

Multiple Cutaneous Granular Cell Tumors: A Case Report and Review of the Literature

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GOAL

To describe a case of multiple cutaneous granular cell tumors

OBJECTIVES

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

1. Outline the epidemiology of granular cell tumors.
2. Describe the clinical manifestations and how to diagnose granular cell tumors.
3. Identify treatment recommendations for granular cell tumors.

CME Test on page 367.

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Granular cell tumors are benign neoplasms derived from Schwann cells. Their clinical presentation ranges from large verrucose nodules, as in our patient, to small, nonspecific, subcutaneous papules. Approximately half of granular cell tumors develop in the head-and-neck region, most commonly on the tongue. Multiple granular cell tumors are not a sign of malignancy and may be more common than generally reported.

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When assessing a painful tumor of the skin, dermatologists often use a differential diagnosis of blue rubber-bleb nevus, leiomyoma, eccrine spiradenoma, neuroma, dermatofibroma, angioliipoma, neurilemoma, endometrioma, glomus tumor, and granular cell tumor. The mnemonic *BLEND AN EGG* is used to remember these tumors. We report a case in which a 56-year-old black woman presented with a painful left-flank tumor diagnosed as a granular cell tumor.

Case Report

A 56-year-old black woman presented with a painful tumor growing from the left flank. The tumor, which the patient first noticed 3 years earlier, had grown slowly and became painful. Medical history was significant for hypertension; surgical history included removal of 3 benign growths from the tongue 20 years earlier and removal of a biopsy-

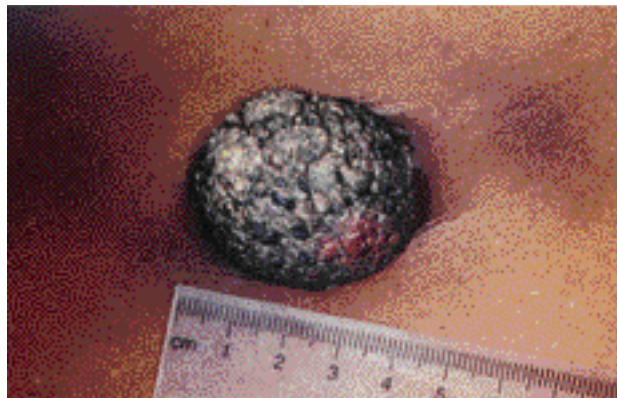


Figure 1. Large verrucose tumor on the left flank (length in centimeters).

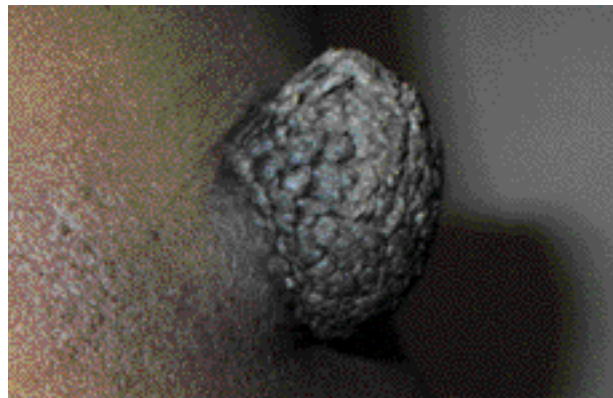


Figure 2. Large verrucose tumor on the left flank (close-up).



Figure 3. Large verrucose tumor on the left flank (side view).

verified granular cell tumor from the left breast in 1994. Medications included nifedipine and furosemide. The patient stated that her father had had benign growths removed, but she did not know his histopathologic diagnosis. She also mentioned that her sister had decided not to have similar growths removed.

The patient was a well-nourished, healthy-looking woman. Her left-flank lesion was a 4×4×1.5-cm verrucose, firm, hyperpigmented, tender nodule (Figures 1–3). Other lesions were found during the physical examination—an 8-mm tongue-colored papule on the tongue (Figure 4); a 2×1-cm soft polypoid papule on the right buccal mucosa; a cyst with a visible punctum on the right cheek; a 1-cm soft, motile, subcutaneous papule on the left arm; a firm, subcutaneous nodule (with overlying hyperpigmentation) on the right antecubital fossa; a 6-mm shiny,



Figure 4. Pink nodule on the tongue.

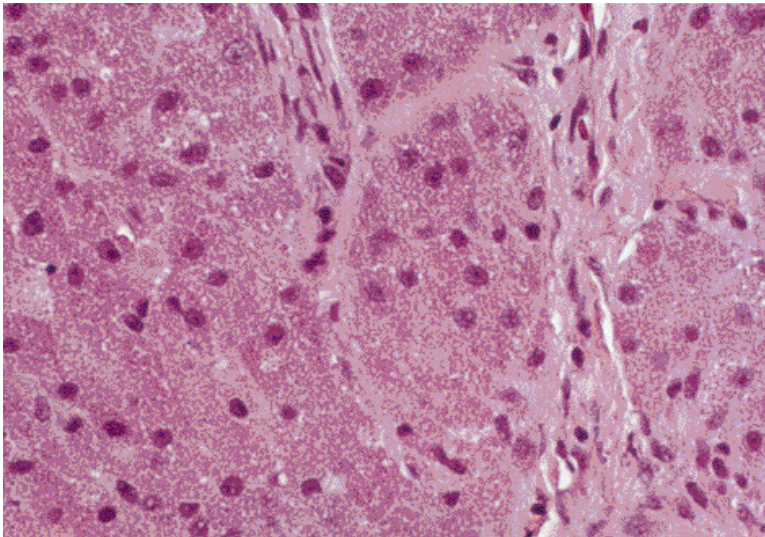


Figure 5. Granular cell tumor (H&E, original magnification $\times 400$).

