When Lightning Strikes Twice ! - Management Of Familial Neuroblastoma

Background

Familial neuroblastoma (NBL) is rare (1-2% of all NBL). In contrast to sporadic cases, it occurs at a younger age, often with multifocal primary tumours. Inheritance pattern is incomplete autosomal dominant. The two most frequent mutations include ALK mutations (80%) and lesser so, germline mutations of PHOX2B (6-7%).

Methods

We present two siblings with familial neuroblastoma and discuss clinical management.

Results

A 3 year-old male presented with classical symptoms of metastatic NBL (fatigue, bone pain and weight loss). Biopsy confirmed a poorly differentiated NBL (MYCN not amplified, 17q gain, segmental chromosomal abnormalities). Staging showed a metastatic tumour (thorax, liver, bone and bone marrow disease). He commenced treatment for stage IV high-risk NBL, with complete response of metastatic disease following rapid COJEC induction. The thoracic mass remained unchanged and required gross total resection. Unilateral ocular miosis was incidentally detected by the surgeon in an asymptomatic 10-month-old sister visiting her brother in hospital. Imaging thereafter in the female sibling showed multifocal NBL tumours with left lung apex, thorax and abdominal paraspinal lesions Biopsy confirmed neuroblastoma (MYCN not amplified, 17q gain, segmental chromosomal abnormalities). The ‘asymptomatic ‘ female commenced treatment for intermediate risk NBL Both patients have been referred to clinical genetics and are awaiting whole genome sequencing.

Conclusion

Cases of familial neuroblastoma provide great opportunity to advance genetic understanding of NBL. Screening of ‘asymptomatic’ children with a history of familial NBL has been proposed in an effort to detect the two most common mutations , ALK and PHOX2B. If positive, surveillance with sonography and urinary catecholamines until age 5 years has been recommended [ Bosse et al Cancer 2016 ]. No robust clinical data exists to support such practice. Familial NBL can be linked to other genetic polymorphisms. Subtle anomalies notably ocular miosis in siblings of children with NBL therefore require careful investigation. Whole genome sequencing may aid further insight into these family(s) / kindreds and the overall heritability of NB.