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Case Report

Granular Cell Tumor

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Abstract

Granular cell tumor is an uncommon, benign tumor that mainly occurs on the skin, tongue, and oral cavity as a single nodule. This tumor was previously thought to be derived from muscle by Abrikossoff and was called as "granular cell myoblastoma." Recent ultrastructural studies and stains such as S100 and neuron-specific enolase confirm that this tumor is derived from Schwann cells of the peripheral nerves. A 48-year-old male patient was admitted to our hospital with the complaint of expanding mass in his left lumbar region for about five months. On his dermatological examination, a 5 x 4 cm sized, pink-–brown tumor was detected in his left lumbar region. The tumor was hard on palpation. There was an ulcer 1 cm in diameter at its center. The borders of the tumor were regular. On histopathological examination, pseudoepitheliomatous hyperplasia in the epidermis and tumoral infiltration in the dermis were detected; the infiltration was composed of cells with large eosinophilic cytoplasm containing fine granules and numerous oval-–round nuclei. Cytoplasmic granules stained positive with PAS and S100 stain. Granular cell tumor was diagnosed on the basis of clinical and histopathological features. The clinical diagnosis of granular cell tumor is difficult and depends on the histopathological findings. Outside of the typical region of involvement, as observed in our case, any region can be involved. Granular cell tumor is a benign neoplasm with good prognosis. A tumor larger than 4 cm in diameter, the presence of ulceration, rapid growth, and lymphadenopathies are signs that suggest malignancy. Although in our case the lesion was greater than 4 cm in diameter, there was ulceration, and rapid growth, the histopathological features were benign. No recurrence was observed for 13 months in its pursuits after wide local excision.

Keywords: Granular cell tumor, lumbar region, ulcer

Introduction

Granular cell tumor was firstly called "granular cell myoblastoma" by Abrikossoff in 1926 (1). Currently, the generally accepted view is that the tumor is of neural origin (2).

The oral cavity is a common localization region, but it can be seen in any part of the body. Cutaneous lesions constitute approximately 30% of cases.

In this study, a case with granular cell tumor localized in the lumbar region and including ulcerative changes is presented.

Case Report

A 48-year-old male patient applied to our outpatient clinic with the complaint of a mass expanding in his left lumbar region for approximately 5 months. No characteristic feature was found in his systemic examination. The results of his laboratory examinations were within normal intervals. In his dermatological examination, a 5x4 cm-sized, pinkish-brown, and hard tumor with regular borders and with a 1-cm diameter clean-based ulcer in its centre was observed (Figure 1). Written informed consent was received from the patient for using his information and pictures in a study. Then, punch biopsy was performed. In the histopathological examination of punch biopsy performed because of the prediagnoses of squamous cell carcinoma and keratoacanthoma, pseudoepitheliomatous hyperplasia was observed in the epidermis (Figure 2). Tumoral infiltration consisting of cells with an oval round nucleus and with an unclear nucleolus were detected in the dermis. Tumoral infiltration consisted of cells with a large cytoplasm, unclear cytoplasmic margins, and fine granules (Figure 3). Cytoplasmic granules were stained positive with periodic acid-Schiff stain (PASS) (Figure 4) and S100 protein (Figure 5). Based on these findings, the patient was diagnosed with a granular cell tumor. His lesion was removed with wide local excision by a plastic surgeon. It was seen in the excision preparation that the tumor filled the whole dermis and was invasive in the superficial subcutaneous fat tissue. An apparent cytological atypia, mitosis, and necrosis were not detected. Surgical margins were without any lesion. Abdominal and thoracic tomographies did not reveal a lesion consistent with metastasis. No recurrence was observed in the 13-month follow-up of the patient.

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Discussion

Abrikossof, who first defined the tumor, called the tumor "granular cell myoblastoma", thinking that it was muscle-originated. Subsequently, different authors came up with new ideas on the tissue from which the tumor was originated. Histiocytes, fibroblasts, and mesenchymal cells were specified as the cells from which the tumor originated. However, at present, the accepted view is that the tumor is of a neurogenic origin (2).

