Granular Cell Tumor of Ocular Adnexa; Report of Three Cases and Review of Literature
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Abstract

Purpose: Granular cell tumors (GCT) are benign unusual neoplasms which have been proven to have a Schwann cell phenotype. They rarely occur in the eye region.

Case reports: We report three cases of GCT in the ocular adnexa including palpebra, subconjunctiva and orbit which rarely occur. Patients are, a young girl with the lesion in orbit and presentation of proptosis, a middle aged man with the lesion in nasal limbus and erythema presentation and as well as an old age woman with the lesion in eyelid and protrusion. Morphologic examination of above cases show similar histology composed of polygonal cells which contained PAS positive eosinophilic granules. The S-100 protein and CD68 tests were positive in immunohistochemical stainings.

Conclusion: GCT occurs in different sites and ages, so they should be considered in the differential diagnosis of eye tumors in children and adults.

Keywords: Granular Cell Tumor, S-100, Orbit, Subconjuctiva, Eyelid

Introduction
Granular cell tumor (GCT) is an idiopathic slow-growing non-encapsulated painless tumor fairly common in soft tissues which infantile and adult forms are recognized. The infantile form involves the gingiva and the adult form occurs primarily in tongue (up to 40%), neck, chest wall, and virtually any organ.¹-⁴ Most of these tumors are benign. Rarely this tumor arises in the orbit, skin of the eyelid, palpebral conjunctiva, lacrimal sac, caruncle, and inferior oblique muscle.⁵-⁷ We report three of these cases with involvement of eyelid, orbit and subconjunctiva which are uncommon locations.

Case reports
Case 1
A 10-year-old girl student came to Farabi Eye Hospital (Ophthalmology center) of Tehran University of Medical Sciences with 3 months history of left eye proptosis and restriction of movement (Figure 1). So, Trans-conjuctival orbitotomy was done for her.
After left medial rectus muscle and adipose tissue dissection an encapsulated mass was seen. CT scan showed a well-defined homogeneous intracranial oval shape mass with pressure effect on optic nerve and involvement of rectus muscles. No scalloping, erosion of bone or invasion to adjacent structure was seen. Globe was normal (Figure 2). MRI shows hypo-signal intensity area on T1-weighted and homogenous intensity on T2-weighted with contrast enhancement (Figure 3).

**Case 2**
A 27-year-old man with raised erythematous lesion in nasal limbus of left eye.

**Case 3**
A 50-year-old woman with recurrent right eyelid protrusion, which was followed by surgery and pathologic diagnosis of Xanthelasma in another center, came to this hospital for consultation and reexamination of pathology slides.

Morphologic examination of above cases show similar histology composed of nests and ribbons of large round and polygonal cells which contained paracentral, vesicular nuclei with prominent nucleoli and abundant cytoplasm replete with striking coarse eosinophilic granules (Figures 4, 5).

Figure 1. Clinical photograph of the first case revealing proptosis in the left eye

Figure 2. MRI shows hyposignal on T1-weighted.

Figure 3. Axial section of a computed scan shows a hyperdense lesion located in the medial.

Figure 4. Morphologic examinations show eosinophilic cells with abundant granular cytoplasm and small oval nuclei (H&E staining).

Figure 5. Subconjunctival region, histopathological examination (H&E staining) (case 2).

The cells lay close to peripheral nerve bundles and normal striated muscles. They were also surrounded by dense fibrous scar tissue.
with a few scattered lymphocytes and plasmacytes. Neither mitotic figures nor necrosis were present.

The cytoplasmic granules were moderately periodic acid Schiff positive, diastase resistant, and stained Indian red with Masson's trichrome. They were negative for luxol fast blue.

The tumor cells in all of three cases were strongly positive for S-100 protein, calcitonin, epithelial membrane antigen (EMA) and CD68, as well as negative for carcinoembryonic antigen (CEA), smooth muscle antigen (SMA), desmin and myogenin.

**Discussion**

GCT described initially by Weber in 1854 and later by Abrikossoff in 1926 as tumor of muscle lineage.\(^6\)\(^-\)\(^9\)

GCTs have been proven to have a Schwann cell phenotype.\(^5\)\(^,\)\(^10\) Almost any organ or body tissue may be affected, though the most common sites are tongue, chest wall, and arm. Other cases have occurred in larynx, digestive tract, breast, female anogenital region, and pituitary stalk.\(^11\)\(^,\)\(^12\) Orbital involvement has previously been described in only 15 patients.\(^13\)\(^-\)\(^25\) Other cases in or near the eye have arisen in uvea, conjunctiva, caruncle, lacrimal sac, eyebrows, and eyelids.\(^12\)\(^,\)\(^25\)

Retrolubbar tumors adjacent to the optic nerve have been reported four times previously.\(^12\)\(^,\)\(^18\)\(^,\)\(^21\)\(^,\)\(^25\) Unlike their counterparts elsewhere in the body, GCTs in the orbit have characteristically been described as discrete and well encapsulated.\(^12\)\(^,\)\(^26\)

The tumor may occur at any age, though is most common between 40 and 70 years. Women are more frequently affected than men.\(^12\)\(^,\)\(^27\)

For unknown reasons they occur more often in blacks than whites. GCT presents as a painless nodule and most are solitary, however, 15% to 25% of patients have multiple nodules.\(^9\)

It may be well circumscribed or infiltrated into the surrounding tissue. Between 10 and 15% of GCTs are multicentric and 1 to 3% are malignant.\(^12\)\(^,\)\(^27\)

However, on histopathological examination, the diagnosis of granular cell tumor can often be made on haematoxylin and eosin sections as a result of its characteristic morphological features. Nevertheless, immunohistochemical studies may be needed to rule out other lesions such as oncocytoma.\(^5\)

They consist of uniform, plump or angulated, polygonal to fusiform cells with granular eosinophilic cytoplasm and central nucleoli with vesicular chromatin. The cells are arranged in nests, trabeculae and sheets that are surrounded by a desmoplastic stroma.\(^2\)

Immunohistochemically the tumor cells are positive for S-100 and CD68. Expression of S-100 in the granular cells supports the neural origin of this tumor.\(^3\) Positive stain with CD68 (a macrophage marker) can be explained by the intracytoplasmic accumulation of phagolysosomes and does not reflect a histiocytic origin. Histochemical staining for Luxol fast blue demonstrates positive staining of the prominent and characteristic cytoplasmic granules suggesting that they are of myelin origin. Additionally, it has been shown that the granular cells are also positive for inhibin-a.\(^3\) Although inhibin-a has been demonstrated to be strongly supportive of a GCT, the relation between this expression and pathogenesis of the granular cell tumor is unclear.\(^5\)

Histologically, the presented cases has shown typical features of GCT on light microscopy and by immunohistochemical staining.\(^5\)

**Conclusion**

In conclusion, GCT occurs in different sites and ages, so they should be considered in the differential diagnosis of eye tumors in children and adults. In the majority of cases, these lesions represent a benign isolated tumor. Surgical excision is the treatment of choice. The tumor has no or minimal potential of recurrence.
References