Granular Cell Tumor of the Larynx: Report of Two Pediatric Cases

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Introduction

Granular cell tumor is an uncommon neoplasm of the head and neck region. The tumors occur more often in blacks than other racial groups, and females are affected twice as often as males, although laryngeal involvement demonstrates a male predilection.[1]

The cause is unknown, but inflammatory, degenerative, regenerative, and congenital abnormalities have all been suggested. Different cells have been proposed for the origin of the tumor, including striated muscle, histocytes, fibroblasts, and neural elements.

In 1926, granular cell tumors were first described by Abrikosoff, who called them granular cell myoblastomas.[2] He first believed that the tumors arose from degenerated striated muscle fibers after injury, but 5 years later, he speculated that they were true neoplasms of embryologic myoblasts. Challenging this theory, other investigators reported that approximately 50% of the tumors occurred in sites that did not contain striated muscle, such as the gallbladder, breast, and hypophysis.

In 1972, it was demonstrated that granular tumor cells resembled Schwann cells associated with regenerating nerves, and studies by Sobel and associates[3] offered evidence that granular cell myoblastoma was a tumor-like lesion of Schwann cell origin. Sobel's group thought that the tumors were the result of a reactive cellular response or, more likely, were true neoplasms. In another investigation, they hypothesized that undifferentiated fibroblast-like mesenchymal cells were precursors of granular cell tumors.[4]

Some investigators have favored a non-neoplastic theory, indicating instead inflammatory, degenerative, regenerative, and congenital causes for these tumors. Azorpardi believed the lesion represented a storage disease rather than a neoplasm.[5] Recent immunochemical studies show the tumor to be positive for S-100 protein, implicating muscle or nerve sheath as the origin.[6] However, the neurogenic theory remains the most popular explanation for these rare tumors.

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Case Reports

Case #1

A 10-year-old black male presented himself to us with stridor and increasing difficulty in breathing. Beginning in January of 1989, he was treated for asthma, but with no improvement. He was referred to an otolaryngologist. Direct laryngoscope and bronchoscopy revealed severe subglottic narrowing. In May, a tracheotomy was performed to relieve upper airway obstruction, and subsequently, two laser surgeries were performed to widen his airway. Because there was no apparent postoperative change in the patient's condition, he was referred to us for further management.

On July 25, direct laryngoscopy and bronchoscopy revealed a huge posterior subglottic mass, for which a biopsy was performed. The biopsy results were consistent with granular cell tumor. The patient was scheduled for surgical excision on July 28.

The tumor was exposed by a vertical neck incision and a laryngofissure. The tumor was widely excised, and clear margins were obtained, as evidenced by examination of frozen sections. The raw area over the cartilage was allowed to granulate, and a Montgomery T-tube was inserted.

After 6 weeks, repeat direct laryngoscopy showed persistent subglottic edema. At that time, the Montgomery T-tube was removed and replaced with a routine tracheotomy tube. Six weeks later, repeat direct laryngoscopy was performed. The airway was patent, and there was no evidence of disease. The tracheotomy tube was removed. Since that time, there has been no recurrence of the symptoms or the disease.

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Case #2

A 6-year-old black female went to another hospital with respiratory difficulty and wheezing on June 8, 1991. The patient was diagnosed as having asthma since early childhood. The girl was treated appropriately for asthma, but because there was no improvement, she was intubated and then transferred to Le Bonheur Children's Medical Center for further management.

The patient remained intubated in the medical center's intensive care unit for 8 hours and was then extubated. On June 10, 1991, the patient was transferred to regular care on another floor, but by June 12, she demonstrated increasing respiratory difficulty and stridor that required intensive care management.

Upper airway obstruction was suspected, and radiographic studies were performed. A chest radiograph was unrevealing. A soft-tissue neck series (Fig. 1) revealed a subglottic prevertebral mass with subglottic narrowing. Airway fluoroscopy confirmed this finding, but an esophagogram was unrevealing. Subsequently, a computed tomography scan of the neck showed a subglottic mass narrowing the airway (Fig. 2).

After a pediatric otolaryngology consultation on June 18, 1991, the patient underwent direct laryngoscopy and bronchoscopy, and a biopsy specimen was taken from the subglottic mass. Results of examination of frozen sections was consistent with granular cell tumor.