The incidence of granular cell tumor was reported to be 0.017%-0.029% in all surgical samples. It is mostly seen in women and in the 4th-6th decades of life. It is threefold more frequent in black people than in whites (3). Although granular cell tumors occur in the head and neck region at a rate of 50%, in the tongue at a rate of 35%, and in the vulva at a rate of 5.3%, it can also involve other parts of the body. It is rarely seen in visceral organs.

The clinical appearance of a cutaneous granular cell tumor is mostly non-specific, and it is difficult to establish its diagnosis clinically. It generally appears as a nodule, which is smaller than 3 cm, solitary, asymptomatic, sometimes tender or itchy, brownish-red, and firm, and the epithelium covering it is generally strong. However, ulcer or verrucous changes can be seen on its surface (4).

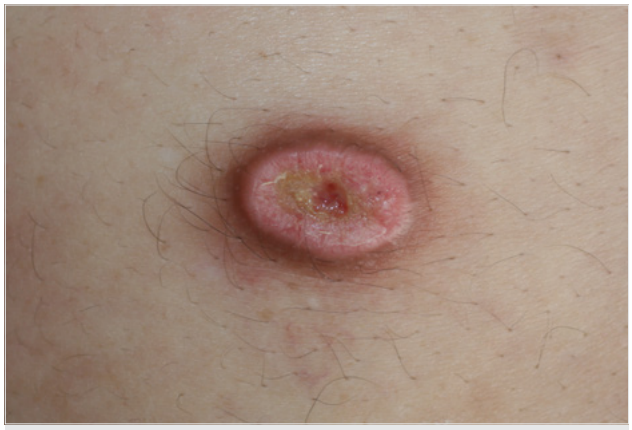

Figure 1. A pinkish-brown tumoral lesion localized in the left lumbar region

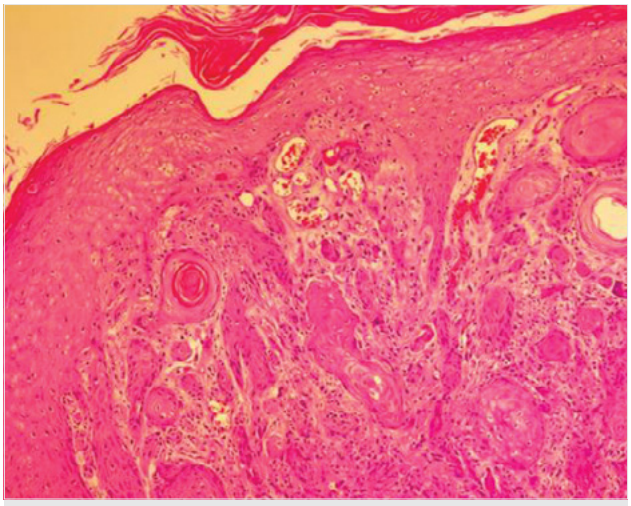

Figure 2. Pseudoepitheliomatous hyperplasia in the epidermis and tumor cells in the dermis

Ulcerative granular cell tumor has been studied as a separate entity in the literature. The clinical feature of these lesions is that they are large; painless; asymptomatic; round or oval; and solitary ulcers with an indurated base, necrotic floor, and elevated bor-

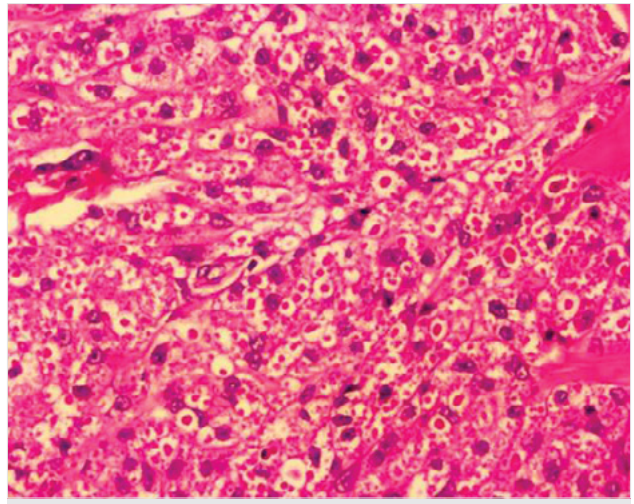

Figure 3. Tumoral infiltration consisting of cells with a large cytoplasm, unclear cytoplasmic margins, fine granules in their cytoplasms, oval round nucleus, and unclear nucleolus in the dermis

