Granular cell tumor: Case report

Mona Bitar *, Khalid A. Al Afif, Mohammad I. Fatani

Department of Dermatology, Hera General Hospital, Makkah, Saudi Arabia

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Abstract   Granular cell tumor (GCT) is uncommon, mostly benign neoplasm that can affect any organ of the body; immunohistochemical studies showed that it has a Schwann cell origin through the positive identification of S-100 protein. GCT can affect both sexes and in any age, although it is most common in females and dark skinned population. The most common occurrence is during the fourth to sixth decades of life, very rarely it occurs as congenital disease. The common locations are the head and neck, the tongue is affected in 25% of cases but any internal organs can be affected such as larynx, bronchus, stomach, rectum, anus, biliary ducts, pancreas and soft tissues. Malignant GCT is extremely rare, it occurs in only 1–2% of cases. Multiple GCTs occur up to 10%. In children, only 20 cases have been reported in the literature.

This paper describes the case of a 6-year-old girl diagnosed with upper right arm granular cell tumor and the patient’s clinical evolution after tumor surgical removal.

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1. Introduction

Granular cell tumors were first described by Abrikossoff in 1926 and named as myoblastomas, as they were considered to derive from smooth muscle. GCTs are also known as Abrikosoff’s tumors (Montijo et al., 1999). Feyrter in 1935, postulated that these tumors were neural in origin and he called them granular cell neuromas. In 1948 Fust and Custer confirmed this theory, and proposed a new name – granular cell neurofibroma. Fisher and Wechsler in 1962 conducted ultrastructural and immunohistochemistry studies to find that Schwann’s cells were the most likely origin of these tumors, and thus named them granular cell schwannomas (Garin et al., 1992). However, granular cell tumor (GCT) is the nomenclature adopted by the World Health Organization (WHO) (Garin et al., 1992).

In spite of the arguments around the origin of GCTs, the apparent connection with Schwann’s cells is based on solid findings: ultrastructural similarity between Schwann’s and granular cells; similarity between the granules in granular cells and altered myelin; concentric arrangement of granular cells around nerve ends; presence of lipoproteins and sphingomyelin in granular cells indicating that the granules in granular cells are made of myelin or the product of its degradation; and positivity for protein S-100, enolase, and myelinic
proteins PO and P2 by immunoperoxidase techniques (Garin et al., 1992).

GCTs are more common in females than males (Apisarnthanarax, 1981), multiple GCTs are more commonly found in African-descendent patients (Garin et al., 1992; Moraillon et al., 1993), between the fourth and the fifth decades of life (Apisarnthanarax, 1981; Moraillon et al., 1993). It is a rare disease especially in children, only 20 cases have been reported in the literature (Lassaletta Atienza et al., 1999; Fried, 1996; Ortiz-Hidalgo et al., 1997).

GCTs grow slowly and insidiously, when an internal organ is involved, patients may need 6–7 months before they seek medical advice (Garin et al., 1992).

GCT diagnosis is done through pathology tests. The tumor is characterized by the presence of a large amount of dense cytoplasmatic lysosomes in different fragmentation stages, giving it a granular aspect under microscopy. The disease manifests itself in the form of subdermal or submucosal tumors with cells arranged in diffuse masses and strings. GCTs are characterized for not being encapsulated and for having imprecise borders. They may also invade and infiltrate adjacent tissues. The tumors are formed by large fusiform or polygonal cells with marked cell membrane and abundant pale cytoplasm, filled with eosinophilic granules.

The most characteristic trait of granular cells is the membrane-contained cytoplasmatic granulation with microvesicles, increased density areas, microtubules, and myelinic formations. Cell nuclei are small, round to oval, located centrally, and some cells may have more than one. The pale, characteristic granules inside the cells are PAS (periodic acid-Schiff) positive and diastase-resistant (Noronha and Dias, 1997; Lazar et al., 1992; Hamid and Alshaikhly, 1993). In immunohistochemistry granular cell tumors are positive for protein S-100 and neuron-specific enolase.

