Cellular Blue Nevus with Massive Regional Lymph Node Metastases

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BACKGROUND. Small, well-differentiated groups of nevus cells have been found occasionally in the marginal sinuses and parenchyma of regional lymph nodes that drain sites of cellular blue nevi.

OBJECTIVE. The histologic, immunohistochemical, and karyometric description of a pigmented cutaneous lesion, with the features of cellular blue nevus and located on the leg of a 14-year-old woman, that was accompanied by synchronic presentation of massive inguinal lymph-node metastases.

METHODS. The excised specimens were processed routinely, embedded in paraffin, and sectioned into 4- μ m-thick slices. The sections were stained using hematoxylin-eosin and the ABC immunohistochemical method for demonstrating S-100 and HMB-45. Karyometric analysis was performed in a static cytometer using Feulgen-stained sections.

RESULTS. The cutaneous lesion had the cytologic and architectural features of cellular blue nevus. The lymph nodes showed massive invasion by pigmented cells and contained extensive necrotic foci. After 3.5 years of clinical follow-up, the patient is free from disease.

CONCLUSIONS. The absence of malignant features in the cutaneous lesion and the bland nuclear features of the pigmented cells in the regional lymph node metastases suggest that this case could be interpreted as an unusual form of benign cellular blue nevus with metastases. Nonetheless, other possibilities, such as malignant melanoma mimicking a cellular blue nevus or primary malignant melanoma of the lymph nodes with concomitant cutaneous cellular blue nevus, cannot be definitively excluded. A conservative surgical approach with close follow-up was recommended. *Dermatol Surg* 1996;22:83-87.

Cellular blue nevus is a relatively large, benign melanocytic tumor of the dermal melanocytes that sometimes produces nonprogressive small seeds in the subcapsular sinuses of regional lymph nodes.^{1,2} Exceptionally, these "benign metastases" grow and form expansive and destructive nodules that suggest metastatic malignant melanoma.³ We describe the histological findings seen in a cutaneous lesion that had the features of cellular blue nevus and produced massive regional lymph node metastases.

Case Report

A 14-year-old Caucasian woman consulted for a 4-month-old pigmented nodular lesion located on the middle third of her inner right leg. The lesion did not produce discomfort or bleed with friction. The pigmented lesion measured 0.7 cm maximum diameter and had a smooth, homogeneous surface. A homolateral inguinal nontender mass measuring 4 cm was

palpated. Abdominal and thoracic computerized tomography disclosed no evidence of enlarged lymph nodes or abnormal visceral masses. The skin lesion and inguinal mass were excised surgically leaving a margin of safety of 2 cm. After 3.5 years of clinical follow-up at 6-month intervals, the patient is free from disease.

The cutaneous ellipse presented a 0.5-cm-thick black nodular lesion. The inguinal specimen contained two dark brown lymph nodes whose maximum diameters were 3.5 and 1 cm, respectively; the largest lymph node had central softening (Figure 1).

Microscopically, the cutaneous lesion was slightly asymmetric, well separated from the epidermis, and reached the depth of the middle reticular dermis (Figure 2A). The proliferating nevocytic cells were clumped in irregular clusters delimited by bundles of dense collagen (Figure 2B). The cells were polygonal or ovoid in shape and had abundant, glassy-looking cytoplasm and, occasionally, fine melanin pigment. Numerous intensely pigmented cells lay close to the glassy-looking cells (Figure 3A). Cellular nuclei were round or oval and contained fine chromatin granules distributed homogeneously and a small, obvious nucleolus (Figure 3A). The superficial areas of the mass contained frequent multinucleated nevus cells (Figure 3B). Dendritic melanocytes located preferentially around vessel walls and adnexal glands were common at the edges of the lesion (Figure 4). The tumor was sectioned in toto but no atypical cells, mitoses, necrosis, or junctional melanocytic activity were identified. The nevocytic cells showed intense cytoplasmic immunostaining for S-100 and HMB-45.

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Figure 1. Gross appearance. A) The larger lymph node shows black central softening. B) The smaller lymph node is partially replaced by a black tumor nodule. C) Cutaneous ellipse with a 0.5-mm-thick black lesion.

