

MULTIPLE GRANULAR CELL TUMOR IN A TEENAGER: REPORT OF A CASE AND REVIEW OF THE LITERATURE

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Abstract- Granular cell tumors are rare neoplasms of uncertain histogenesis but with a typical histologic appearance composed of cells with characteristic granular cytoplasm. These tumors occur most often in adults as an asymptomatic solitary papule or nodule. Multiple granular cell tumors are rare, especially in children and teenagers. We represent a case of multiple granular cell tumors in a 19-year-old girl presented with multiple cutaneous and mucosal nodular lesions. The diagnosis was documented by histopathology and immunohistochemistry.

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INTRODUCTION

Granular cell tumor (GCT) was first described by Abrikossoff in 1926. It is rare and usually presents as a benign asymptomatic solitary lesion. Although GCT is a well-recognized entity, its biologic nature and histogenesis remain controversial.

The old term "granular cell myoblastoma" implied a muscle cell origin, but immunohistochemical studies have generally supported a Schwann cell origin through the positive identification of S-100 protein, neuron-specific enolase and myelin-related protein and negative reaction to epithelial and muscular markers. Most authors consider the tumor to be a true neoplasm and it is now commonly accepted that GCT originates from Schwann cells (1-3).

GCT occurs among all races, both sexes and in any age, although it is most common in females and in the black population (4). The most common occurrence is during the fourth to sixth decades of life although there are rare instances of congenital occurrence (4,5). The common locations are the head and neck, the tongue, and the vulva (6), but any organ

can be involved and there are reports of involvement of internal organs such as larynx, bronchus, stomach, rectum, anus, biliary ducts, pancreas and soft tissues. Malignant GCT is extremely rare and occurs in only 1-2% of cases (7,8). Multiple GCTs are rare, especially in children and teenagers. This report introduces a case of multiple GCTs in a 19-year-old Iranian girl with a review of similar cases in the literature.

Case Report

A 19-year-old girl presented for evaluation of multiple, firm skin-colored to red nodules on her chest, back, abdomen, face, scalp, extremities, as well as in oral mucosa, tongue (Fig. 1), and external genitalia. When she was 5 years old, the first lesion had appeared on her upper chest and since that time, she had developed more than 40 other similar lesions, the largest being about 2cm in diameter (Fig. 2). She was otherwise in good health and family history was negative for skin and developmental disorders such as neurofibromatosis. Laboratory data were all normal. Multiple skin biopsies were performed and light microscopy revealed an ill-defined infiltrative tumor composed of polygonal cells with small central nuclei and abundant cytoplasm filled with diastase-resistant granules with a positive periodic acid-Schiff stain result. Immunohistochemistry was done, and granular cells were strongly positive for S-100

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protein. These findings suggested the diagnosis of granular cell tumor (GCT).



Fig. 1. A large nodule in the tongue



Fig. 2. The largest nodule of approximately 2 cm on the upper back

DISCUSSION

Credit for the first description of GCT was given to Abrikossof, who named the tumor as granular cell myoblastoma, because of its presumed skeletal muscle origin (4), but nowadays electron microscopy and immunohistological studies generally support a Schwann cell origin.

GCT is an infrequent soft tissue neoplasm. It occurs among all races, both sexes and in any age, although a slight female predominance exists and most patients are middle-aged, with a peak incidence in the fourth to sixth decades of life. Typically, GCTs are asymptomatic, slow-growing, rarely over 3 cm in diameter, smooth-surfaced or hyperkeratotic, solitary nodules or tumors (4). They are commonly intradermal, subcutaneous, or submucosal lesions and not encapsulated (4). Almost half of the tumors (43%) occur in the skin and subcutaneous tissues, 40% in the oral cavity, and 35% in the tongue (9).

Multiple cutaneous GCTs are rare and have only been reported in less than 10% of cases (2), although some believe that this percentage is probably higher and in a long-term follow-up, a number of patients with solitary GCT may develop new lesions elsewhere in the body (4).

Multiple lesions are especially very rare among children (10,11). In a review of literature in 1986, Rubenstein *et al.* recorded only 12 cases of multiple GCTs in patients younger than 16 years of age and in another review in 1990, Martin *et al.* found only 26 reports of multiple cutaneous GCTs among patients younger than 19 years (12,13). Dorta *et al.* reported a Spanish girl with progressive multiple GCTs since the age of 7 years (14).

There are many reported associations with multiple GCTs including neurofibromatosis, Watson's syndrome, Lentiginosis profusa, Noonan syndrome, facial and ocular alterations, cardiovascular abnormalities, muscle and bones malformations, and neurologic deficits (15-19). According to Bakos, this combination seems to be more than accidental and suggests a distinct syndromic entity (20). Another point of interest in GCT is a possible association with malignant neoplasias of other organs. Squamous carcinoma of the esophagus, adenocarcinoma of the prostate and

small cell lung cancer are among the reported cases of this association (21-23). In our case, clinical findings include multiple asymptomatic cutaneous and mucosal papules and nodules of different sizes and colors. Light microscopy revealed polygonal cells with small round centrally located nuclei and granular eosinophilic cytoplasm without mitosis and pleomorphism, and immunohistochemical investigation showed positive staining for S-100 protein. All of these findings are compatible with the diagnosis of multiple GCT.

Histological examination is usually necessary to separate GCT from other soft tissue tumors. Clinically, squamous cell carcinoma is the most common preoperative entity in the differential diagnosis of solitary GCT, which may also be confused pathologically if pseudoepitheliomatous hyperplasia of the epithelium is present (1,14). Dermatofibroma, keloid and lipoma are among the other differential diagnoses. It is not surprising that in all 16 cases reported by Apisarnthanarax, the preoperative clinical diagnoses were incorrect (4). In multiple lesions, diagnosis is even more difficult because the lesions can resemble prurigo nodularis or even nodular forms of mastocytosis (24). The histopathologic picture of GCT is usually highly characteristic, although histologically, many cutaneous neoplasms of diverse lineage, such as leiomyoma, leiomyosarcoma, atypical fibroxanthoma, dermatofibroma and even basal cell carcinoma should be considered in the differential diagnosis, because all of these neoplasms may occasionally have granular qualities (1,25). The best treatment for solitary tumor is surgical removal with wide margins, and further follow-up due to the possibility of recurrence or malignant transformation (4). Intralesional corticosteroid injection has been reported to induce some regression in multiple GCT (24). To our knowledge this case is the first reported case of multiple GCT in a teenager from Iran, and involvement of both mucosa and skin was another aspect of interest in this patient. Although we could not find any significant association in this case, the possibility of associated anomalies, malignant degeneration and other organ malignancies should be meticulously considered in any case of multiple GCT.

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