

Rhabdomyosarcoma Arising in a Giant Congenital Melanocytic Nevus

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GOAL

To understand rhabdomyosarcoma in giant congenital melanocytic nevi (GCMNs)

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Discuss the histologic presentation of rhabdomyosarcoma.
2. Explain the staging of rhabdomyosarcoma.
3. Describe the treatment of rhabdomyosarcoma in GCMN.

CME Test on page 44.

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We report the case of a 6-week-old girl who presented with a pedunculated embryonal rhabdomyosarcoma arising in a giant congenital melanocytic nevus (GCMN) on her lower back. There was no associated leptomeningeal involvement. The patient underwent surgical resection of the rhabdomyosarcoma at age 2 months, with subsequent chemotherapy consisting of actinomycin D and vincristine. No recurrences or metastases of tumor have been noted at 5 months of age.

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Figure 1. Pigmented hairy nevus extending from the lower back onto the abdomen with an enlarging, soft pink pedunculated polyp measuring 3 cm in diameter present centrally.

Giant congenital melanocytic nevus (GCMN), defined as measuring or predicted to measure greater than 20 cm in diameter by adulthood, uncommonly occurs in newborns.¹ Concerns arise regarding malignant degeneration, with melanoma developing in 4.5% to 8.5% of cases.^{2,3} Other malignancies rarely have been reported in a GCMN, including rhabdomyosarcoma, melanosarcoma, undifferentiated spindle cell tumor, neuroblastoma, melanoblastoma, myoblastic sarcoma, liposarcoma, and malignant peripheral nerve sheath tumor.^{1,4} We report a case of rhabdomyosarcoma arising in a GCMN.

Case Report

A 6-week-old infant girl presented with an 18×13-cm pigmented hairy nevus extending from the lower back onto the abdomen. A rapidly enlarging, soft pink pedunculated polyp measuring 3 cm in diameter had been present centrally at birth (Figure 1). An ultrasound of the spine revealed no abnormalities.

The polyp was surgically resected, along with a portion of the GCMN. Results of the histologic examination disclosed a rhabdomyosarcoma, embryonal type, located superficially within the dermis (Figure 2). The deep and lateral margins showed no evidence of tumor. Immunohistochemistry results of the neoplastic cells showed marked positivity for desmins, smooth muscle actin, and vimentin; results of tests for S100, neuron-specific enolase, chromogranins, synaptophysin, leukocyte common

antigen, and CD57 were negative. Myoglobin stain was noncontributory.

No evidence of metastatic disease was noted on computed tomography of the chest, abdomen, and pelvis; bone scan; and bone marrow examination. The patient was started on a chemotherapy regimen consisting of actinomycin D and vincristine.

