chordoma. Notochordal-type vertebral lesion is additionally denominated as benign chordoma, notochordal rest, giant notochordal rest, giant notochordal hamartoma, ecchordosis physaliphorous vertebralis, benign notochordal lesion or benign notochordal cell tumour.

Benign notochordal cell tumour is a benign, intraosseous tumefaction engendered from cells of the notochord. The neoplasm was initially scripted by Darby., *et al*. in 1999 and designated as an "intraosseous chordoma" [1]. The intraosseous neoplasm is contemplated to be diverse from a notochordal rest or hamartoma.

Neoplasms originating from cells of the notochord are common and demonstrate an estimated prevalence of 20%. Application of magnetic resonance imaging (MRI) has significantly enhanced tumour detection although cogent disease discernment of the contemporary neoplasm may be challenging.

Disease characteristics

Notochord induces configuration of the vertebral column during third week of gestation with emergence of vertebral bodies, intervertebral disc and nucleus pulposus [2]. Subsequently, the notochord degenerates and is undiscernible beyond 10 weeks of gestation. Nevertheless, the notochord may be discernible in infants, children or middle-aged adults [2,3].

Of notochordal differentiation, the neoplasm demonstrates a wide age of disease emergence with an equivalent gender distribution. Tumefaction is generally discerned beyond > 40 years [2,3].

Tumour magnitude usually varies from one millimetre to 13 millimetres and the neoplasm is frequently discerned at multiple sites such as the vertebral column, sacrum, clivus, cervical spine or lumbar vertebral region [2,3].

The neoplasm may coexist with chordoma or appear as a precursor lesion to chordoma. Nevertheless, concurrence between chordoma and benign notochordal cell tumour remains debatable. Tumour progression of benign notochordal cell tumour is generally absent [2,3].

Clinical elucidation

Majority of neoplasms are miniature lesions which are discovered incidentally, at autopsy or are associated with diverse disorders. The miniature neoplasm usually appears within axial bones. Incrimination of entire vertebral column is exceptional [2,3].

Enlarged benign notochordal cell tumour may be initially detected due to accompanying back pain. Benign notochordal cell tumour usually incriminates a singular vertebral body. Also, non-contiguous, multi-centric neoplasms are exceptional [3,4].

Histological elucidation

Grossly, the neoplasm may be well demarcated or poorly demarcated, non lobulated and appears yellowish or grey/white. Certain dark red foci of bone marrow are intermingled within the aggregates of neoplastic cells [3,4].

Microscopy of the incriminated bone or vertebral bodies displays bone trabeculae with maintained architecture. Tumefaction is composed of sheets or nests of characteristic physaliferous cells imbued with a singular vacuole. Essentially, the neoplasm is composed of solid, sheet-like proliferation of univacuolar or mul-

tivacuolar physaliferous cells. The cellular component permeates between existing bone trabeculae.

The neoplastic cellular component supplants the bone marrow and incorporates medullary spaces between bony trabeculae although trabecular architecture is well preserved. Islands of hematopoietic cells or mature adipose tissue aggregates confined to the bone marrow appear intermingled between sheets of neoplastic cells [3,4].

Bone trabeculae demonstrate thickened, dense, cement lines and configuration of appositional, reactive new bone formation. Upon low power examination, the cellular component may be misinterpreted as clusters of mature adipose tissue [3,4].

Upon high power examination, the characteristic physaliferous cells demonstrate a clear, vacuolated cytoplasm and eccentric, elliptical or spherical nuclei [3,4].

Microscopically, bone trabeculae and bone marrow are permeated and partially replaced by poorly circumscribed nests of neoplastic cells which characteristically display a clear, vacuolated cytoplasm. Tumour cells configure aggregates, nests, clusters and a cord-like pattern [3,4].

Foci of viable, cellular bone marrow are exemplified. Diffuse dissemination or focal accumulation of red blood cells is intermingled within the tumour cell nests [3,4].

Phyasilferous tumour cells are imbued with singular or multiple vacuoles. Tumour cell nuclei are miniature, centric or confined to the cellular perimeter. Mature adipocytes arising as a component of the bone marrow are admixed with aggregates of neoplastic cells. Also, cells with minimally vacuolated, eosinophilic cytoplasm and centric, spherical nuclei are observed [4,5].

The well demarcated, un-encapsulated neoplasm is composed of sheets of adipocyte-like, vacuolated cells admixed with eosinophilic cells with minimal vacuoles. The cytoplasm is frequently imbued with eosinophilic hyaline globules or colloid-like substance. Nuclei are bland, spherical and depict minimal cellular or nuclear pleomorphism [4,5].