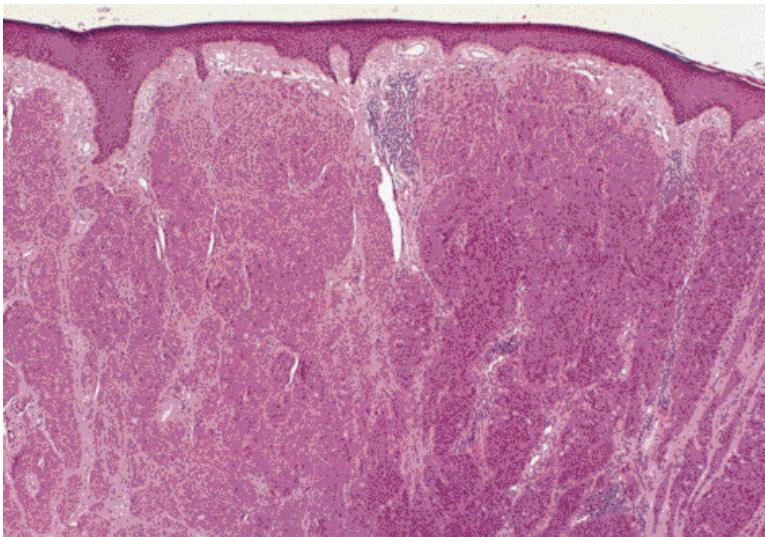


Figure 6. Granular cell tumor (H&E, original magnification $\times 40$).

flesh-colored, dome-shaped, buttonholing papule in the central area of the chest; and a soft, motile, subcutaneous nodule on the right thigh.

Results of biopsies of the large verrucose lesion on the left flank showed nests of granular cells weaving between dermal collagen bundles (Figures 5 and 6). Granular cell tumor was diagnosed, and the tumor was surgically excised. At the same time, a biopsy was performed on the papule in the central area of the chest (this papule also was diagnosed as a granular cell tumor), and the papule on the left arm was removed (diagnosis: lipoma). Biopsies were not performed on the other lesions.

Comment

In 1854, Weber was the first to report a case of granular cell tumor. In 1926, Abrikosoff named this type of tumor *granular cell myoblastoma* (he thought its origin was muscular).¹ In 1935, Feyrter suggested

an origin of neural differentiation.² In the 1960s, convincing clinical and pathologic evidence of Schwann-cell origin was reported.^{3,4}

Granular cell tumors are most often found from the second to sixth decade of life. They are more common in women and in blacks.⁵ Half of these tumors develop in the head-and-neck region. The tongue is the most common site. One third of granular cell tumors develop on the tongue, one third on the skin, and one third in internal organs. Granular cell tumors develop in almost every internal organ, including the esophagus, stomach, appendix, larynx, bronchi, pituitary gland, and uvea, as well as the skeletal muscle.^{2,6} Up to 25% of granular cell tumors develop in multiples.^{6,7} A patient with a biopsy-verified granular cell tumor should undergo a complete physical examination, as presence of another tumor is very likely. Some patients have both granular cell tumors and malignant tumors (one patient

had both a granular cell tumor and a ductal carcinoma on one breast⁸). A patient with a mass suggestive of malignancy should have a biopsy performed. Approximately 1% to 2% of granular cell tumors are malignant.⁹ The diagnosis of malignancy usually is based on the clinical behavior of the tumor, as there is no set of diagnostic histologic criteria for malignancy. Features suggestive of malignancy include size greater than 4 cm, necrosis, metastases to lymph nodes, aggressive clinical behavior and fast growth, nuclear pleomorphism, and ulceration.

The clinical manifestations of granular cell tumors are varied. Many of these tumors present as subcutaneous nodules. (The overlying skin may be normal, hyperpigmented, or covered with a tuft of hair.) These tumors often are verrucose, can be pruritic or painful, and can develop within scars. The cut surface of the tumor is white to yellowish, similar to the color of nerve bundles.

In the biopsy specimen, broad fascicles of tumor cells infiltrate the dermis among collagen bundles arranged in nests or sheets. Pseudoepitheliomatous hyperplasia often overlies the tumor cells,^{2,6} which are round to polygonal and have distinct membranes. Small, uniform, eosinophilic granules fill the cytoplasm. Scattered, laminated cytoplasmic globules have peripheral halos (residual bodies). Nuclei are small, round to oval, and centrally located. Evidence of mitosis, though uncommon, is not necessarily a sign of malignancy. Neurotropic spread along peripheral nerves occurs.

Immunostain is positive for S-100 protein, peripheral nerve myelin proteins, and neuron-specific enolase. The lysozymes in the granular cell cytoplasm stain positively for CD68. Under electron microscope, degenerated myelinated axons are seen in the cytoplasm of these tumor cells. These degenerated axons reportedly are similar to the granules and whorled filaments found after wallerian degeneration of altered Schwann cells.¹⁰ When an axon is transected, its distal part breaks down (ie, undergoes wallerian degeneration). When this occurs, Schwann cells proliferate, which suggests that local injury causes these granular alterations.¹¹

Although granular cell tumors rarely grow back after simple excision, wide local excision usually is recommended.¹² Of course, recurrence is possible.¹³ According to some reports, intralesional steroids have caused regression.¹ Evidence of successful treatment with either systemic chemotherapy or radiation is lacking.¹²

Granular cell tumors (tumors of the nerve sheath) are rare. Multiple granular cell tumors are probably more common than generally reported. Diagnosis of a granular cell tumor warrants a complete physical examination for other tumors.

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