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CASE REPORT

Laryngeal gigant cell tumor

Tumor de células gigantes de laringe

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ABSTRACT

Giant cell tumors (GCT) are usually benign, typically found in the epiphyseal area of long bones, affect individuals in the third decade, and have a slight female predilection. GCT represent about 4% to 9.5% of all bone tumors and 20% of all benign ones. Approximately 2% of all GCT occur in the head and neck region. However, primary laryngeal GCT is an infrequent entity, with 43 cases reported to date. Therefore, the present study aimed to report an issue of laryngeal GCT in a young male patient. Given the uncertainty of clinical and radiological distinction between the wide variety of differential diagnoses, histopathological examination is indispensable for a definitive diagnosis and therapeutic management. The treatment of GCT is controversial. However, currently, the literature supports surgical management. The incidence of GCT is not a common situation in medical practice, and the diversity of differential diagnoses is quite broad, which may lead the physician to suspect other diseases that affect the larynx. GCT is rarely considered among the diagnostic hypotheses, its incidence is sporadic, and management data must be studied.

Keywords: Giant cell tumors; Larynx; Dysphonia.

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RESUMO

Os tumores de células gigantes (TCG) são geralmente de natureza benigna, tipicamente encontrados na área epifisária de ossos longos, acometem indivíduos na terceira década e têm uma leve predileção pelo sexo feminino. TCG representam cerca de 4% a 9,5% de todos os tumores ósseos e 20% de todos os tumores ósseos benignos. Aproximadamente, 2% de todos TCG ocorrem na região da cabeça e pescoço. Entretanto, TCG primário de laringe é uma entidade extremamente rara, com 43 casos relatados até o momento. Portanto, o presente artigo teve por objetivo relatar um caso de TCG de laringe em paciente jovem de sexo masculino. Dada a incerteza de distinção clínica e radiológica entre a ampla variedade de diagnósticos diferenciais, é indispensável exame histopatológico para um diagnóstico definitivo e conduta terapêutica. O tratamento do TCG é controverso, porém, atualmente, a literatura apoia o manejo cirúrgico. A incidência de TCG não é uma situação corriqueira na prática médica, sendo que a diversidade de diagnósticos diferenciais é bastante ampla, podendo induzir o médico a suspeitar de outras doenças que acometem a laringe. A TCG raramente é considerada entre as hipóteses diagnósticas, sua incidência é extremamente rara e dados de manejo devem ser estudados.

Palavras-chave: Tumores de células gigantes; Laringe; Disfonia.

Introduction

Giant cell tumors (GCTs) are generally benign, typically found in the epiphyseal area of long bones. They affect individuals in the third decade of life, and have a slight female predilection[1]. GCT represent about 4% to 9.5% of all bone tumors and 20% of all benign bone tumors. Approximately 2% of all GCT occur in the head and neck region[2]. However, primary GCT of the larynx is an extremely rare entity, with 44 cases reported to date, including the present case.

GCTs have a small incidence in medical practice and the diversity of differential diagnoses is quite wide, which may lead the physician to suspect other diseases that affect the larynx. GCTs are rarely considered among the diagnostic hypotheses, its incidence is extremely rare, and management information should be studied. Therefore, the present study aims to report a case of giant cell tumor of thyroid cartilage submitted to surgical treatment for tumor exeresis.

Case Report

A 37-year-old male patient was referred to our service with diplophonia for three months. He was a mechanic, an ex-smoker with a light smoking load (1.5 year/pack) and had a prior personal history of dyslipidemia. Laryngoscopy revealed bulging of the vestibular region of the right larynx with displacement of the right vocal fold medially, without vocal fold paralysis (Figure 1). Neck computed tomography (CT) showed an expansile lesion measuring 2.9x1.9x2.6 cm located on the right wing of the thyroid cartilage, with no signs of aggressiveness, demonstrating marked thinning of the thin calcified margin of the cartilage, bulging contours with no significant signs of invasion of adjacent soft tissues and retraction of the laryngeal structure, with medial displacement of the vocal fold (Figure 2). Nuclear magnetic resonance (NMR) showed an expansive nodular lesion measuring 3.5x2.2x2.7 cm, located in the right laryngeal region, involving the right wing of the thyroid cartilage, with high T2 signal, low T1 signal, demonstrating restriction in the diffusion sequence and intense enhancement after intravenous contrast (Figure 3). Distinctly the lesion caused a mass effect displacing the laryngeal air column, with no signs of mucosal invasion in either the vestibular or vocal fold region. The histopathological findings obtained by incisional biopsy indicated a giant cell tumor of the larynx. The immunohistochemical study revealed a patchy lesion characterized by proliferation of ovoid cells with minimal atypia permeated by numerous osteoclast-like multinucleated giant cells (Figure 4A), sparse and typical mitosis figures and expression of histone H3.3 G34W (Figure 4B), findings consistent with a diagnosis of primary giant cell bone tumor. Patient underwent protective tracheostomy and exeresis of thyroid cartilage tumor (Figure 5). After decannulation, one week after surgery, the patient presented voice recovery. Histopathological study of thyroid cartilage tumor exeresis specimen confirmed laryngeal giant cell tumor. A control CT scan of the neck 6 months after surgery showed no recurrence of the lesion. At follow-up, 1 year after surgery, the patient remains asymptomatic.