Nuclear atypia is minimal whereas cellular and nuclear pleomorphism, mitoses and foci of necrosis are absent. Occasionally, microcystic spaces are delineated which are incorporated with colloid- like substance. Although soft tissue extension is absent, tumefaction may depict expansion along adjoining extra-osseous tissue [4,5].

Bone trabeculae are usually sclerotic. Foci of bone destruction, intercellular myxoid matrix, necrosis or mitotic activity is absent. Trabeculae of incriminated bone are thick, dense and demonstrate deposition of new bone upon the trabecular surface [4,5].

The neoplasm is devoid of lobular architecture, fibrous bands, morphological heterogeneity, nuclear atypia, mitotic activity, necrosis, decimation of adjoining bone trabeculae, myxoid stroma, syncytial cell strands or soft tissue invasion [4,5].

Immune histochemical elucidation

Tumour cells are diffusely immune reactive to pan-cytokeratin (AE1/AE3), low molecular weight cytokeratin, epithelial membrane antigen (EMA), S100 protein and vimentin. Immune reactivity to CK18, galectin-3 and HBME-1 may also be discerned. Brachyury is a transcription factor implicated in development of the notochord and appears consistently immune reactive. Intracellular eosinophilic hyaline globules can be stained with Periodic acid Schiff's (PAS) stain and are resistant to digestion by diastase [5,6].

Tumour cells are immune non reactive to CD10, smooth muscle actin (SMA), calponin, desmin, high molecular weight cytokeratin and glial fibrillary acidic protein (GFAP). Ki-67 proliferative index is minimal and appears at approximately 1%. Currently, cytokeratin 18 is considered as a dubious immune marker for differentiating benign notochordal cell tumour from diverse notochordal neoplasms [5,6].

Differential diagnosis

Benign notochordal cell tumour requires a segregation from conditions such as:

- Haemangioma confined to the vertebrae is a commonly discerned benign neoplasm composed of endothelium layered vascular articulations. The neoplasm depicts significant image enhancement and increased signal intensities upon T1 weighted and T2 weighted magnetic resonance imaging (MRI). Computerized tomography (CT) depicts a typical "polka-dot sign" which is indicative of thickened bone trabeculae of incriminated vertebral bodies [6,7].

- Chordoma is an osteolytic neoplasm consistently located within the axial skeleton, especially vertebral column and sacrococcygeal or sphenocciptal region. The lobulated tumefaction is constituted by cords, strands or sheets of vacuolated physaliferous cells enmeshed within a myxoid matrix and segregated by attenuated fibrous tissue septa. Tumour cells depict mild to marked nuclear atypia. Chordoma stains intensely with alcian blue and the extracellular sulphated muco-polysaccharides are resistant to digestion with hyaluronidase. Chordoma is immune reactive to cytokeratin such as CK1, CK7, CK10, CK19, CK20, CK19, CK12 to CK17 and immune non reactive to type IV collagen [6,7].

- Giant notochordal rest or notochordal vestiges are comprised of cords or strands of notochordal cells entangled within a myxoid background. Constituent cells are imbued with minimally vacuolated, abundant, eosinophilic cytoplasm and pyknotic, spherical nuclei. The cellular component is immune non reactive to CK18. Notochordal vestiges are usually substituted by fibrocartilage within ~ 3 years [6,7].

- Metastatic cancer composed of vacuolated cells such as clear cell renal cell carcinoma is discerned within the adult age group. Typically, tumefaction delineates an extraneous golden tinge on account of lipid rich cellular component. Nests of clear cells are segregated by a vascular framework. Tumour parenchyma depicts foci of tumour necrosis and haemorrhage. Neoplasm appears immune reactive to pan-cytokeratin (AE1/AE3), epithelial membrane antigen (EMA) or vimentin and is immune non reactive to S100 protein [6,7].

- Vertebral adipose tissue metaplasia is constituted by aggregates and nests of benign, mature adipocytes imbued with vacuolated, lipid-rich cytoplasm and eccentric nuclei. Metaplastic adipose tissue aggregates are traversed by fine, vascularized fibrous tissue septa and are immune non reactive to pan-cytokeratin (AE1/AE3), epithelial membrane antigen (EMA) or S100 protein [7,8].

