A Rapidly Changing Skin Lesion in an 11-year-old Boy

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PRESENTATION

An 11-year-old Black boy with obesity presents to a pediatric outpatient clinic with a 3-month history of an evolving, brown, nevus-like lesion in his left axilla. The lesion first appeared 3 months ago and started as a small, asymptomatic, hyperpigmented macule but progressively became raised and painful to the patient, prompting an appointment. At the time of the visit, the patient’s physical examination reveals a blood pressure of 118/67 mm Hg and a pulse of 61 beats/min. A temperature was not obtained. The area of concern is a soft, homogeneous, brown, fleshy papule located in the left axilla, 3 mm in diameter with regular borders. The papule is oval shaped and appears symmetrical. There is no palpable lymphadenopathy in the neck or axillae. The remainder of the physical examination findings are normal. Due to progression and symptoms, pictures are obtained (Fig 1), and a referral is made to pediatric dermatology for evaluation.

During the next 2 months, the papule is noted to increase in size, develop color variation, and appear fluid-filled. It has become persistently bothersome to the patient, rubbing against the surrounding axillary skin and causing him significant pain and discomfort daily. Days before repeated evaluation, the papule and surrounding skin became pruritic and a transient violaceous rash developed surrounding the lesion, which has almost resolved by the time of his dermatology visit. The patient has tried applying cold compresses to the area, which provides temporary relief. No topical creams or ointments have been applied. The patient denies using new deodorants, detergents, or soaps or wearing new clothing. At the time of pediatric dermatology evaluation, the appearance of the mass has changed significantly from the previous visit 2 months earlier (Fig 2), increasing in size to approximately 1 cm in diameter, becoming more raised, changing in color from brown to a purple hue, and with dry, smooth skin in surrounding axilla. There is no surrounding erythema, swelling, streaking, bleeding, or drainage from the lesion. The lesion is described by pediatric dermatology as an approximately 1-cm, pink/brown, pedunculated papule with a purple/dark brown homogeneous pattern notable on dermoscopy that is thought to be either an irritated soft fibroma or a pyogenic granuloma.

DISCUSSION

Differential Diagnosis

At the time of the first visit, the lesion (Fig 1) is thought to be an acrochordon (also known as a soft fibroma or a skin tag). At the time of the second visit
(Fig 2), the differential diagnosis is expanded to either an inflamed acrochordon with surrounding contact dermatitis or a thrombosed acrochordon. The common differential diagnoses for acrochordons include neurofibromas, dermal nevi, and seborrheic keratoses. (1) Neurofibromas are usually rubbery and dome shaped, dermal nevi are not usually pedunculated (attached by a stalk or stem), and seborrheic keratoses are benign growths found in older adults; however, biopsy may at times be the only way to distinguish among these lesions.

As a brief review, a melanocytic nevus can be classified based on where it is in the skin, and this correlates with what is seen clinically: 1) a junctional nevus is histologically located at the dermoepidermal junction and clinically appears as a flat brown macule; 2) a compound nevus is histologically located at the dermoepidermal junction extending into the dermis and clinically appears as a brown, raised papule; and 3) a dermal nevus is histologically located solely in the dermis and clinically appears as a skin-colored papule.

Many melanocytic nevi can go through a maturation process, and they can often descend deeper in the skin as the patient ages. This results in clinical and histologic changes over years where the melanocytic nevus may progress from a junctional nevus to a compound nevus to a dermal nevus.