The cells of the inguinal lymph nodes were replaced partially by proliferating melanin-pigmented cells (nevocytes and melanophages). The smaller lymph node showed partial cellular replacement by proliferating pigmented cells (Figure 5A and 5B) and the larger lymph node showed extensive cellular replacement and large necrotic areas (Figure 6A). After melanin clearance the tumor cells were well defined and had a polygonal or fusiform shape and slightly irregular nuclei with prominent nucleoli (Figure 6B). Mitosis and marked cellular atypia were absent. Cellular DNA was quantitated on Feulgen-stained sections⁴ using a SAMBA 2000 static cyclometer (Alcatel; TITN, Grenoble, France). A diploid pattern was evident in the primary tumor and in metastases.

Discussion

Allen and Spitz⁵ were the first to report the presence of nevus cells in the peripheral sinuses of regional lymph nodes in patients operated for cellular blue nevus. In a review of the literature, Rodriguez and Ackerman⁶ found nodal nevus cells in 14 cases, all of which had certain common characteristics: patients were younger than average; the cellular blue nevi were located in the sacrococcyx or lower limbs; the cutaneous lesion and metastases were synchronous; inguinal or axillary nodes were involved; and metastases consisted of small, well-differentiated groups of nevus cells located in the marginal sinuses and parenchyma.

More recently, Temple-Camp et al³ described a case of combined nevus in the course of a clinicopathological study of 30 cases of benign and malignant cellular blue nevi. The combined nevus was located on the calf and consisted of a broad mixture of biphasic type cellular blue nevus with junctional activity; 5 years later, an inguinal lymph node metastasis appeared. The lymph node had a central cystic area surrounded by abundant fibrous tissue containing dendritic and epithelioid melanocytes as well as melanophages. No necrosis or mitotic activity was present, but melanocytes showed some atypia. The patient was well and alive and had no evidence of recurrent or metastatic disease 9 years after lymphadenectomy.

Our case shares some features of the Temple-Camp et al case,³ as well as notable differences: our patient's cutaneous lesion looked like a cellular blue nevus with a component of Spitz nevus (combined nevus) that had no junctional component; the lymph node metastases and skin lesion were synchronous; two lymph nodes were involved; and, most importantly, the largest node showed necrosis and fibrosis rather than cystic changes. Our case could be interpreted as an unusual case of benign cellular blue nevus with massive lymph node

Figure 2. Cutaneous lesion. A) Low-power view showing a slightly asymmetric lesion with no involvement of the epidermis (H&E, $\times 16$). B) Clusters of melanocytic cells intersected by bundles of collagen fibers (H&E, $\times 200$).

Figure 3. Cutaneous lesion. A) The proliferating cells were polygonal or ovoid in shape and had abundant glassy cytoplasm. The nuclei were round and showed fine, uniformly dispersed chromatin granules and a small but obvious nucleolus. Numerous intensely pigmented cells lay close to the glassy cells (H&E, $\times 400$). B) The papillary dermis contained numerous glassy multinucleated cells and pigmented cells immersed in a dense collagen stroma (H&E, $\times 400$).

metastases, as a malignant melanoma mimicking cellular blue nevus, or as a primary malignant melanoma of the lymph node with concomitant cutaneous cellular blue nevus. According to the current criteria for diagnosing metastatic malignant melanoma (permeative growth in the pulp of the lymph node and necrotic

Figure 4. Cutaneous lesion. Dendritic melanocytes and intensely pigmented polygonal cells were distributed around the eccrine glands (H&E, $\times 200$).

foci),⁶ our case should be considered as a malignant melanoma; nonetheless, the absence of architectural and cytologic features of malignancy in the cutaneous lesion coupled with the bland nuclear features of the pigmented cells in the regional lymph node favor the unusual possibility of a benign, metastasizing cellular blue nevus with massive metastases. The cellular features in themselves are not absolute criteria for differentiating cellular blue nevus from melanoma because malignant melanoma may show bland nuclear features, low mitotic rate, and a nuclear DNA content of diploid pattern.^{7,8} Immunohistochemistry using primary HMB-45 antibody does not help to resolve this problem because cellular blue nevus may show extensive immunostaining.⁷ To the best of our knowledge, the third diagnostic possibility, benign cellular blue nevus with massive metastases, has not been reported in the literature. Only restriction fragment length polymorphism analysis might reveal the clonal differences between cellular blue nevus and malignant melanoma. A primary malignant melanoma arising from a lymph node was described by Shenoy et al,⁹ but, unlike our case, this melanoma involved only one lymph node and evolved from precursor nevus cell aggregates located in the lymph node capsule and was associated with blue nevi in the axillary lymph nodes. A conservative surgical approach with close follow-up was recommended.

