SKIN

BRIEF ARTICLE

Malignant Melanoma within a Giant Congenital Melanocytic Nevus in a Pediatric Patient

Jackson Green, BS[4], Jessica Nye, BS[4], Kelly Turner, PA[3,4], Matthew R. Greives, MD[3,4], Kate Mowrey, MS, CGC[1,4], Adelaide A. Hebert, MD[1,2,4], Autumn Atkinson, MD[1,4]

[1]Department of Pediatrics, University of Texas Health Science Center at Houston, Houston, TX
[2]Department of Dermatology, University of Texas Health Science Center at Houston, Houston, TX
[3]Department of Plastic Surgery, University of Texas Health Science Center at Houston, Houston, TX
[4]University of Texas McGovern Medical School at Houston, Houston, TX

ABSTRACT

While giant congenital melanocytic nevi are rare lesions in the pediatric population, malignant transformation within these lesions remains even more rare. A 22-month-old male patient developed a 6.5 mm Clark's Level IV melanoma within a giant congenital nevus with an activating *NRAS* variant. The need for frequent surveillance and screening of giant congenital melanocytic nevi is essential to identify early signs of melanoma, even in the pediatric population.

INTRODUCTION

Congenital melanocytic nevi (CMN) pose a constellation of challenges that include cosmetic and functional disfigurement, reduction in self-esteem, and the potential to develop into malignant melanoma.[1, 2] Giant CMNs are defined by pigmented proliferations that are greater than 20 cm^2 in diameter, and these occur in 1 in 20,000 births, most commonly on the trunk, upper extremities and head and neck regions.[2, 3] CMNs can change in size and appearance with age from a flat brown plaque to a pigmented and hairy plaque with erosions, ulcerations, or a thickened verrucous surface.[4] While all CMNs have the potential to transform into malignant melanoma, the highest risk of malignant transformation resides in giant congenital melanocytic nevi with reports of this transformation being as high as 14%.[1-5] Regular dermatologic screenings by pediatricians are vital to assess changes in giant congenital nevi over time.[4] Early biopsy and possible surgical intervention can help identify early transformation and potentially reduce the sequelae of melanoma.[4]

CASE REPORT

A male infant was born at 39 weeks and 6 days gestation to a 23-year-old primigravida mother who obtained appropriate prenatal care throughout the pregnancy. At the time of birth, the newborn was noted to have a large black plaque with tufts of hair from the scalp to mid-back with numerous smaller satellite lesions on the face, trunk, and extremities. The patient received an MRI at 2 days of age to rule out neurocutaneous melanosis. The patient was evaluated in the Vascular

Anomalies Clinic at UTHealth McGovern Medical School at 1 month of age and diagnosed with a multifocal congenital melanocytic nevus, congenital ear deformity and positional plagiocephaly (**Figure 1**). The patient was to be followed in our outpatient clinic every six months to screen for possible foci of transformation within the giant congenital nevus. Due to the COVID-19 pandemic, the patient was delayed in returning to clinic initially.

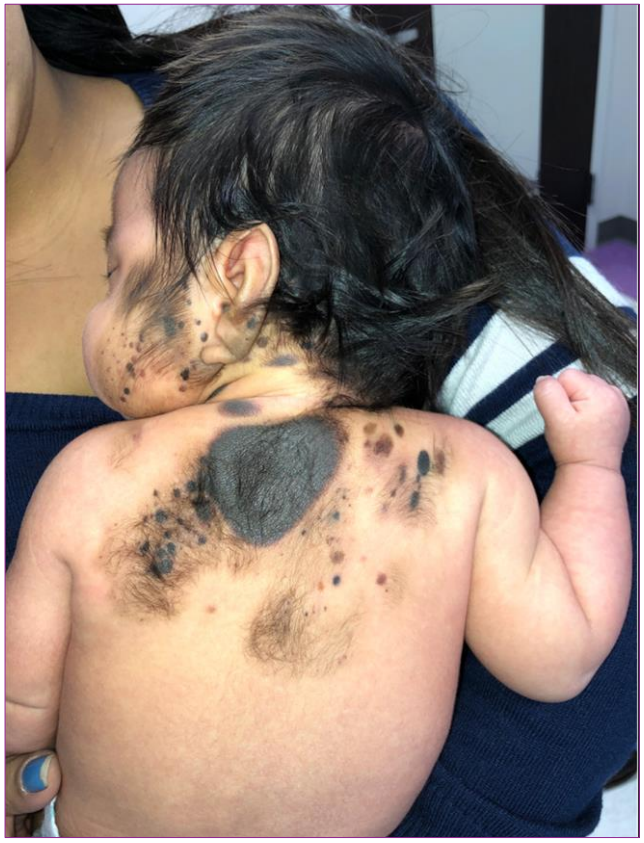

Figure 1. Large multifocal congenital pigmented nevus at 2 months of age.