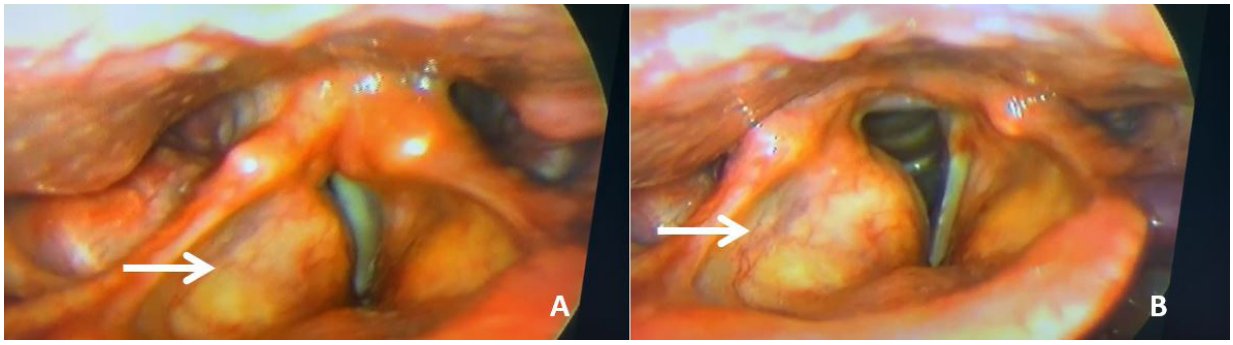


Figure 1. Laryngeal telescopy. **A.** Adducted vocal folds; **B.** Abducted vocal folds.

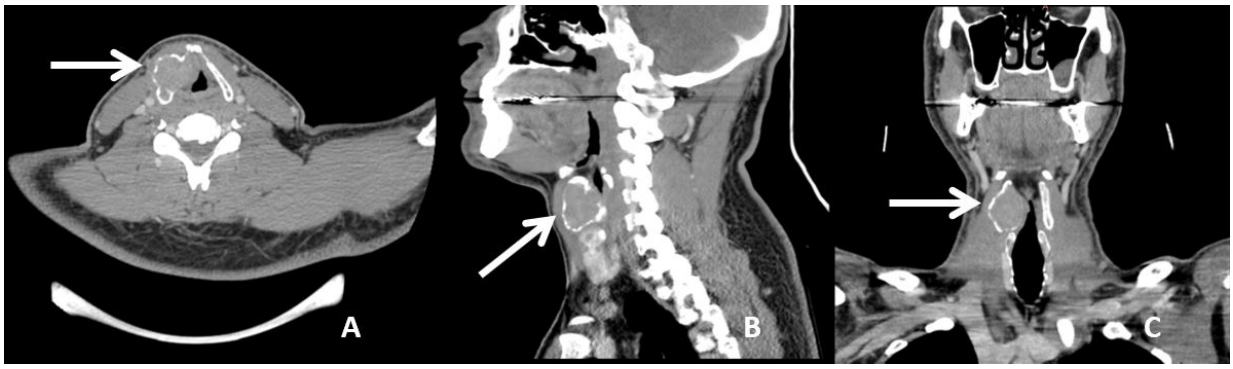


Figure 2. Neck TC. **A.** Axial incidence; **B.** Sagittal incidence; **C.** Coronal incidence.



Figure 3. Neck RNM. **A.** Sagittal incidence - T1; **B.** Sagittal incidence - T2; **C.** Coronal incidence - T1; **D.** Coronal incidence - T2; **E.** Axial incidence - T1; F. Axial incidence - T2.