- Malignant vertebral neoplasms morphologically delineate diverse configurations such as irregular tumour perimeter, aberrant intrinsic tissue architecture, tumour necrosis and extra-osseous tumour extension. Computerized tomography displays foci of osteolysis or osteosclerosis. Magnetic resonance imaging of malignant vertebral neoplasm depicts a minimal signal intensity upon T1 weighted imaging and enhanced signal intensity upon T2 weighted imaging. Also, significant image enhancement of the hyper-vascular malignant vascular neoplasm is observed upon administration of gadolinium contrast medium [8,9].

Associated bone diseases with a component of vacuolated cells are immune non reactive to cytokeratin (AE1/AE3), epithelial membrane antigen (EMA) and S100 protein [8,9].

Additionally, entrapped, intra-lesional bone marrow fragments comprised of significant quantities of haematopoietic cells require a demarcation [8,9].

Investigative assay

Plain radiographs may display an osteolytic defect, pathological fracture or moderate sclerosis as the non expansive neoplasm is confined to the bone [9,10].

Computerized tomography (CT) may be unremarkable with absence of vertebral anomalies or may demonstrate moderate sclerosis of vertebral bodies in the absence of bone destruction [9,10].

Upon plain radiographs and computerized tomography (CT), benign notochordal cell tumour may or may not be accompanied by sclerosis or may demonstrate minimal to significant radio-density. Radio-density visualized upon plain radiographs and computerized tomography (CT) is concurrent to dense bone trabeculae and articulated new, reactive bone. Upon computerized tomography (CT), the neoplasm depicts minimal intraosseous sclerotic alterations and mild thickening of uninvolved bone trabeculae. Nevertheless, absence of extra-osseous invasion or osteolytic features is indicative of benign notochordal cell tumour [9,10].

Magnetic resonance imaging (MRI) can be beneficially adopted for appropriate tumour discernment. Upon MRI, the intraosseous tumefaction depicts a clear perimeter with an intrinsic, homogeneous signal intensity. Tumefaction displays minimal to intermediate signal intensity upon T1 weighted imaging and intermediate to enhanced signal intensity upon T2 weighted imaging. Administration of gadolinium exhibits occasional heterogeneity with absence of tumour enhancement. Extra-osseous extension of lesion is usually absent [10,11].

Bone scan is usually unremarkable although cold spots may be detected upon the lesion site. Prevalence of benign notochordal cell tumour upon imaging is around 0.76% [10,11].

Radiographically, architecture of benign notochordal cell tumour is usually maintained with occurrence of bone trabeculae, absence of bone expansion, bone destruction, tumour extension into adjoining soft tissue and lack of tumour enhancement following contrast administration, features which are absent in a chordoma [10,11].

Therapeutic options

The contemporary, preferable treatment strategy is periodic monitoring of the neoplasm in the absence of specific therapy [11,12].

Surgical extermination of benign notochordal cell tumour is recommended with emergence of osteolytic lesions or tumours demonstrating extra-osseous expansion [11,12].

The benign, non-progressive benign notochordal cell tumour may necessitate surgical eradication in instances demonstrating malignant transformation. Additionally, debilitating, chronic pain associated with the neoplasm or fracture of vertebral body may require surgical intervention or resection of incriminated vertebral body [11,12].

Diverse treatment strategies are comprised of curettage of the neoplasm, comprehensive vertebrectomy or vertebral reconstruction fixation. Injection of bone cement into vertebral bodies may also be employed [11,12].

The neoplasm may undergo malignant metamorphoses and emerge as a classic chordoma [11,12]. Benign notochordal cell tumour is devoid of tumour reoccurrence or distant metastasis [11,12].

Figure 1: Benign notochordal cell tumour depicting clusters of physaliferous cells with a singular vacuole, eosinophilic cytoplasm, bland spherical nuclei and a cord-like pattern [13].

Figure 2: Benign notochordal cell tumour demonstrating multi-vacuolated physaliferous cells with central uniform nuclei and adjoining thickened bone trabeculae [14].

Figure 3: Benign notochordal cell tumour delineating aggregates of multi-vacuolated physaliferous cells with bland nuclei and abutting thickened bone trabeculae [15].

Figure 6: Benign notochordal cell tumour exemplifying nests of physaliferous cells with singular or multiple vacuole, uniform centric nuclei and thickened trabeculae of adjacent bone [16].

Figure 5: Benign notochordal cell tumour displaying cords of vacuolated physaliferous cells with bland nuclei and intermingled thickened bone trabeculae [17].

Figure 6: Benign notochordal cell tumour enunciating cords of vacuolated physaliferous cells with intertwined thick bone trabeculae [18].

Figure 7: Benign notochordal cell tumour demonstrating thickened, dense, sclerotic bone trabeculae [19].

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