The patient had his first follow up evaluation at 8 months of age, and an area of the nevus in the preauricular space was biopsied due to concern for a rapid change in texture and thickness. The results of the biopsy were normal. A secondary biopsy was performed at 11 months of age due to a new scalp growth, which was found to be a pyogenic granuloma and was excised with normal pathologic findings. At the 16 month follow up, three new lesions of concern were biopsied, and wide excision was performed due to highly proliferative margins and atypical cells. At the 22 month follow up, a previous lesion showed abnormal coloration and borders, and there was found to be an enlarged posterior cervical lymph node raising concern for possible metastasis (**Figure 2**).

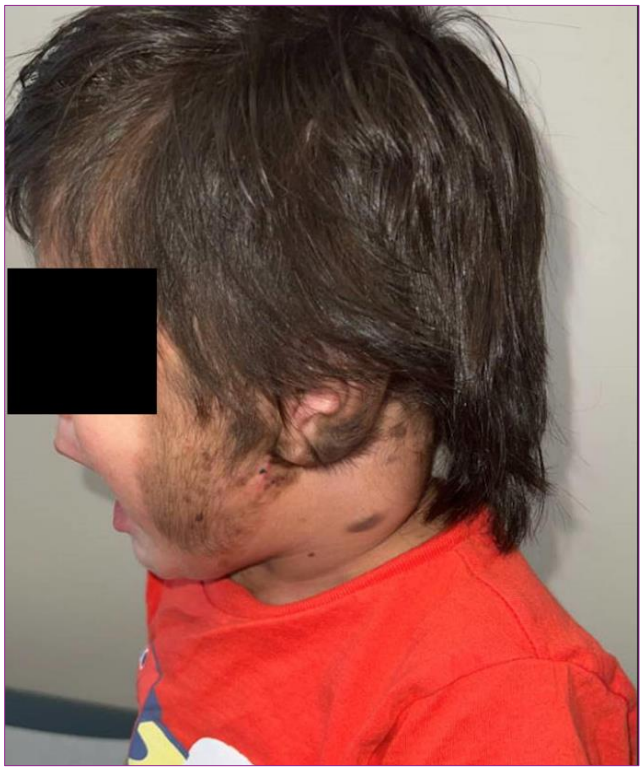

Figure 2. Swelling of posterior cervical lymph nodes at 22 months of age after initiation of nivolumab and ipilimumab.

As a part of an oncology work-up, a multiplanar, multisequence MRI was performed with and without IV contrast showing a new enlarging posterior cervical lymph node prompting concern for malignant transformation or metastatic disease. Skin biopsy showed an invasive, nodular, Clark Level IV, and Breslow thickness 6.5 mm melanoma with mitotic figures and ulceration. The patient had a next generation sequencing analysis that demonstrated an

NRAS variant. A repeat multiplanar, multisequence MRI of the abdomen and pelvis was performed to evaluate for metastases. Results of the MRI showed metastases to the bones of the legs and the patient was referred to MD Anderson to initiate therapeutic intervention with ipilimumab and nivolumab. A PET scan demonstrated enlarging left cervical lymph nodes with central necrosis and increase tracer uptake in T3 vertebra and the intertrochanteric region of the right femur suspicious for bony metastases (**Figure 3**).

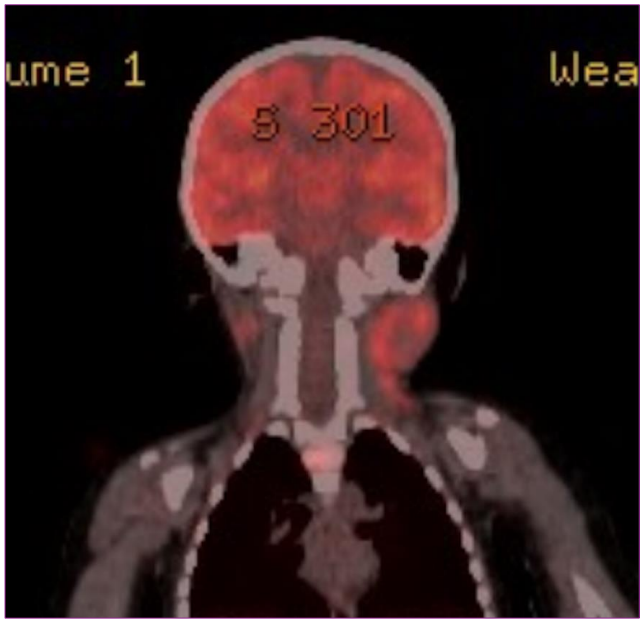

Figure 3. PET scan at 22 months of age exhibiting enlargement of the left cervical lymph nodes with central necrosis, likely metastatic in nature.

