CEO Clinical and Experimental Otorhinolaryngology Vol. 3, No. 1: 52-55, March 2010 DOI 10.3342/ceo.2010.3.1.52

Case Report

Granular Cell Tumor on Larynx

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Granular cell tumors (GCTs) are uncommon neoplasm. They can originate in any part of the body. The most common sites of origin are in the head and neck, while the larynx is a relatively uncommon location. Patients affected with a laryngeal GCT typically present with persistent hoarseness, stridor, hemoptysis, dysphagia, and otalgia but, the tumor may be asymptomatic. Care must be taken to differentiate this lesion from others due to the presence of pseudo-epitheliomatous hyperplasia which overlies the GCT and may occasionally mimic squamous cell carcinoma. Therefore, a confirmative diagnosis should be made histopathologically and should be supported by immunohistochemical staining. These tumors are treated by complete surgical resection. Examining the complete removal of the tumor through securing a negative free margin is considered to be a consequential procedure. We experienced a 64-yr-old man with a laryngeal granular cell tumor involving the right true vocal cord. He was treated by surgical resection under a fine dissection laryngomicroscope. Here we present this case and a review of literature.

Key Words. *Granular cell tumor, Larynx*

INTRODUCTION

A granular cell tumor is one whose histologic origin has not yet been determined. This tumor can develop in any part of the body and 50% of all cases occur in the head and neck area, especially in the tongue (1, 2). Granular cell tumors (GCTs) appearing in the larynx are reported to be as rare as 3% to 10% of all cases (3). More than 98% of these tumors are benign, but 1% to 2% of all cases occur as malignant tumors (4). Therefore, we present herein a case of a granular cell tumor which occurred in the larynx and a review of the literature.

CASE REPORT

A 60-yr-old man presented with a 1-yr history of hoarseness. The patient had been receiving antihypertensive medication for 2 yr. Otherwise, there were no specific past and family histories. At presentation, indirect laryngoscopic examination revealed an irregular marginated protruding mass at the mid portion of the right true vocal cord. On physical examination, there were no specific findings in the head and neck area. Laboratory analysis, cervical computed tomography (CT) and chest radiography demonstrated no abnormalities. Stroboscopic examination showed no mucosal wave during phonation and incomplete closure of the true vocal cord with the normal vocal cord movement due to the mass. For distinguishing a benign from a malignant lesion, he underwent direct laryngeal biopsy and resection.

Direct laryngoscopic examination performed under general anesthesia showed that the 0.5×0.3 cm sized yellowish mass was confined to the epithelial layer at the mid portion of the right true vocal cord (Fig. 1A). Frozen biopsy was not performed due to the small size of the tumor. The anterior and posterior margins of the tumor were identified, and the tumor was then removed using a laser with a 2 mm free margin. The free margin was set at 2 mm considering the resection margin of early stage (T_{1a}) glottis carcinomas are usually 1-2 mm (5). Histopathological examination of the surgical specimen revealed pseudoepitheliomatous hyperplasia with no capsule. Hematoxylin and eosin staining revealed that there were oval-shaped tumor cells with abundant eosinophilic granular cytoplasm but without interstitial tissue. The majority of the nuclei were small and thick and did not show definitive nucleoli or mitotic processes (Fig. 2A).

• Received January 24, 2009
Accepted after revision February 5, 2010

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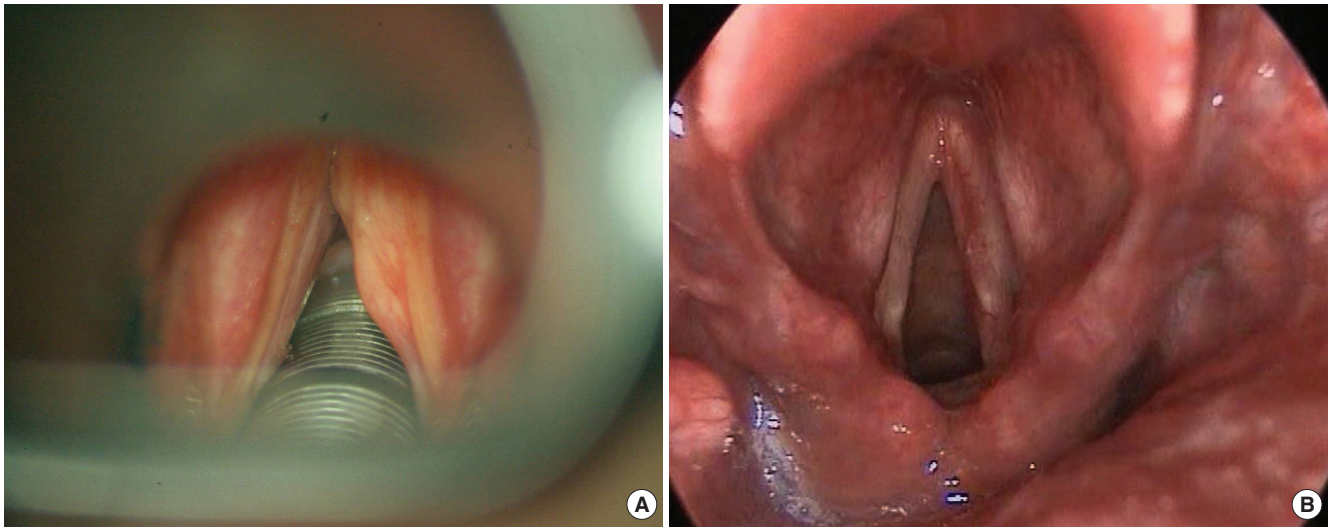