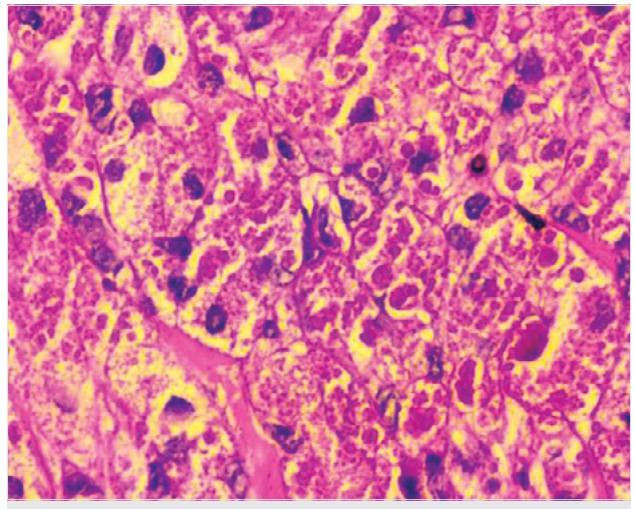

Figure 4. PAS (+) staining of cytoplasmic granules

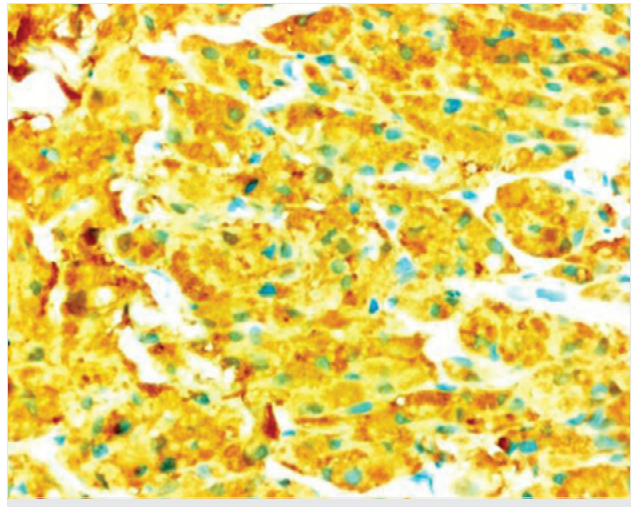

Figure 5. Staining of cytoplasmic granules with S100 (+)

Table 1. Differential diagnosis of diseases in the histopathologies of which granular cells are observed

Granular cell tumor	**Pseudoepitheliomatous hyperplasia in the epithelium, pale stained polygonal cells with, eosinophilic granular cytoplasma, and oval nucleus; granular PAS+, S100+, NSE+**
Rhabdomyoma	Wide, polygonal cell layers with granular, eosinophilic cytoplasma desmin and myoglobin strong+, S100 sometimes poor+
Hibernoma	Vacuole cells besides small cells with a granular cytoplasm
Atypical fibroxanthoma	Pleomorphism, atypical and oddly-shaped cells, mitotic figures; vimentin, actin+, S100 rarely+
Dermatofibroma	Granular cell variant, generally together with typical regions; FXIIIa+, vimentin+, CD34 –
Dermatofibrosarcoma protuberans	Granular cell variant; CD34+, FXIIIa –, S100 –
Schwannoma	Encapsulated, Verocay body characteristic; S100+
Neurofibroma	Random proliferation of fusiform cells in the fibrillary matrix
Paraganglioma	Polygonal large cell nests, with central oval nucleus, abundant eosinophilic granular cytoplasm; chromogranin, synaptophysin, vimentin, NSE+
Melanoma, compound nevus	S100, HMB45, Melan-A+; nuclear pleomorphism in melanoma, abnormal mitotic figures
Leiomyoma, leiomyosarcoma	Fusiform or polygonal cells with a rough granular eosinophilic cytoplasm; desmin+, S100 –
Basal cell carcinoma	Granular variant; large cells with an abundant eosinophilic granular cytoplasm out of conventional BCC regions; Ber-EP4+, PAS+, keratin+

