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Peripheral Primitive Neuroectodermal Tumor and Neurofibromatosis Type 1 in an Adolescent Male

Tristan E. Knight, MD*,

Department of Pediatrics, University of Hawaii John A. Burns School of Medicine, Honolulu, Hawaii

Samantha W. E. Knight, BSc,

Royal College of Surgeons in Ireland, Dublin, Ireland

Wade Kyono, MD,

Department of Pediatrics, University of Hawaii John A. Burns School of Medicine, Honolulu, Hawaii

Karen Thompson, MD,

Department of Pathology, University of Hawaii John A Burns School of Medicine, and Clinical Laboratories of Hawaii, Honolulu, Hawaii

John Hicks, MD, PhD, DDS, and

Department of Pathology, Texas Children's Hospital, Baylor University Medical Center, Houston, Texas

Bruce Shiramizu, MD

Department of Pediatrics, University of Hawaii John A. Burns School of Medicine, Honolulu, Hawaii

To the Editor

We present the first reported case of a peripheral primitive neuroectodermal tumor (pPNET) in an adolescent male with Neurofibromatosis Type 1 (NF1). This case illustrates the need to be cognizant of rare tumors in adolescent patients with NF1, and the need for larger case series to understand the genetic mechanisms linking NF1 and pPNET.

A healthy 14-year-old male with a negative family history presented with 6 months of left upper back/lower neck pain and swelling, and 1 month of progressive left arm weakness/paresthesia. Physical examination revealed a firm 5 × 6 cm mass in the posterior left lower neck associated with hyperesthesia and hypoesthesia in the left hand and arm, respectively, and reduced strength throughout the left upper extremity. Bilateral axillary freckling was noted with multiple 2–5 cm cafe-au-lait spots on the body.

*Correspondence to: Tristan Knight, Kapi'olani Medical Center for Women and Children, University of Hawaii Pediatric Residency Program, 1319 Punahou Street, 7th floor, Honolulu, HI, 96826. ; Email: knighttr@hawaii.edu

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Computed tomography (CT) scan revealed extramedullary masses within the cervical spine with cord compression; MRI showed a left T2 hyperintense heterogeneous soft tissue mass from C2-T4 with multiple enhancing, enlarged foramina nerve roots from C2–C7 extending into the epidural space. The bilateral axillary freckling and café au lait spots suggested previously undiagnosed NF1, with multiple plexiform neurofibromas therefore included in the differential diagnosis. Pathology showed a cellular tumor with sheets of small, poorly differentiated, malignant round cells within a variably myxoid background with geographic necrosis (Fig. 1A, 4×). Nuclei were round-to-oval with multiple fine nucleoli and minimal amphophilic cytoplasm with brisk mitoses (Fig. 1B, 40×). Immunohistochemical staining was positive for nuclear FL-1, nuclear WT-1, and membranous CD99 consistent with pPNET (Figs. 1C–1E, 40×). Even though EWSR1-FLI1 and EWSR1-ERG translocations were absent by RT-PCR, other variant translocations involving EWSR1 and other partner genes have been described in Ewing sarcomas.[1] Additionally, Ewing sarcomas lacking EWSR1 translocations with a Fused in Sarcoma (FUS)-associated translocation are known. [1] Despite negative RT-PCR results, the histopathologic and immunohistochemical features of the tumor were consistent with Ewing sarcoma/pPNET. Following initial radiotherapy and chemotherapy, repeat imaging showed disease progression, and the patient passed away 4 months after diagnosis.

In addition to neurofibromas, patients with NF1 are at an increased risk of malignant peripheral nerve sheath tumors and pheochromocytomas, leukemia, rhabdomyosarcomas, and brain tumors.[2–4] The risk of malignant transformation is higher among individuals with NF1.[5] PNETs, rarely diagnosed in NF1, are malignant neural crest-derived tumors from remnants of the neuroectoderm and are divided into central nervous system PNET and pPNET. pPNETs are within the family of Ewing sarcoma tumors, but differ in their degree of neural differentiation.[6] Three previous reports described NF1 patients with pPNET;[7–9] however, our unique adolescent male highlights a category of patients (adolescents and young adults [AYA]) whose outcomes are influenced not only by treatment but also by “host” biology.[10] Further cases of AYA with NF1 and pPNET and other rare tumors are necessary to contribute to understand genetic mechanisms linking NF1 and pPNET.

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Fig. 1.

Tumor histopathologic findings consistent with pPNET. (A) Low-power view with sheets of malignant small round cells with significant geographic necrosis and perivascular sparing (H&E, 4x). (B) Tumor cells containing minimal amphophilic cytoplasm, round nuclei with fine nucleoli, and brisk mitotic rate (H&E, 40x). (C) FLI-1 immunohistochemical stain showing strong nuclear positivity (40x). (D) WT-1 immunohistochemical stain showing strong nuclear staining (40x). (E) CD99 stain demonstrating membranous staining (40x).