Fig. 1. (A) Preoperative direct laryngoscopic finding. An irregular margined mass occupying the right true vocal cord. (B) A laryngeal stroboscopic finding after the operation. The tumor was completely excised and no evidence of recurrence was found 1 yr after the operation.

The cytoplasm of tumor cells contained periodic acid-Schiff (PAS)-positive materials (Fig. 2B). The tumor cells showed immunoreactivity for S-100 protein (Zymed, San Francisco, CA, USA) (Fig. 2C) and neuron-specific enolase (Biogenex, San Ramon, CA, USA) (Fig. 2D) and no immunoreactivity for smooth muscle actin (Biogenex) (Fig. 2E). Based on the aforementioned results, the patient was diagnosed with a granular cell tumor.

He made a complete recovery of his voice and had no evidence of tumor recurrence after undergoing his 1-yr follow-up laryngeal stroboscopy (Fig. 1B). He has been undergoing regular follow-up at the outpatient clinic and didn't have any post-operative complications or recurrence.

DISCUSSION

In 1926, Abrikossoff first described a granular cell tumor which was named myoblastic myoma based on the differentiation of the skeletal muscle (6). Although much controversy exists concerning the origin of this type of tumor, immunohistochemistry shows positivity for the S-100 protein, neuron-specific enolase and negativity for muscle-related antigens. Additionally, electron microscopy reveals a cluster of squamous cells with a continuous perineurium-like basement membrane, dehydrated axons and angulated bodies around them (7-9), which supports the Schwann's cell theory.

Laryngeal GCTs appear as small, rounded, firm submucous tumors covered with whitish gray or yellow, flat and normal mucosa, and they often resemble vocal fold polyps or granulomas. Their small size (less than 2 cm) and their well-circumscribed, but nonencapsulated feature is typical (10). These tumors mostly involve the posterior third of the true vocal cords, but are also found on the anterior commissure, arytenoids, the false vocal folds, subglottis, and the postcricoid region. In contrast, polyps are usually connected to vocal abuse and are gel-like, smaller structures when compared to GCTs which are more on the fibrotic side. Laryngeal local trauma is connected to the etiology of granuloma, whether it is physical or chemical. They are similar to GCTs macroscopically, but are also smaller and usually located in the posterior larynx. They do not evolve so slowly. GCTs may tend to be solid and homogenously enhancing on CT scans, often mimicking a squamous cell carcinoma (11), but in this case we had no specific findings. The diagnosis was made after histologic examination of biopsied material from direct laryngoscopy. In 50-65% of all cases, there is development of "squamous pseudoepitheliomatous hyperplasia" in the overlying epithelium. An endoscopic biopsy specimen including only the mucosa may result in a misdiagnosis of a well-differentiated squamous cell carcinoma (12). Therefore, a biopsy specimen should include sufficient normal tissue adjacent to a tumor. The cytoplasm of a granular cell tumor contains ill-defined, spindle-shaped or polygonal, vacuolated nuclei and eosinophilic granules (13). These granules are strongly positive for the PAS reaction and immunohistochemistry reveals strong positivities for S-100 protein and neuron-specific enolase (7-9). These tumors also stain for vimentin, myelin-associated glycoprotein (Leu-7) and CD 68 (KP-1).

