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GLI ACTIVATED NESTED MALIGNANT EPITHELIOID CELL TUMOUR

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Soft tissue neoplasms displaying a nested epithelioid morphology and abnormalities of the GLI-1 locus are emerging as a distinctive new tumour type. In 2018, a series of 6 such tumours was published, showing frequent S100 positivity and a tendency for aggressive clinical behaviour. Recently, a case series was published describing a related group of tumours showing morphologic overlap with the earlier examples and harbouring GLI-1 amplification as an alternative pathway of GLI-1 activation. We report a 9-year-old female who presented with a 5-year history of a slowly growing lesion on the left great toe. Microscopy revealed a dermally-based tumour with a multinodular growth pattern, arranged in tight nests separated by thin fibrovascular septa. The tumour cells had uniform ovoid nuclei with granular chromatin and inconspicuous nucleoli. Necrosis was absent, but mitoses were frequent. There was strong positivity for BCL2, Glut A, and CD56. S100 was seen in isolated cells. FISH for GLI-1 and DDIT3 showed amplification of both loci. We propose the term 'GLI-activated nested malignant epithelioid cell tumour' to describe this entity. This case also highlights the utility of FISH for DDIT3, which lies in close proximity to GLI on chromosome 7, as a surrogate marker for GLI-1 amplification.

MUTATIONAL ANALYSIS OF UNDIFFERENTIATED MELANOMA

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In recent years, the use of checkpoint inhibitors and targeted molecular therapy has dramatically improved survival in metastatic melanoma. Accurate and prompt diagnosis is essential to initiate appropriate management. Dedifferentiated tumours, i.e., those that have lost some or all morphologic and immunohistochemical features of melanoma, pose a major challenge to this

endeavour. In these instances, identification of a melanoma-related mutation can be a useful ancillary investigation. The aims of this study were to describe the histological, immunochemical, and molecular features of undifferentiated melanomas. A search of our institutional database (2012–2019) identified 23 cases of undifferentiated malignant tumours that underwent subsequent mutational analysis. Of these, 15 tumours were found to harbour a melanoma-related mutation including BRAF V600E (3/15), BRAF V600K (3/15), and NRAS Q61R (5/15) among others. On the basis of the molecular findings, a diagnosis of melanoma was favoured. Sites of disease included lymph nodes (5/15), skin or subcutis (5/15), lung (2/15), small bowel (1/15), mediastinum (1/15), and epidural space (1/15). A prior history of melanoma was documented in 10 cases. This study illustrates the value of mutation testing in establishing a diagnosis in cases of undifferentiated malignancy, particularly when melanoma metastases are clinically suspected.

GENOMIC ALTERATIONS IN METASTATIC BASAL CELL CARCINOMA

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Basal cell carcinoma (BCC) is the single commonest human malignancy. Histologically, BCC is classified into one of several subtypes based on the growth pattern, a feature that correlates with risk of aggressive behaviour. Metastasis is exceptionally rare and portends a poor prognosis. Although the genome of BCC has been fully characterised, little is known about genomic events associated with metastatic potential. We sought to identify clinicopathologic and molecular features associated with an increased risk of metastasis in BCC. Cases were identified from a search of our institutional database. The pathology of each primary tumour and corresponding metastasis was reviewed, followed by DNA extraction and whole-exome sequencing. The detected molecular alterations were compared between the primary tumour and the corresponding metastasis. The findings were compared to publicly available genomic data. 9 patients were identified, with matched primary tumour tissue available in 7 cases. 6 cases originated in the head and neck. Sites of metastasis were local lymph nodes (7/9) and lung (2/9). Most primary tumours were at least partially infiltrative (4/7) or morphoeic (2/7). Results of genomic analyses will be presented and will provide insights into molecular events that may serve as biomarkers for the rare complication of metastasis in BCC.