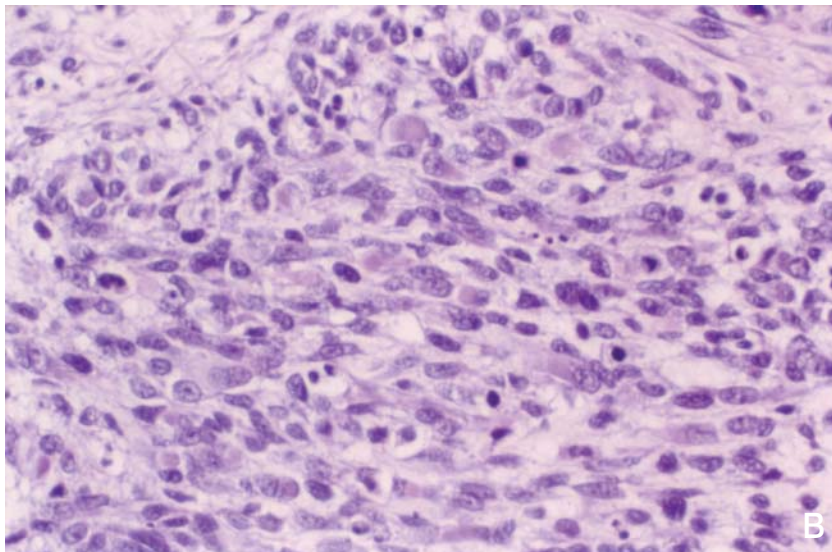
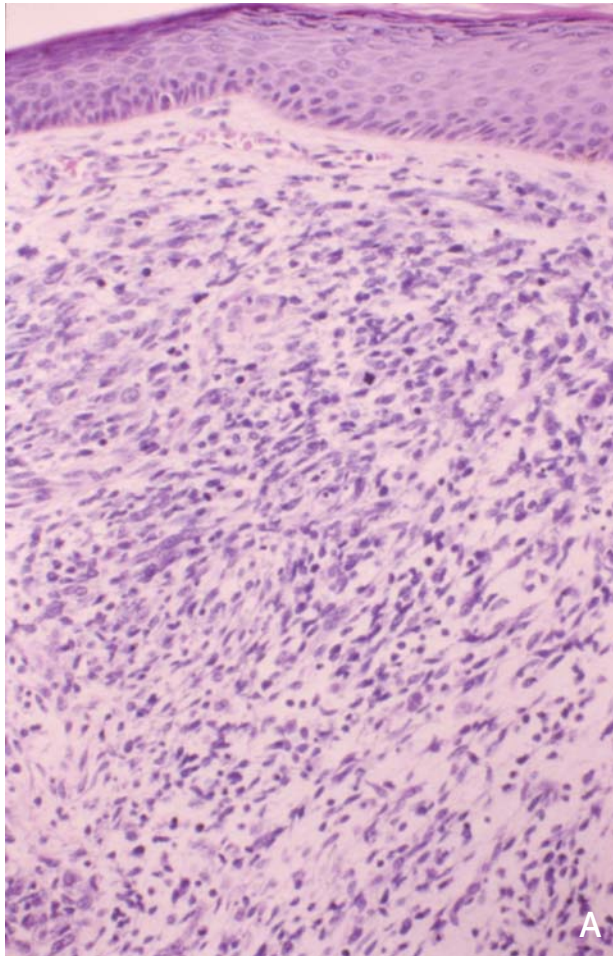
Comment

Although controversy exists regarding the precise risk of malignant degeneration in GCMN, it presents a major concern. Often, extensive surgical procedures are undertaken to eliminate or manage the risk of malignancy, primarily to minimize the risk of melanoma, the most commonly associated malignancy.⁵

Rhabdomyosarcoma is the most common soft tissue sarcoma and the third most common extracranial solid tumor of childhood. It is responsible for up to 25% of malignant cutaneous neoplasms in the pediatric population.⁶ Most tumors occur in the head and neck region, as well as the genitourinary tract; other areas include the extremities and trunk. Rhabdomyosarcoma occurring in the skin *de novo* may present as an asymptomatic, firm red nodule or as a lobulated mass with a shiny erythematous surface and telangiectatic vessels.^{6,7} The differential diagnosis includes hemangioma, lymphangioma, hygroma, lymphoma, leukemia cutis, amelanotic melanoma, and angiofibroma.⁷

The 4 most common histologic subtypes of rhabdomyosarcoma include the following: embryonal,

embryonal-botryoid, alveolar, and pleomorphic. The embryonal and embryonal-butryoid subtypes account for 50% to 60% of childhood rhabdomyosarcomas. The alveolar pattern is seen more commonly in older children, and the pleomorphic pattern is seen more in adults.⁷



Immunohistochemical stains used to identify rhabdomyosarcoma include the intermediate filaments vimentin and desmins. Vimentin highlights undifferentiated cells of mesenchymal origin, whereas desmins become positive as a cell becomes committed to rhabdomyoblastic differentiation. Because myoglobin is also found in skeletal muscle, myoglobin stains less consistently in rhabdomyosarcomas. This is most likely a result of its expression later in the development of skeletal muscle.^{7,8} Other muscle-specific proteins used in identification are Myo-D, myogenin, muscle-specific actin, and Z-band protein.⁹

