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Neuroblastoma in Adolescents and Children Older than 10 Years: Unusual Clinicopathologic and Biologic Features

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Neuroblastoma in Adolescents and Children Older than 10 Years: Unusual Clinicopathologic and Biologic Features

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IRB Number: n/a

Describe role of Submitting/Presenting Trainee in this project (limit 150 words):

I retrospectively collected data on each patient in regards to clinical course and outcomes and wrote that section of the manuscript that was submitted to Journal of Pediatric Hematology/Oncology for publication (acceptance pending).

Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words

Background:

Neuroblastoma is one of the most common malignancies in children and accounts for 15% of pediatric cancer deaths. It is most common in young children where the median age at diagnosis is 2 years. The survival of patients depends on the presence of numerous prognostic factors including age. The occurrence of neuroblastoma in children over 10 years of age is rare and few clinical studies are published in this age group emphasizing their poor outcome.

Objectives/Goal:

Describe 4 cases of neuroblastoma in children older than 10 years old and highlight their unusual clinicopathologic and biologic features, including results of deep targeted exome sequencing, single nucleotide polymorphism DNA microarray, and ATRX immunohistochemistry results.

Methods/Design:

This is a case series. We reviewed our archives for patients with neuroblastoma aged 10-18 years and summarized their clinicopathologic and genetic records. Of 96 patients with neuroblastoma, four patients with five tumors were identified in this age group.

Results:

Four tumors were abdominal and one presacral. Tumor sizes ranged from 3-20cm. All tumors were high risk at clinical stages 3 and 4, with metastasis to bone marrow and other areas. Four tumors were poorly differentiated with unfavorable histology and one patient with bilateral adrenal disease had an intermixed ganglioneuroblastoma on one side. Another tumor exhibited pheochromocytoma-like morphology. *MYCN* amplification was present in bone marrow metastasis in only one case. The same case had partial loss of ATRX immunohistochemistry in the primary tumor. Complex chromosomal gains and 19p deletions were common. Exome sequencing revealed *ALK* variants in two cases and previously unreported *MAGI2*, *RUNX1* and *MLL* mutations. All patients initially received standard therapy per Children's Oncology Group protocols (including ANBL0532 and ANBL1232), and two patients eventually received ALK-targeted trial therapy. Three patients died of disease, ranging 18-23 months after diagnosis. One patient has active disease and is receiving trial therapy.

Conclusions:

Neuroblastoma in children older than 10 years may exhibit unusual clinicopathologic and genetic features with large tumors, bilateral adrenal disease, rare morphologic features, complex DNA microarray findings and novel mutations. Patients have grim prognoses despite genomic profiling-guided targeted therapy.