Case Report

Granular Cell Tumor of the Tongue: A Case Report and Literature Review

Maria Giulia Cristofaro1, Eugenia Allegra2*, Serena Trapasso2 and Francesco Conforti3

1Department of Oral and Maxillofacial Surgery, University of Magna Graecia of Catanzaro, Italy
2Department of Medical and Surgical Sciences, Otolaryngology – Head and Neck Surgery, University Magna Graecia of Catanzaro, Italy
3Department of Pathology, University Magna Graecia of Catanzaro, Italy

Abstract

Background: The granular cell tumor (GCT), or Abrikossoff’s tumor, is a rare benign neoplasm of soft tissue characterized by clusters of cells with abundant presence of cytoplasmic granules. It can affect any area of the body, but the head and neck, it has a predominance ranging from 45% to 65%; in 70% of these cases, it has intra-oral localization (tongue, oral mucosa, hard palate).

Case presentation: We describe a case of GCT of the tongue in a 47-year-old man presenting like a papillomatous lesion.

Discussion: Histopathological features, differential diagnosis, and therapeutic implications of GCT of the oral cavity are discussed, together with a review of the recent literature.

Conclusion: Immunohistochemistry besides helping to establish the correct diagnosis has allowed one to improve the knowledge of the controverter origin of this tumor, especially when clinical diagnosis is uncertain.

ABBREVIATIONS

GCT: Granular Cell Tumor; HE: Hematoxylin-Eosin; NGCT: Congenital Granular Cell Tumor; AFIP: Armed Forces Institute of Pathology.

INTRODUCTION

The granular cell tumor (GCT), or Abrikossoff’s tumor, is a rare benign neoplasm of soft tissue characterized by clusters of cells with abundant presence of cytoplasmic granules. The histological origin of GCT is controversial, since different derivations have been postulated by various authors, including fibroblasts, myoblasts, undifferentiated mesenchymal cells, Schwann cells, histiocytes, and neural cells. Accordingly, different definitions have been applied to this entity, such as myoblastoma, granular cell neurifibroma, and granular cell schwannoma [1].

It has a prevalence ranging from 0.003% to 0.019% of all neoplasms [2]. It can affect any area of the body; in the head and neck, it has a predominance ranging from 45% to 65%; in 70% of these cases, it has intra-oral localization (tongue, oral mucosa, hard palate). Typically, it occurs in adults between the third and sixth decade, and women are more affected than men with a ratio M:F = 1:2 [1]. Even if the biological behavior of GCTs is usually benign, accurate histological examination is mandatory, because in 2% of cases, they can be malignant and with high risk of recurrence [3]. We describe a case of GCT in a 47-year-old man. Histopathological features, differential diagnosis, and therapeutic implications of GCT are discussed, together with a brief review of the recent literature.

CASE PRESENTATION

A 47-year-old male reported with a rounded neoformation on the lingual body since about 4 years, which is increasing in size in the last 6 months. The swelling was initially small in size and slowly progressed to a present size of 0.5 cm in maximum diameter. The patient gave no history of trauma, pain, bleeding, ulceration, or pus discharge. Past dental history, family history, and drug history was not contributory. The patient gave history of mild smoking (15/day) since 25 years.

Intraoral examination revealed a well-circumscribed and elevated swelling, rounded, appearance like papillomatous with a regular surface, shape like a chickpea, and measuring 1 cm approximately in maximum diameter on the middle third of the lingual back. On palpation, the neoformation had
tense-elastic consistency, hardly movable, not bleeding and not painful, adherent to the underlying structures with no regional lymphadenopathy. The examination of the remaining ENT districts was within normal limits. A clinical diagnosis of verrucoid papilloma was made. Routine hematological investigations revealed normal values.

Excisional biopsy with local anesthesia was performed and the specimen was sent for histopathological examination. Histological examination classified the lesion as GCT. Gross examination revealed a tender tissue mass, purplish-brown color, with well-defined borders, 1 cm in diameter, oval in shape, and tense in consistency. Pathological examination showed an epithelium with hyper-ortho-parakeratosis, with a diffuse hyperplasia pseudo-epithelioid (HE 4x), in association with the proliferation of medium-sized cellular elements with granular cytoplasm and pattern of growth pseudo infiltrative (HE 20X, HE 40X) associated with a proliferation of cellular elements medium with granular cytoplasm and pseudo-infiltrative growing (HE 20X, HE 40X) (Figure 1). Investigations of molecular morphology by immunohistochemistry showed negativity for Cytokeratin (AE1-AE3 clone) (cytokeratin AE1-AE3, 4X, 20X) and positivity for S100 (S100 4X, 20X, 40X) (Figures 2, 3). Resection margins were free.

Based on histopathological findings, the final diagnosis of GCT was made.

The patient was included in a follow-up program with quarterly checks. At present the follow-up time is approximately one year. Currently, there are no signs of relapse.