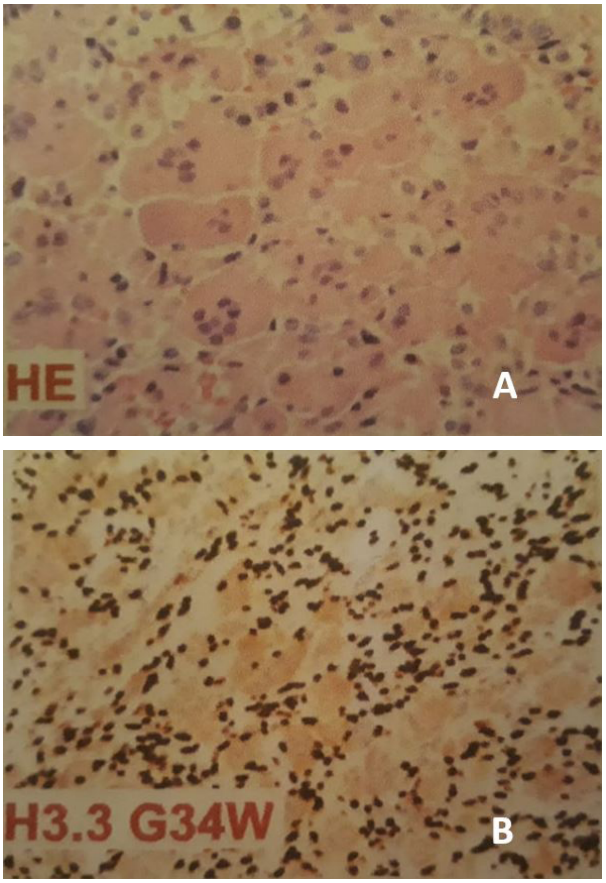


Figure 4. Immunohistochemistry. **A.** Hematoxylin-eosin staining showing osteoclast-like multinucleated giant cells; **B.** Histone H3.3 G34W expression.

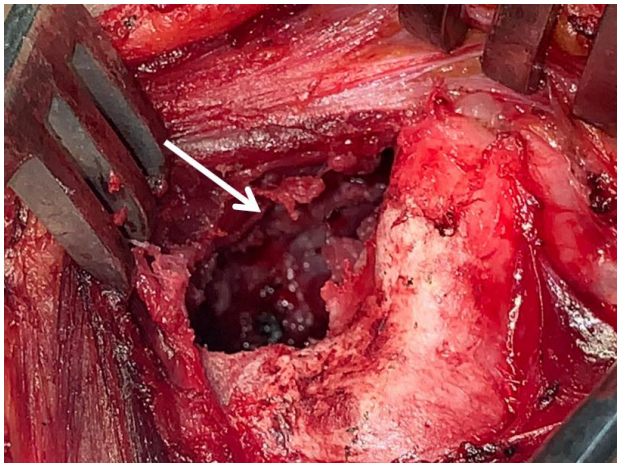


Figure 5. Whitish tumor in thyroid cartilage on the right.

Discussion

GCTs are typically found in the metaphyseal-epiphyseal area of long bones, especially the distal femur, proximal tibia, distal radius, proximal humerus and sacrum[3]. In the head and neck, it accounts for 2% of the cases of GCTs, and is most commonly found in the sphenoid, ethmoid or temporal bone, and very rarely in the hyoid bone and cartilaginous structure of the larynx, the thyroid cartilage being the most frequently involved[1,2]. Primary GCT of the larynx is extremely rare, with 44 reported to date, including the present case report.

GCTs of the larynx usually develops in people between the ages of 23 and 76, with a mean age at presentation of 44.6 years and a higher frequency in males. The clinical presentation depends on the origin and patients usually present with hoarseness, anterior cervical mass, dyspnea and dysphagia[1]. Other less common findings include sore throat and changes in vocal folds mobility[4]. The most commonly affected site is the thyroid cartilage, followed by the cricoid and epiglottis cartilages[1].

These tumors, although characteristically benign in course, can be locally aggressive, recurrent, and occasionally develop into lung metastases[1]. Six to ten percent of GCTs exhibit malignant features that manifest as a high-grade sarcoma occurring at the site of a prior benign GCT or as a sarcoma in juxtaposition to the GCT[4], but only one case has been reported as a laryngeal GCT with osteosarcomatous malignant transformation[5].

Radiologically, it is difficult to differentiate GCT from other neoplasms. The differential diagnosis includes but is not limited to: giant cell reparative granuloma, brown tumor of hyperparathyroidism, osteoblastoma, chondroblastoma, chondrosarcoma, chondroma, aneurysmal bone cysts, non-ossifying fibroma, foreign body reaction, benign fibrous histiocytoma, malignant fibrous histiocytoma, osteosarcoma with abundant giant cells, and spindle cell or sarcomatoid carcinoma with giant cells[1].