Figure 5. Lymph node. A) The smaller lymph node showed partial replacement by proliferating tumor cells (H&E, $\times 16$). B) The proliferating cells were polygonal and spindle shaped and contained abundant melanocytic pigment (H&E, $\times 200$).

Figure 6. Lymph node. A) The larger lymph node showed total cellular replacement by tumor cells and fibrosis (H&E, $\times 16$). B) The bleached sections show tumor cells with bland nuclear features (H&E, $\times 400$).

The primary cutaneous lesion of cellular blue nevus should be differentiated from so-called atypical blue nevus and from malignant blue nevus. The term "atypical blue nevus" designates cellular blue nevi that have cytologic atypia and a mitotic count of two figures per square millimeter; most of these lesions behave benignly and do not metastasize except after local recurrence or progression of an incompletely excised lesion.^{10,11} In contrast, malignant melanoma is a highly pleomorphic tumor that may recall, or arise from, a cellular blue nevus. Unlike our case, most malignant melanomas that simulate cellular blue nevi show some degree of cellular atypia, a destructive and infiltrative pattern, epidermal invasion, and necrosis.⁷ Malignant blue nevus is a malignant melanoma that originates from a preexisting cellular blue nevus or from its site of excision. Most of these tumors have a spindle-cell pattern, are located on the head, usually behave aggressively (80% of cases present metastases at time of diagnosis), and have a high mortality rate in the first 5 years.^{12,13}

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References

Rodriguez HA, Ackerman LV. Cellular blue nevus: clinicopathological study of forty five cases. *Cancer* 1968;21:393-405.

- Lambert DC, Brodtkin RH. Nodal and subcutaneous cellular blue nevi. *Arch dermatol* 1984;120:367-70.
- Temple-Camp CRE, Saxe N, King H. Benign and malignant cellular blue nevus. A clinicopathological study of 30 cases. *Am J Dermatopathol* 1988;10:289-96.
- Deicht AD. Cytophotometry of nucleic acid. In: Wied GL, ed. *Introduction to Quantitative Cytochemistry*. New York: Academic Press, 1966;327-54.
- Allen AC, Spitz S. Malignant melanoma. A clinicopathological analysis of criteria for diagnosis and prognosis. *Cancer* 1953;6:1-45.
- Merkow LP, Burt RC, Hayeslip DW, Newton FJ, Slifkin M, Pardo M. A cellular and malignant blue nevus. A light and electron microscopic study. *Cancer* 1969;24:888-96.
- Elder DE, Murphy GF. Melanocytic tumors of the skin. In: Rosai J, Sobin L, eds. *Atlas of Tumor Pathology*. Washington, DC: Armed Forces Institute of Pathology, 1991;103-98.
- Björnhagen V, Auer G, Lagerlöf, et al. Nuclear DNA analysis in archival material from primary malignant melanoma. A pilot study. *Anal Quant Cytol Histol* 1991;13:335-42.
- Shenoy BV, Fort III L, Benjamin SP. Malignant melanoma primary in the lymph node. The case of the missing link. *Am J Surg Pathol* 1987;11:140-6.
- Avidor I, Kressler E. Atypical blue nevus. A variant of cellular blue nevus: presentation of three cases. *Dermatologica* 1977;154:39-44.
- Goette DK, Robinson JW. Atypical cellular blue nevus. *J Assoc Milit Dermatol* 1980;6:6-8.
- Connelly J, Smith JL. Malignant blue nevus. *Cancer* 1991;67:2653-7.
- Boi S, Barbareschi M, Cristofolini M. Malignant blue nevus. Report of four new cases and review of the literature. *Histol Histopathol* 1991;6:427-4.