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Conceptual Paper

Dedifferentiated Chordoma of the Skull Base in Children: An Enigmatic Rare Tumour

Mark Yoi Sun Soo*

Senior Lecturer in Clinical Radiology, Faculty of Medicine and Health Science, University of Sydney and Visiting Medical Officer, Department of Radiology, Westmead Hospital, Westmead, NSW, Australia

***Corresponding Author:** Mark Yoi Sun Soo, Senior Lecturer in Clinical Radiology, Faculty of Medicine and Health Science, University of Sydney and Visiting Medical Officer, Department of Radiology, Westmead Hospital, Westmead, NSW, Australia.

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Abbreviations

AT/RT: Atypical Teratoid/Rhabdoid Tumour; CC: Conventional Chordoma; DC: Dedifferentiated Chordoma; GTR: Gross Total Resection; MFH: Malignant Fibrous Histiocytoma; PDC: Poorly Differentiated Chordoma; PBT: Proton Beam Therapy; SB: Skull Base

The tendency for skull base (SB) chordomas in childhood to turn malignant is well documented. In keeping with its capricious biological nature, the clinical course among children under the age of five is strikingly short and terminal. An unusual high incidence of cellular atypia inevitably leads to malignant change and distant metastases. Such poor prognosis is further illustrated by the fact that despite surgical excision and adjuvant radiotherapy, the five year overall survival is 14% compared with 66% among children over five years of age. Arguably, conventional chordoma (CC) affecting very young children is a different condition.

In 1993, a group from a children's hospital in St Louis, Missouri, USA, described their own experience on 12 children treated for chordomas. Six of them had originated from the SB, all but one died of the disease between four weeks and 4.5 years following initial presentation. Death from distant metastases accounted for 33%. Yet, these figures were on chordomas with histological cellular atypia only. The truly malignant form is when a CC differentiates, over time, into a high-grade sarcoma.

During the mid-1980s and 1990s, research scientists in North America, Europe and Japan discovered the histopathological pathways whereby a CC would spontaneously morph into a dedifferentiated chordoma (DC), known as a de-novo process. More commonly, a DC can originate from a recurrent or incompletely excised CC. One should realise oncological scientists of the past four decades conducted their research of DC on the more common sacral chordoma in adult patients; a scientifically acceptable practice since those stricken with DC irrespective of age share identical cyto-morphologies.

It has been revealed DCs affecting adults and children, especially the latter, are rare. The actual number of cases occurring in children is rather inconsistent as case reports are also published in the French and Italian literature. A series from Boston MGH (2020) analysed

87 cases of DC between 1914 and 2019, the youngest being a 15-year-old. Contrarily, the New York Sloan Memorial Kettering Cancer Centre series (2019) described three children below the age of seven among 11 patients with DC over a 23-year period. Two of them have remained well and disease free following gross total resection (GTR) with negative margins.

Of 10 cranial CCs described by Toronto's Sick Children Hospital (2016), two died because their lesions turned sarcomatous 12 months after incomplete resection and radiotherapy. Data from a paediatric series in Beijing (2019) listed 63 SB CCs, including a single case of DC, possibly originating de novo. Additionally, in 2016, an eight-year-old girl developed DC two years following proton beam therapy (PBT) treatment for a SB CC. Despite the above discussion on children, DC is more a tumour of young and older adults.

Freshly excised specimens show no major differences in appearance between CC and DC although in the latter the cut surface might be a little haemorrhagic and necrotic. Presence of fibrous septations is characteristic but not diagnostic of CC as Ewing's tumour may remotely have such features. However, it is the cytological findings that determine DC as a different neoplastic entity. These are based on the invariable presence of sarcomas (from 30% to 90%) within the lesion in question. The histological feature of a DC is typified by a sharp demarcation of CC with an adjacent sarcomatous component. The commonest components include malignant fibrous histiocytoma (MFH), fibrosarcoma with malignant spindle cells and anaplastic sarcomas. In later years, other researchers found the demarcation between CC and sarcoma indistinct that might have caused laxness in criteria. It led to over-diagnosis of DC. Additionally, some specimens were inadequately examined histologically. The exact cyto-morphologic features of a DC consist of short atypical spindle cells with moderate extents of granular cytoplasm. The classic physaliferous cells are absent and only scant amount of extra-cellular myxoid material is discernible. Nuclear inclusions and mitotic figures are occasionally present. Sarcomatous cells are the predominant (between 40 to 98%) cell type.

Of late, another subtype of chordoma popularly known as poorly differentiated chordoma (PDC) has been described mainly in the oncology/pathology literature. There is some similarity of PDC in clinical presentation and patient population to DC. The inclination of PDC to affect the paediatric and adolescent population is even more pronounced. Cyto-morphologically, a PDC consists of epithelioid cells characterised by prominent nucleoli and with a rich vein of cellular pleomorphism and eosinophilic cytoplasm. The classic physaliferous cells are notably absent; crucially, sarcomatous changes are not present.

A remote possibility exists whereupon a young child with a SB DC can be mistaken for an infratentorial atypical teratoid/rhabdoid tumour (AT/RT) as they share certain gross morphological features. There is the similarity in cellular heterogeneity, intratumoral calcifications and occasional scattered tiny haemorrhagic foci. But AT/RT tends to form cysts that do not occur in DCs. The favoured location for AT/RT is cerebello-pontine angle but CCs and DCs arise primarily from the clivus in which clival floor erosion is the hallmark of the disease. But immunohistochemical findings are the final arbitrator. Although both AT/RT and DC show loss of the tumour suppressor gene SMARCB1, only DC with its inherent chordoma component expresses the transcription factor gene T brachyury.

GTR remains the only avenue of cure for both CC and DC. In paediatric practice there is the traditional trans-sphenoidal approach and also a lateral retrosigmoid craniotomy for petroclival tumours. Recent advances in endoscopic endonasal surgery have made it safe and effective even for six-year-old children for excision of clival CCs and DCs. The most suitable scenario that is free of serious postsurgical complications relate to tumours in the extradural space and patients without history of prior surgical interventions. The anatomical complexities of the clival regions make it difficult for surgical removal without causing partial cranial nerve damage or possible injury to the cavernous internal carotid artery.

But adjuvant radiotherapy to treat incompletely excised tumour has proven to be effective. The Bragg effect of PBT renders a low incidence of immediate and remote complications, maintaining a good quality of life for children for many years.

One cannot over-emphasise the wisdom of referring those afflicted with SB DC to management of a multi-disciplinary team. The resources of a paediatric teaching institution can be relied on. Its well-trained staff on neurosurgical nursing and post-surgical adjuvant radiation therapy are fully conversant of the patients' care and long-term follow-up.

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