Staging of rhabdomyosarcoma by the Intergroup Rhabdomyosarcoma Study (IRS) initially was based on a clinical grouping that sorted patients according to the extent of disease after surgical resection: group I, complete resection; group II, microscopic residual disease after gross resection, with or without nodal involvement; group III, gross residual disease after surgery; and group IV, metastatic disease at diagnosis. Now, the IRS is incorporating a more prognostically significant TNM staging. The TNM Staging System, in addition to clinical grouping, includes favorable versus unfavorable sites, along with increasing the stage number for bulky disease measuring greater than 5 cm in diameter or for nodal involvement. Favorable sites include the orbit, eyelid, head and neck, nonparameningeal, and genitourinary areas not including bladder or prostate. Unfavorable areas include extremities, bladder, prostate, parameningeal, retroperitoneum, and, as in our patient, the trunk.^{8,9} According to the latest IRS staging, our patient falls into the clinical group I, TNM stage II category, which places her in the low-risk rhabdomyosarcoma group.

Figure 2. Embryonal type rhabdomyosarcoma. Proliferation of spindle-shaped neoplastic cells with hyperchromatic nuclei in a fibromyxoid stroma located within the dermis (A). Cross striations characteristic of rhabdomyoblasts are seen, along with numerous abnormal mitotic figures (B) (H&E, original magnifications $\times 40$ and $\times 400$).

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Reference	Patient Age	Location	Leptomeningeal Involvement	Treatment	Outcome
Hendrickson and Ross ⁵	7 mo	Left scalp and cheek	None	Excision without subsequent chemotherapy	Recurrence noted at 3-mo follow-up; subsequently excised with no recurrence by age 3 y
Zuniga et al ¹¹	Newborn	Posterior neck and upper trunk	Associated with melanosis of leptomeninges and central nervous system	Excision and chemotherapy (actinomycin D, vincristine, cyclophosphamide)	Death at age 1 mo
Schmitt et al ¹²	7 mo	Trunk and thighs	None	Excision and chemotherapy (actinomycin D, vincristine, adriamycin, cyclophosphamide)	No recurrence at 18-mo follow-up
Hoang et al ⁴	4 y	Left gluteal and sacral areas	None	Excision. Parents refused chemotherapy and radiation therapy	Death at age 5 y
Current case	6 wk	Lower back	None	Excision and chemotherapy (actinomycin D, vincristine)	No gross evidence of recurrence noted to date

The treatment of rhabdomyosarcoma in a GCMN consists of surgical resection and combination chemotherapy with or without radiation therapy, depending on the clinical grouping of the patient. According to the IRS definition of low-risk patients, the chemotherapy regimen consists of actinomycin D and vincristine with or without cyclophosphamide, depending on stage and location. Radiation therapy is added for patients with groups II through IV disease and for some unfavorable locations with a high risk of recurrence.^{9,10}

Rhabdomyosarcoma arising in a GCMN has been reported rarely, with only 4 cases to date in the literature (Table).^{4,5,11,12} Three of the 4 cases occurred in infants, with a fatal outcome reported

in one of the infants. In 3 of 4 cases, the trunk was indicated as the site of the rhabdomyosarcoma, with only one case associated with leptomeningeal involvement. In all cases, the rhabdomyosarcoma was excised, with subsequent chemotherapy in 2 of the 4 previously reported cases.

The occurrence of rhabdomyosarcoma arising in a GCMN could be explained by the pluripotential nature of undifferentiated neural crest cells. These cells likely maintain the ability for rhabdomyoblastic differentiation. This mesenchymal derivative originates from the cranial or cephalic portion of the neural crest. The term *ectomesenchyme* applies to the potential of the ectoderm to give rise to mesenchymal tissue and indeed may be the pathway by which a rhabdomyosarcoma arises.⁵

Conclusion

We report a fifth case of rhabdomyosarcoma arising in a GCMN. Our patient underwent surgical resection of the rhabdomyosarcoma at age 2 months, with subsequent chemotherapy consisting of actinomycin D and vincristine. She has tolerated outpatient chemotherapy well, with no gross evidence of local recurrence, and will complete 12 months of therapy for her low-risk rhabdomyosarcoma.

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