The malignant type of granular cell tumor is uncommon and accounts for only 1% to 2% of all cases (4). Although criteria for malignant GCTs have not yet been determined, this malignant tumor is suspected in cases which have nuclear pleomorphism, frequent mitoses, and an increase in the nucleus/cytoplasm ratio, spindle-shaped cellularity, necrosis and vacuolated nucleus with large nucleoli. It is also clinically suspected in cases where the

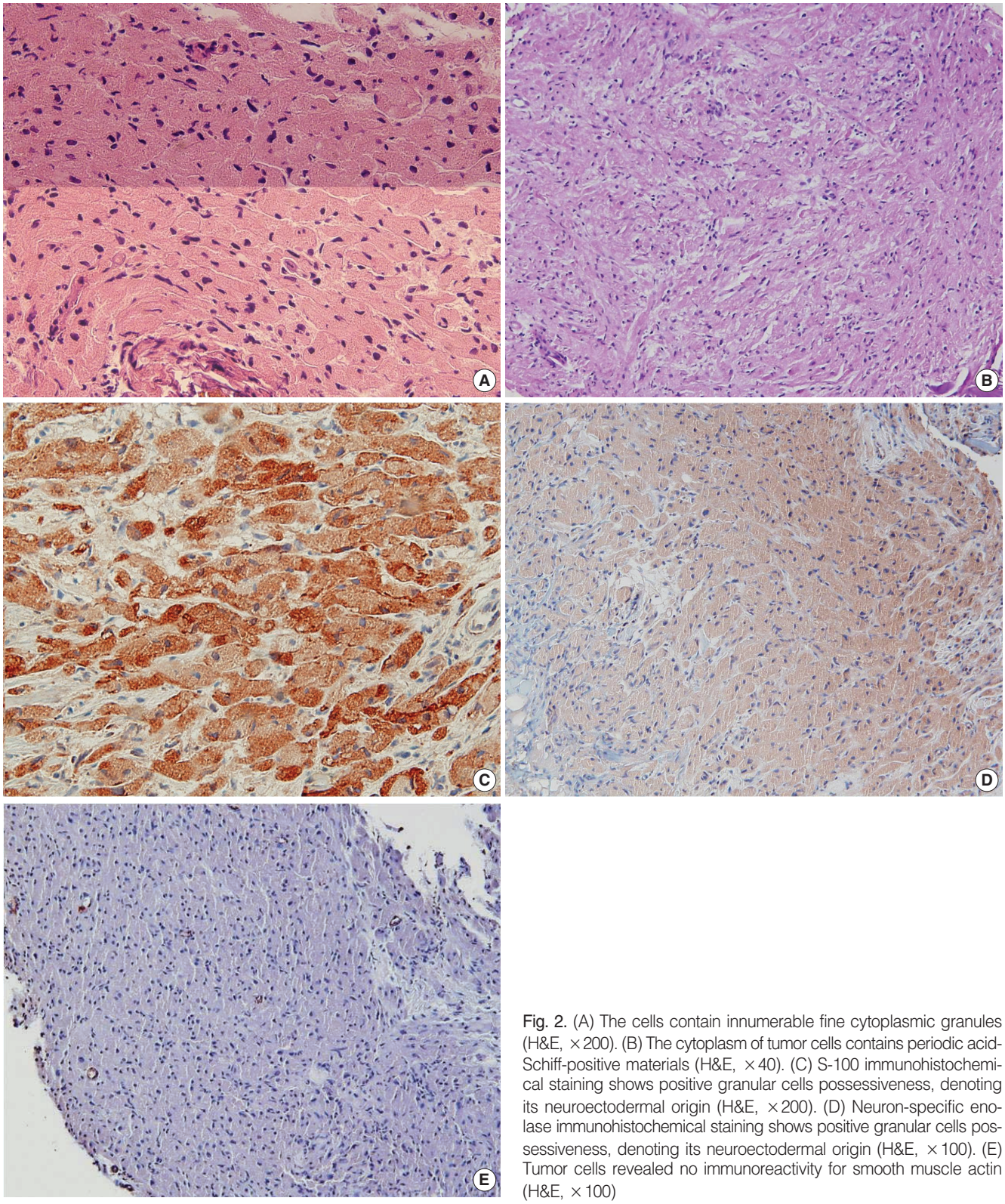

Fig. 2. (A) The cells contain innumerable fine cytoplasmic granules (H&E, ×200). (B) The cytoplasm of tumor cells contains periodic acid-Schiff-positive materials (H&E, ×40). (C) S-100 immunohistochemical staining shows positive granular cells possessiveness, denoting its neuroectodermal origin (H&E, ×200). (D) Neuron-specific enolase immunohistochemical staining shows positive granular cells possessiveness, denoting its neuroectodermal origin (H&E, ×100). (E) Tumor cells revealed no immunoreactivity for smooth muscle actin (H&E, ×100)

tumor size is ≥4 cm and where the tumor grows rapidly and shows recurrence or infiltration into the adjacent tissue.