der. The lesion slowly progresses, and ulceration often occurs after a time longer than 1.5 years. It is more frequently seen in men during the 2nd and 3rd decades of their lives, and the most common localization is the extremities. Although our patient's lesion included ulcerative changes, he presented a different feature with the localization of the lesion and a relatively more rapidly formation of the ulcer. Histologically, an ulcerative granular cell tumor looks like a typical granular cell tumor (5).

The diagnosis of granular cell tumor is mostly based on histopathological findings. Histologically, granular cell tumor is composed of well-demarcated dermal proliferations of pale-stained polygonal cells with characteristic eosinophilic granular cytoplasma and an oval nucleus. Characteristic large cytoplasmic granules are called pustulo-ovoid bodies. The granules stain positive with PAS but are resistant to diastase. It rarely has a perineural pattern, but it is deprived of axone. The epithelium covering the tumor often displays pseudoepitheliomatous hyperplasia. A plexiform growth pattern has been defined occasionally. Although the histological criteria of rare aggressive tumors, which are prospectively determined, are not well-demonstrated, the presence of necrosis, increased mitotic velocity, and fusiform cells are accepted as the indicators of aggressive behavior (5). Despite the fact that the lesion of our patient grew relatively rapidly and the diameter of the lesion reached 5 cm, the finding reminiscent of malignant transformation was not observed in his histopathological examination.

The presence of immunohistochemical and electron microscopic findings confirms the diagnosis of granular cell tumor. The diagnosis is verified using immunohistochemical staining showing S100 and neuron spesific enolase positivty. The S100 protein is demonstrated in Schwann cells and satellite cells of autonomic ganglion. The tumor is stained with inhibin-a, calretinin, galectin-3, and mesothelioma marker antibody (HBME) at different rates, and it is expressed with vimentin, protein gene product (PGP 9.5), and melanoma-directed monoclonal antibody NKI/C3 ve CD68 (6).

Granular cell tumor is generally benign. Only 1%–3% of all cases are malignant. Malignancy often develops in visceral or deep lesions. The diameters of such lesions are bigger than 5 cm. It grows rapidly and displays the risk of metastasis (7).

Because of evident pseudoepitheliomatous hyperplasia in the upper epithelium, the lesions, especially in the tongue, can be confused with squamous cell tumors. Similar to that in our patient, the clinical features of ulcerative granular cell tumors may resemble infectious granulomatous ulcers, including cutaneous leishmaniasis and tuberculosis, in addition to malignant neoplasms such as squamous cell carcinomas and cutaneous lymphomas. There are some diseases that show granular cell changes histopathologically. Their differential diagnosis with granular cell tumors is addressed in Table 1 (5, 8).

A great number of granular cell tumors have been successfully treated with wide local excision. In benign granular cell tumors excised locally, the recurrence rate has been 2%–8% in the presence of negative surgical margins and >20% in the case of positive surgical margins. Therefore, the control of surgical margins is important (9). The lesion of our patient was removed with wide local excision, and no recurrence was observed during his 13-month follow-up. In the literature, there are also patients who underwent Mohs surgery with successful results (10).

Conclusion

Although a large diameter, rapid growth, and ulceration of granular cell tumors are the features reminiscent of malignant transformation, this study reported a rare case with granular cell tumor which did not present malignant features, and localized in lomber region, despite it having a diameter of 5 cm, growing rapidly, and being ulcerated.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

Peer-review: Externally peer-reviewed.

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