**Actual Diagnosis**

A shave biopsy is performed, and the sample is sent to the pathology laboratory. Histopathologic analysis of the excision shows an ulcerated fragment of skin with confluent sheets of uniform nevomelanocytic cells in the dermis. They are morphologically epithelioid with large nuclei and prominent nucleoli, and they extend to the deep margin. They do not exhibit any significant maturation. Ki-67 immunocytochemical stains (stains that help assess the mitotic rate of cell populations in tumors) reveal a Ki-67 expression level of 10%, with some Ki-67–positive melanocytic cells in the deep portion of the lesion. The higher the level of Ki-67–positive cells, the more rapidly the tumor cells are proliferating, and the value is an important prognostic factor to consider. (2) For example, one study found that Ki-67 expression greater than 20% in melanoma was associated with a significantly poorer prognosis (higher 10-year metastasis rates). (3)

Although the histologic features of the patient’s biopsy sample favor those of a severely atypical Spitz nevus, based on the architecture of the lesion, the presence of ulceration, the cytologic atypia noted, and the lack of maturation, a Spitzoid melanoma could not be excluded.

An experienced dermatopathologist, dermatologic surgeon, and pediatric dermatologist discussed the clinical and pathologic features and felt that, overall, the most likely diagnosis was a spitzoid melanoma.

The depth at which the tumor cells are found (or, the thickness of the tumor) is used as a prognostic factor in melanoma diagnoses (4) and it is used as 1 of the staging criteria included in the American Joint Committee on Cancer’s Eighth Edition Cancer Staging Manual, which was most recently updated in 2017. (5)

The patient’s tissue is tested for BRAF mutation and is negative (a mutation that is regularly tested to guide the oncologist’s treatment decisions because BRAF mutations are found in >50% of melanomas, and targeted BRAF inhibitor molecular therapy can be used in those cases). (6)
The Condition

Pediatric melanoma is a rare diagnosis accounting for 1% to 4% of all melanoma diagnoses. (7)(8) with fewer than 500 cases diagnosed annually in the United States. (9) There are 5 types of pediatric melanomas: spitzoid melanoma, melanoma arising from a congenital nevus (this is the official name), conventional (or adult-type) melanoma, congenital melanoma, and leptomeningeal melanoma associated with neurocutaneous melanosis. (10) The first 3 types are by far the most common.

Spitzoid melanoma most commonly affects patients younger than 20 years, and it is the most common melanoma diagnosed in prepubescent children. It typically presents as a nodule, papule, or polyp of any color (typically pink or red), can resemble a benign lesion such as a wart or a pyogenic granuloma, and does not necessarily present on sun-exposed skin. It has a high incidence (~50%) of sentinel lymph node metastasis but tends to have excellent outcomes. Histopathologic findings, as well as certain genetic aberrations (including specific kinase gene fusions of ROS1, NTRK1, ALK, BRAF, and RET) can distinguish spitzoid melanoma from the other types of melanomas found in the pediatric population. (10)(11)(12)

Melanoma arising from a congenital melanocytic nevus most commonly presents before age 10 years from a lesion that was present at birth, as the name suggests. It typically presents as a nodule in the deep dermis or subcutaneous tissue of a congenital melanocytic nevus. The risk of malignant transformation increases with the size of the congenital nevus, with melanomas arising from large or giant nevi being highly aggressive. (10)(11)(12)

Conventional (or adult-type) melanoma accounts for approximately half of all pediatric melanomas. There are several subtypes of conventional melanoma, including superficial spreading type, nodular type, lentigo maligna, and melanoma of acral (glabrous) skin (which is rare in children). In prepubescent patients, conventional melanoma more commonly affects nonwhite patients, with lesions commonly seen on the head, face, and neck, and it does not follow the adult ABCDE (asymmetry, border irregularities, color variation, diameter ≥6 mm, evolving lesion) criteria for melanoma. (10)(11)(12)(13) In postpubescent patients, conventional melanoma typically affects fair-skinned patients with poor tanning ability, more commonly follows the adult ABCDE melanoma criteria, and is genetically very similar to adult melanoma. (10)(11)(12)