Malignant GCT is very rare and has a poor prognosis, as patients die within 2–5 years after diagnosis. It occurs in only 1–2% of cases (Kamal and Othman, 1998; Parayno and August, 1996; Jardines et al., 1994). Differential diagnoses are rhabdomyosarcoma, paranglioma, oncocyctic tumor, melanoma (Brandwein et al., 1990). All these can be excluded by histopathological features.

2. Case report

A 6-year-old girl was presented to the dermatology clinic complaining of a painless nodular lesion on the right upper arm evolving for about a year with good general condition. Actually, 8 months ago, the patient has attended the surgical clinic, inquiring about a small slowly growing, skin colored nodular lesion, not resolving with classical medication. A surgical excision has been done without histopathological study. Several weeks later, the lesion reappeared in the same site, and had considerably increased in size, but remained asymptomatic. The examination showed on the upper right arm a solitary, yellowish, firm nodule, with shiny lobulated surface, central umbilication and regular border, of 2–3 cm in diameter (Fig. 1). The clinical picture was mostly consistent with keloid formation on an old scar. An intralesional steroid injection was attempted, and it resulted in only mild reduction of the size of the nodule. Then a biopsy was performed and showed on histopathological study, a mild acanthosis of the epidermis, the entire dermis was deeply infiltrated with a proliferation of large polygonal, and oval cells with abundant, fine granular eosinophilic cytoplasm, and small acenetrically located nuclei (Fig. 2). Immunostaining has been done and showed clear S-100 protein positivity (Fig. 3) features diagnostic of a benign granular cell tumor. The patient underwent a complete surgical resection.

3. Discussion

GCTs are rare benign neoplasms, they may involve any organ of the body, about 50% of the tumors are found in the head and neck area. (Kamal and Othman, 1998; Leache Pueyo et al., 1997).
Granular cell tumors are more frequently found in adults, with rare occurrences in the pediatric population. Usually include benign tumors as they account for 98% of the cases (Lazar et al., 1992).

Congenital GCT is in fact a variation of GCT with similarities under the microscope but with immunohistochemical, and ultrastructural differences (Scala et al., 2008).

GCTs are almost always benign, but malignant manifestations are found in 1–2% of the patients. They are preferentially located in the skin and subcutaneous region. They involve the regional lymph nodes, although distal metastasis is uncommon. Malignancy is suspected from a series of factors (Garin et al., 1992):

1. Cases of tumors macroscopically similar to benign GCTs, however quickly relapsing locally after surgical removal.
2. Tumors above 4 cm; Gamboa (1955) and Batsaki and Manning (1986) reported GCT cases with malignant clinical and histological characteristics, with larger tumors (averaging 9 cm in diameter) in relation to benign GCTs.
3. Tumor evolving slowly that suddenly begins to grow quickly.
5. Presence of atypia and pleomorphism, although not always present in malignant GCT.

The name Atypical GCT in which malignant histological traits and clinical aggressiveness was given for cases are present, even without signs of metastasis (Brandwein et al., 1990).

This study presents the case of a 6-year-old girl with tumor on upper right arm which recurred after surgical excision.

Investigations showed on skin biopsy, microscopic proliferation of benign granular cells, which stained positivity for S-100 protein. These traits were suggestive of benign granular cell tumor. The most common benign neoplasms at this age range are papillomas and hemangiomas. Papillomas are caused by HPV (human papilloma virus) infection, which are characterized by verrucous surface.

Hemangiomas rank second in prevalence among children, but they occur much less frequently than.

GCTs are not pre-malignant tumors, nor do they evolve into malignancy; but they may coexist with carcinoma. When not combined with carcinoma, the diagnosis of malignant manifestations is based on accentuated cell pleomorphism and increased mitotic activity; characterizing it though as a malignant tumor can be a quite difficult task. This fact should be taken into account when planning patient treatment, as an over-conservative approach may allow aggressive tumors to remain undiagnosed. GCT treatment is principally surgical, and the tumor must be removed with broad margins.

In the case described in this paper the tumor removed but it recurred again. This may be because of the incomplete resection of the margins. Presently, the patient is in her sixth year of post-operative without relapse.

We may, therefore, conclude that GCTs are rare neoplasms that must be considered in the differential diagnosis of cutaneous and mucosal tumors. Early diagnosis combined with careful follow-up is required to increase the chances of cure.

References