**DISCUSSION**

The GCT, or Abrikossoff’s tumor, is unusual in the first and second decade; therefore, in children and adolescents, many other benign lesions should be considered in the differential diagnosis, amongst which are minor salivary gland tumors, dermoid cysts, vascular lesions, lipomas, benign mesenchymal neoplasm, neurofibroma, and traumatic fibroma [4]. GCTs are usually small, sharp margins can be both single and multiple, nonulcerated, and are never accompanied by lymphadenopathy. They are slow-growing, approximately 0.5-1 mm per year [5]. Typically, they occur in adults between the third and sixth decade, and women are more affected than men with a ratio M:F = 1:2. There seems to be a significant association with the use of alcohol: ethanol would seem to influence the proliferation of Schwann cells and myelin formation in vitro [1].

The histological origin of GCT is controversial, since different derivations have been postulated by various authors. Although Weber had already published a case of TCG in 1854, the literature gives the first reports to Abrikossoff in 1926, who defined this tumor as “myoblastoma,” assuming its origin from muscle cells of embryonic type [6]. This theory was opposed by Klinger in 1928, which presented two cases of myoblastoma insurgents in areas of the body deprived of muscle tissue [7]. In the 1930s, Schirmer and later Klemperer and Meyer confirmed histogenetic relationships between the muscle fibers and granule cells [8-10]. In 1939, Leroux and Delarue supported the hypothesis of histiocytic origin, but did not have any result [11]. At the end of the 1940s, Fust and Custer proposed the neurogenetic theory, attributing to the Schwann cell the origin of cancer. In the 1950s, with Bangle and Stout, the myogenic theory came into vogue, but in the 1960s, this theory has been seriously questioned through the use of electron microscopy, while evidence was in favor of a neural origin, which currently seems to be the most reliable [12-14].

Immunohistochemistry can confirm the diagnosis of GCT.
when PAS positive cells show positivity for S100 and granular CD68. In literature were presented some cases of GCT in adolescent patients and were considered as congenital nGCT; the differential diagnosis between adulthood GCT and congenital nGCT is conducted through the immunohistochemical research of S-100 protein, which is negative in the congenital form. Adverse prognostic factors are the presence of positivity for p53 [1]. An accurate histological analysis must also include the search for other proliferation markers, with particular attention to Ki-67, which is a nuclear antigen expressed during all the phases of the cell cycle except G0 phase, representing an important predictor which is a nuclear antigen expressed during all the phases of the cell cycle except G0 phase, representing an important predictor of malignancy (the expression rate greater than 10% is an index of malignancy) [15]. The 1-3% of GCT can be malignant, based on the presence of at least three of the six histological criteria established by the Armed Forces Institute of Pathology (AFIP) [16]:

1) high mitotic activity (the presence of more than two mitosis in 10 fields at a magnification of 200x);
2) necrosis;
3) high presence of cytoplasmic nuclei;
4) tapered appearance;
5) presence of vesicular nuclei with large nucleoli;
6) pleomorphism.

The presence of one or two criteria classifies the lesion as atypical; presence alone of a pleomorphic nucleus, without any other criterion, classifies the lesion as benign [17,18].

Barbieri et al described a case of GCT of the tongue in a 14-year-old boy, while Angiero et al have described seven cases of GCT of the oral cavity, and observed how the neoplasm has tendency to relapse if not completely removed with laser surgery [19]. Eguia et al analyzed 8 cases of intraoral GCT, noting that if its extirpation was carried out with enough safety margins, the prognosis was positive, due to its slow growth, uncommon aggressiveness, and low tendency to recurrence [5] Platiau reached the same conclusion, observing three cases of GCT of the oral cavity and shared that the treatment must consist of a wide surgical excision, ensuring a prolonged survival [20].

There are cases in literature describing the association between GCT and squamous-cell carcinoma of esophagus, tongue, and larynx, and association with adenocarcinoma of bronchi, stomach, and mammary glands. In all these cases, the pathogenesis seems to be correlated to a process of chronic irritation of the mucosa, which then resulted in carcinoma [21-23].

About the treatment, surgical excisional biopsy of the tumor represents the first choice, both for diagnosis and treatment and, in the majority of cases; it is curative, although removal of the lesion should be wide enough to grant oncological radicality, irrespective of the final histological diagnosis. The risk of recurrence is related to the margins of resection.

CONCLUSION

In conclusion, we suggest that every oral lesion of unknown nature should undergo physical examination or appropriate imaging to reveal the clinical extension of the disease, and then, when feasible, surgically removed. Further clinical management can vary depending on the final histological diagnosis: when GCT is diagnosed, close follow-up should be planned to prevent any relapse.

REFERENCES

20. Platiau R. [Granular cell tumors of the oral cavity: apropos of 3 cases].