DISCUSSION

Melanoma represents the deadliest form of skin cancer and the fifth most common cancer by incidence across all races in the United States.[6] A 35-year review of pediatric patients found that 2.5 per one million children are diagnosed with melanoma, exhibiting an exceptionally rare occurrence.[7] Of these children, only 22% are diagnosed with melanoma before puberty.[7] Preadolescent patients are more likely to present with melanoma on the head and neck and are more likely to be non-Caucasian, as in this case.[8] Early detection and treatment are vital for survival, as prognosis is directly correlated with disease staging.[4]

When evaluating pediatric nevi, CMNs require a unique algorithm of care because their natural history varies from acquired pediatric nevi. Acquired melanocytic nevi (AMN) are ubiquitous in children, typically appearing in early childhood and increasing in size and number. However, AMNs only account for 1% of all melanomas in patients younger than 20 years and have a lifetime risk of transformation into melanoma of 1 in 10,000.[9] Studies indicate the risk of melanoma ranges from 6-14% in giant congenital nevi, while other smaller congenital nevi only have a 1.4% incidence of melanoma.[1,3] Immunohistochemical and somatic genetic testing may be necessary for diagnosis in unique or recurrent cases of melanoma.[3] Thus far, the proto-oncogenes, *NRAS* and *BRAF*, have been identified in approximately 95% and 5-10% in giant CMNs, respectively.[5] As a pediatrician, it is vital to recognize early indications of transformation to melanoma to provide better outcomes for patients.

CONCLUSION

This case stresses the importance of early detection, serial evaluation, and prompt treatment of melanoma in a giant congenital melanocytic nevus. Giant CMNs are particularly difficult to manage due to the diagnostic challenge, operative treatment required, and lifelong follow-up and management. A multidisciplinary team encompassing pediatrics, dermatology, plastic surgery, and genetics – as seen in

many vascular anomalies centers – is uniquely positioned to play an especially important role in managing this subset of patients and provide timely quality care for these rare and deadly conditions.

Consent: The parents have provided written consent for the use of the patient's photos

Conflict of Interest Disclosures: None

Funding: None

Corresponding Author:
Autumn Atkinson, MD, FAAP
The University of Texas Health Science Center at Houston
6341 Fannin St, Suite JJL 495
Houston, TX 77030

References:

1. Ehud A, Zuker RM. The shifting paradigm in the management of giant congenital melanocytic Nevi. *Plastic and Reconstructive Surgery*. 2014;133(5):1312. doi:10.1097/prs.0000000000000342.
2. Gosain AK, Santoro TD, Larson DL, Gingrass RP. Giant congenital nevi: A 20-year experience and an algorithm for their management. *Plastic and Reconstructive Surgery*. 2001;108(3):632-636. doi:10.1097/00006534-200109010-00005.
3. Belysheva TS, Vishnevskaya YV, Nasedkina TV, et al. Melanoma arising in a giant congenital melanocytic nevus: Two case reports. *Diagnostic Pathology*. 2019;14(1). doi:10.1186/s13000-019-0797-1.
4. Arneja JS, Gosain AK. Giant congenital melanocytic Nevi. *Plastic and Reconstructive Surgery*. 2009;124(Supplement). doi:10.1097/prs.0b013e3181ab11be.
5. Lalor L, Busam K, Shah K. Prepubertal melanoma arising within a medium-sized congenital melanocytic nevus. *Pediatric Dermatology*. 2016;33(6). doi:10.1111/pde.12961.
6. Howlader N, Noone AM, Krapcho M, et al., eds. Seer Cancer Statistics Review, 1975-2018. SEER. https://seer.cancer.gov/csr/1975_2018/.
7. Dean PH, Bucevska M, Strahlendorf C, Verchere C. Pediatric melanoma. *Plastic and Reconstructive Surgery - Global Open*. 2017;5(3). doi:10.1097/gox.0000000000001252.
8. Austin MT, Xing Y, Hayes-Jordan AA, Lally KP, Cormier JN. Melanoma incidence rises for children and adolescents: An epidemiologic review of pediatric melanoma in the United States. *Journal of Pediatric Surgery*. 2013;48(11):2207-2213. doi:10.1016/j.jpedsurg.2013.06.002.
9. Levy R, Lara-Corrales I. Melanocytic Nevi in children: A Review. *Pediatric Annals*. 2016;45(8). doi:10.3928/19382359-20160720-07.