The mass was excised through a laryngofissure approach, and a Montgomery T-tube was inserted. The patient was discharged to her home on June 28. On August 20, she had another direct laryngoscopy and bronchoscopy with removal of the Montgomery T-tube. A regular tracheostomy tube was inserted, and decannulation was postponed because some granulation tissue was found at the tracheostomy site. On October 29, 1991, the patient underwent another direct laryngoscopy and bronchoscopy with decannulation. She has been doing well since then with no signs of recurrent disease.

FIGURE 1 Lateral view of the soft tissues of the neck (case #2) shows a subglottic, prevertebral mass with subglottic narrowing

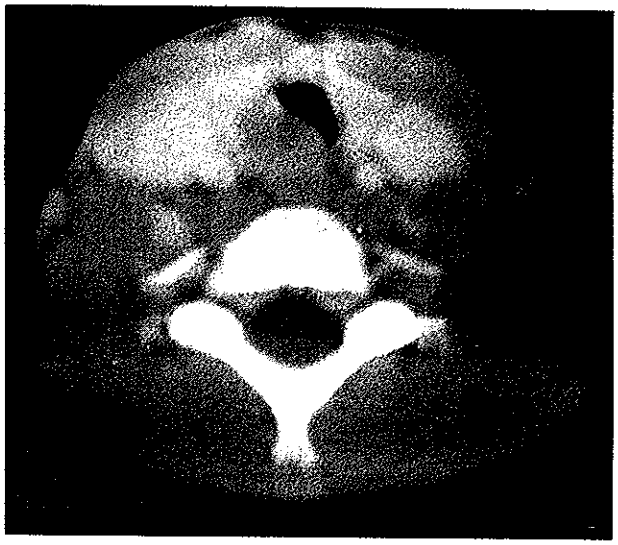

FIGURE 2 Computed tomography scan of the neck (case #2) shows a subglottic mass with subglottic narrowing.

Comment

Half of all granular cell tumors occur in the head and neck region, with 33% of these occurring in the tongue. Less common sites include the maxilla, lips, buccal mucosa, soft palate, trachea, and bronchi. Granular cell tumors have also been reported in skin, subcutaneous tissue, breast, and mucosa of the rectum, anus, and esophagus.

Laryngeal involvement accounts for 7% to 10% of the reported cases.[7] These tumors occur most often in the third through the sixth decades of life.[8] Pediatric laryngeal granular cell tumors are rare, with only 8 other cases reported to date.[9-14] The posterior vocal cords and arytenoid area are the most commonly affected sites in the larynx, but in the pediatric population, 3 patients had tumors in the anterior subglottis, and 2 patients had extensive glottic involvement.[15] The two patients discussed here are the only cases of posterior subglottic involvement that have been reported.

The first symptoms are usually hoarseness, stridor, hemoptysis, dysphagia, and otalgia, but the tumor may be asymptomatic and be discovered incidentally.

Macroscopically, granular cell tumors are usually smooth, sessile or polypoidal, and covered with mucosa. The tumor is firm to the touch, and the mucosa is usually intact.

The cells have a histologically distinctive appearance. They are polymorphic and have abundant pale-staining acidophilic and granular cytoplasm. The nuclei are small, vesicular, or densely chromatic. Mitoses are rare, and the tumor cells are embedded in variable amounts of connective or reticular tissue (Fig. 3).

The tumor is usually not encapsulated, but it is well-circumscribed. Tumor cells may interdigitate with adjacent fibrous stroma, and there can be poor delineation at the periphery of the lesions, giving the impression of invasiveness.

The cytoplasmic granules are periodic acid-Schiff (PAS) positive and react positively with Sudan black. Using electron microscopy, Mittal[16] concluded that the granules were formed by infoldings of the cell membrane by a process similar to the myelin formation around axons. These infoldings are subsequently phagocytosed by lysosomes, yielding the typical granules of the granular cell tumor.

Another phenomenon almost exclusive to these tumors is a covering of pseudoepitheliomatous hyperplasia, which occurs in 50% to 60% of laryngeal granular cell tumors.[4] The squamous cells demonstrate hyperplastic and reactive changes (Fig. 4). The nuclei should not show hyperchromatism, pleomorphism, or other evidence of malignancy. A superficial biopsy of the specimen may lead to an erroneous diagnosis of invasive squamous cell carcinoma if the underlying granular cell tumor has not been recognized. Pseudoepitheliomatous hyperplasia has not been reported in the cases of pediatric laryngeal granular cell tumors, including ours.