Once the diagnosis of a benign granular cell tumor is confirmed, complete surgical resection becomes the appropriate treatment. During removal, securing a negative free margin is a strongly demanded goal. In our case, frozen biopsy was not done due

to the small size of the tumor but through a permanent biopsy the absence of malignancy was determined. A frozen section is recommended to confirm properly performed surgical resections without leaving any tumorous remains (14). Radiation therapy or chemotherapy is not recommended because it may be less responsive or induce malignant transformation (13). Even though surgical resection is performed properly, there is an 8-21% recurrence rate, usually at the primary site. Some of these recurrences may be due to a failure in to diagnose multiple lesions. Moreover, in cases of inadequate removal with the remnant of the tumor at the resection margins, it may recur (15).

Although it is rare for GCTs to occur in the larynx, accurate diagnosis and appropriate treatment follow-up are mandatory. Regular long term follow-ups are required using fiber-optic laryngoscopy to confirm its recurrence. In our case, follow-up was done at 1 an year after surgery, considering that GCTs grow slowly and evolve on average between 6 and 7 months before patients perceive a sensible discomfort and seek medical advice (16).

The above case demonstrates that although GCTs of the larynx are rare and typically benign tumors, clinicians must be aware of the need to make an accurate diagnosis and to provide appropriate treatment. Undergoing surgical resection including having a negative free margin is highly recommended to rule out GCTs in the larynx. When the tumor size is relatively small for complete surgical resection, it should be performed with regular follow-up to provide proper care and to result in a complete recovery, even with occasional treatments. In consideration of the satisfactory result acquired through the whole procedure above, we report on this case for clinicians who regularly see GCTs.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Berkowitz SF, Hirsh BC, Vonderheid E. Granular cell tumor: a great masquerader. Cutis. 1985 Apr;35(4):355-6.
2. Strong EW, McDivitt RW, Brasfield RD. Granular cell myoblastoma. Cancer. 1970 Feb;25(2):415-22.
3. Lazar RH, Younis RT, Kluka EA, Joyner RE, Storgion S. Granular cell tumor of the larynx: report of two pediatric cases. Ear Nose Throat J. 1992 Sep;71(9):440-3.
4. Enzinger FM, Weiss SW. Granular cell tumor. In: Enzinger FM, Weiss SW, editors. Soft tissue tumors. 3rd ed. St. Louis: Mosby; 1995, p.864-75.
5. Brøndbo K, Fridrich K, Boysen M. Laser surgery of T1a glottic carcinomas; significance of resection margins. Eur Arch Otorhinolaryngol. 2007 Jun;264(6):627-30.
6. Abrikossoff A. Myoma, starting with the discretionary skeletal muscles. Virchows Arch Pathol Anat Physiol Klin Med 1926;260(1):215-33.
7. Fisher ER, Wechser H. Granular cell myoblastoma-a misnomer. Electron microscopic and histochemical evidence concerning its Schwann cell derivation and nature (granular cell schwannoma). Cancer. 1962 Sep-Oct;15:936-54.
8. Kurtin PJ, Bonin DM. Immunohistochemical demonstration of the lysosome-associated glycoprotein CD68 (KP-1) in granular cell tumors and schwannomas. Hum Pathol. 1994 Nov;25(11):1172-8.
9. Mazur MT, Shultz JJ, Myers JL. Granular cell tumor. Immunohistochemical analysis of 21 benign tumors and one malignant tumor. Arch Pathol Lab Med. 1990 Jul;114(7):692-6.
10. Sataloff RT, Ressue JC, Portell M, Harris RM, Ossoff R, Merati AL, et al. Granular cell tumors of the larynx. J Voice. 2000 Mar;14(1):119-34.
11. Mukherji SK, Castillo M, Rao V, Weissler M. Granular cell tumors of the subglottic region of the larynx: CT and MR findings. AJR Am J Roentgenol. 1995 Jun;164(6):1492-4.
12. Alessi DM, Zimmerman MC. Granular cell tumors of the head and neck. Laryngoscope. 1988 Aug;98(8 Pt 1):810-4.
13. Yoo YS. A case of granular cell tumor in the larynx. Korean J Otorhinolaryngol-Head Neck Surg. 1994 Apr;37(4):833-7.
14. Pernas FG, Younis RT, Lehman DA, Robinson PG. Management of pediatric airway granular cell tumor: role of laryngotracheal reconstruction. Int J Pediatr Otorhinolaryngol. 2006 Jun;70(6):957-63.
15. Fanburg-Smith JC, Meis-Kindblom JM, Fante R, Kindblom LG. Malignant granular cell tumor of soft tissue: diagnostic criteria and clinicopathologic correlation. Am J Surg Pathol. 1998 Jul;22(7):779-94.
16. Garín L, Barona R, Basterra J, Armengot M, Alemany P, Martorell MA. Granular cell tumor (Abrikossoff's tumor): a review and our experience. An Otorrinolaringol Ibero Am. 1992;19(3):249-64.