Histologically, GCTs show multinucleated giant cells and mononuclear cells in a fibroblast rich, loose, hemorrhagic vascular stroma, and the nuclei of the giant cells are very similar to those of the mononuclear cells. The mononuclear component of the GCT expresses alkaline phosphatase and receptor activator of nuclear factor kappa-B ligand (RANKL), markers of osteoblast lineage, whereas, the multinucleated component expresses tartrate-resistant acid phosphatase and vitronectin receptor, markers of osteoclast lineage[4].

Giant cell reparative granulomas (GCG) can histologically mimic GCT and distinguishing between GCT and GCG can be challenging for the pathologist. GCTs have a more uniform distribution of large giant cells with more than 20 nuclei. In contrast, GCGs have more fibrotic stroma with hemosiderin deposition and more prominent hemorrhage. Head and neck GCGs occur most commonly in the mandible as a central lesion, are more common in women than men, and in individuals under 30 years of age. They have a lower recurrence rate (13-35 vs. 60% of GCTs). Furthermore, only isolated cases of metastasis or sarcomatous transformation have been reported with GCG, as opposed to the 6-10% sarcomatous transformation rate and 2% metastasis rate seen in GCT4. Another important distinguishing factor is the H3F3A (histone 3.3) G34W gene mutation reported in more than 90% of GCTs[6]. Gomes et al. (2014)[7] evaluated nine cases of GCG for this mutation and found that all cases were negative. Such a mutation is found in the immunohistochemical study of the present case.

In the case of a foreign-body giant cell reaction, the distribution of the giant cells would be less regular, their number smaller, and they would aggregate around the foreign material[4].

The brown tumor of hyperparathyroidism may appear grossly and microscopically similar to GCT and GCG. Therefore, it is essential to evaluate the patient to discard hyperparathyroidism[4].

GCTs may have histologic features similar to those of osteosarcoma. However, the radiographic findings (heavy mineralization in an invasive tumor), combined with the histological features of delicate strands of osteoid around pleomorphic cells, atypical mononuclear cells and atypical mitotic figures with necrosis, should confirm a diagnosis of osteosarcoma[1]. Such findings are not reported in the pathological and immunohistochemical study of the present case.

Given the uncertainty of clinical and radiological distinction among the wide variety of differential diagnoses, histopathological examination is indispensable for a definitive diagnosis and therapeutic management.

The treatment of GCT is controversial, but the literature currently supports surgical management. Three surgical modalities have been reported: total laryngectomy (TL), partial laryngectomy (PL) and tumor excision (TE). Factors that will influence the decision between the two techniques include: potential recurrence; postoperative function and quality of life; and if PL is chosen, radiotherapy, chemotherapy or additional salvage surgery may be required.

In addition, given the fact that the mean age at presentation is 44.6 years, the risk of sarcomatous transformation by radiation therapy is a factor to be considered. However, there is still no strong consensus to support this conjecture due to the rarity of the case[1].

However, there is an evolving role for new therapeutics, such as Denosumab, to potentially minimize the morbidity of treatment and should be considered the best first-line treatment option for patients with inoperable or metastatic GCT.

Denosumab is a fully human monoclonal antibody that binds to RANKL and inhibits RANK-RANKL interactions. RANK is expressed on the surface of osteoclast precursors. To differentiate into osteoclasts, their RANK receptors must interact with RANKL that is expressed on osteoblasts. It is theorized that this interaction is prevented by the presence of Denosumab. However, its safety and long-term efficacy for GCT of the larynx are unknown, as only two reported cases have been treated with Denosumab so far[1,4].

Although the results of surgical resection of GCT are better in terms of eliminating recurrence, Denosumab is a viable alternative therapy for bone GCT when function-preserving surgery is not considered possible[4].

Conclusion

Based on the foregoing, the incidence of GCT of the larynx is not a common situation in medical practice, and the diversity of differential diagnoses is quite wide, which may lead the physician to suspect other diseases that affect the larynx and is rarely considered among the diagnostic hypotheses. They are benign tumors with an apparently high cure rate. The main management dilemma centers on the extent of laryngeal surgery, that is, laryngeal preservation. The literature related to functional outcomes and quality of life as factors in the decision about management is scarce, requiring further studies.

Authors' Contributions:

The authors' contributions are structured according to the taxonomy (CRediT) described below:

Michelly Macedo de Oliveira wrote the article under the guidance of Antônio Fernando Salaroli and Sulene Pirana. Daniel Pirana Calzavara was responsible for translating the article.

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