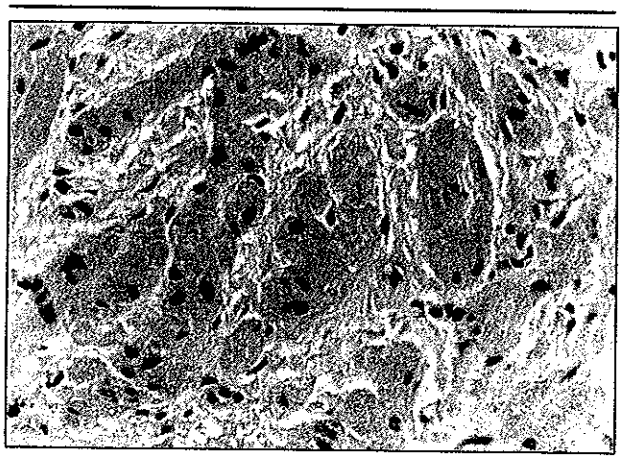

FIGURE 3 High-power view of granular cell tumor of the larynx shows the typical morphology of granular cells embedded in stroma.

The diagnosis is usually made from histologic examination of the tumor specimen. Fine-needle aspiration, frozen sections, electron microscopy, and histochemistry have also been used for evaluation.[17] All cases of laryngeal granular cell tumors have been histologically benign, although granular cell tumors have an overall 3% incidence of malignancy. The tumors are multicentric in 10% of patients, and the incidence is higher if the site is the respiratory tract.[1] Therefore, wisdom dictates bronchoscopy if there is laryngeal involvement.

Case 1 originally had wheezing and stridor. The symptoms initially were mistaken for asthma. Moreover, the subglottic mass was mistaken for a subglottic stenosis on the initial laryngoscopic examination. Subsequently, the patient received a tracheotomy and two laser procedures to widen his subglottic space. Because no improvement occurred, another direct laryngoscopy and biopsy were required to render the correct diagnosis.

Case 2 was also initially mistaken thought to have asthma. After there was no improvement despite maximal treatment and hospitalization, the upper airway obstruction was suspected. Radiographic studies suggested a subglottic mass, but they were not diagnostic. The definitive diagnosis of the nature and location of the obstructive tumor was made only after direct laryngoscopy and bronchoscopy and evaluation of the biopsy specimen. Surgical excision was curative.

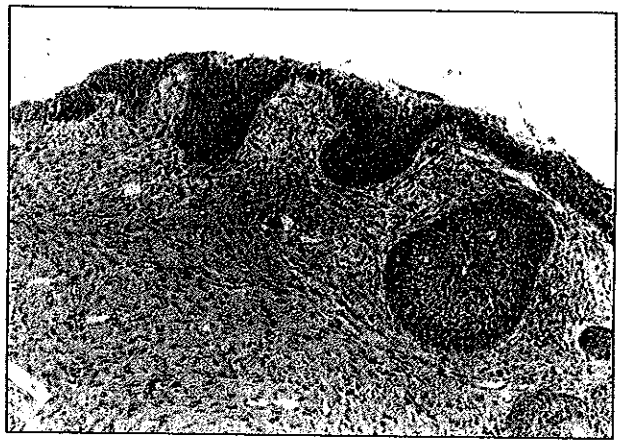

FIGURE 4 Low-power view of granular cell tumor of the larynx shows the squamous epithelium and subepithelial granular cells.

Because recurrence is unlikely, treatment of laryngeal granular cell tumors is accomplished by endoscopic excision, using a cold knife or laser. Larger lesions may require laryngofissure, as in our two cases, or laryngectomy.[10,11] An attempt should always be made to achieve microscopic clearance of the margins, but the recurrence rate for granular cell tumor is low even if the original resection was incomplete.[3,12,18]

Because granular cell tumors of the larynx are rare in children, the abnormality may be mistaken for other causes

of upper airway obstruction. However, the physician should include the possibility of granular cell tumor in the differential diagnosis whenever a laryngeal mass is detected by direct laryngoscopy. The ultimate diagnosis must be made by biopsy of the lesion.

Summary

Granular cell tumors are uncommon neoplasms of the head and neck that usually involve the tongue. The larynx is an atypical site of involvement in adults and a rare site in children. We report two cases of subglottic granular cell tumors, one in a 10-year-old boy and the other in a 6-year-old girl. Although both were initially misdiagnosed as having asthma, radiologic, laryngoscopic, and histologic evaluation of the obstructions eventually furnished the correct diagnosis. The patients were successfully treated by surgical excision of their subglottic masses. The history, presentation, pathologic findings, management, and prognosis of this rare pediatric laryngeal tumor are explored.

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