Melanoma can be difficult to diagnose in the pediatric population due to the often-atypical appearance of the lesion, which does not always conform to the conventional ABCDE adult criteria for melanoma. (13) In recognition of this, there have been 2 proposed additional criteria to be used in conjunction with existing adult ABCDE criteria for the enhanced diagnosis of pediatric melanoma. These include an additional ABCD criteria: “amelanotic, bleeding/bump, color uniformity, and de novo/any diameter,” (14) as well as the CUP criteria: “color (pink or red)/changing, ulceration/upward thickening, and pyogenic granuloma–like lesions/pop-up of new lesions.” (15)

In addition, pediatric melanoma lesions often mimic benign skin lesions, such as congenital nevi, melanocytic nevi on particular anatomical sites such as the scalp, proliferative nodules, aceniform lesions, Spitz nevi, hemangiomas, blisters, warts, or pyogenic granulomas. (10)(11)(16) Pediatric patients with melanoma are more likely to present with thicker lesions and with sentinel lymph node positivity, although there are differences in the pediatric population itself; prepubescent patients are more likely than adolescent patients to be nonwhite, have spitzoid tumors, and have thicker lesions. (17)

The overall 5-year prognosis for pediatric melanoma is 90.9%. This ranges from 57.3% for distant metastatic disease to 100% for in situ disease (disease confined to the epidermis). (9) Spitzoid melanomas in pediatric patients have better outcomes than conventional melanomas in adults, but distant metastases are still possible.

Treatment/Management

Treatment varies based on staging and genetic factors. Staging follows the adult guidelines and considers 3 characteristics: depth of lesion (T), number of lymph nodes involved (N), and presence or absence of metastases (M). (9)

Treatment starts with wide local excision of the lesion in question. If the depth of the lesion is greater than 1 mm (T2, T3, and T4), then a sentinel lymph node biopsy is performed for staging purposes, and if this is positive, a complete lymph node dissection is performed. For metastatic disease, several chemotherapy and immunotherapy agents are currently approved. (9)

Patient Course

A wide local excision and a sentinel lymph node biopsy were performed, the histopathologic analysis of which revealed no residual disease at the primary site. However, there was microscopic disease present in the sentinel node, indicating at least stage IIIc metastatic malignant melanoma. Brain magnetic resonance imaging and whole-body positron emission tomography were performed to complete staging and showed no evidence of metastatic disease. He was started on nivolumab for his stage IIIc
melanoma. Nivolumab is a monoclonal antibody that binds to PD-1, a protein on the surface of T cells that, if bound by ligands PD-L1 or PD-L2 (which many cancer cells produce), renders the T cell inactive and unable to attack the cancer cells. By nivolumab binding this receptor site on T cells instead, it allows the T cells to attack the cancerous cells. (18) The patient initiated treatment approximately 5 months after initial presentation.

Nivolumab was discontinued 3 months after initiation due to the development of lichen planus pemphigoides (Fig 3), which was considered a serious grade 3 cutaneous toxicity. According to the Common Terminology for Adverse Events, a National Cancer Institute protocol, grade 3 cutaneous toxicity is defined as an exanthem that covers greater than 30% of body surface area, disrupts activities of daily living, and affects quality of life, requiring interruption and possibly discontinuation of immunotherapy. (19)(20)

Because the original tumor was BRAF mutation negative, targeted BRAF therapy would be of no benefit. Given the absence of other effective therapies, observation was chosen. At this time (1.8 months since presentation), no residual disease or recurrence has been identified. He will undergo skin checks by pediatric dermatology every 3 months for 2 years after diagnosis, then every 6 months thereafter for the first 5 years after diagnosis.

Lessons for the Clinician

- A rapidly evolving, painful, bleeding, or friable skin lesion should raise suspicion for malignancy, and an expedited referral to pediatric dermatology should be made for evaluation.
- Photographs of skin lesions at each visit are helpful to document evolution.
- All skin lesions (even if they appear benign) that undergo excision or biopsy should always be sent to the pathology laboratory for further testing.

References for this article can be found at https://doi.org/10.1542/pir.2020-004671.