Synaptophysin Positive Glomus Tumor of Trachea Simulating Typical Carcinoid: A Potential trap

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Abstract

Glomus tumors (GTs) are uncommon benign tumors, accounting for <2% of all soft tissue tumors and usually occur within the dermis or subcutis of distal extremities. Primary tracheal GT is rare, and to date less than 40 tracheal GTs have been reported. Tracheal GT usually present as a polypoidal mass. They express smooth muscle markers, and are negative for cytokeratin (CK) and neuroendocrine markers on immunohistochemistry (IHC). We here report a case of tracheal GT showing diffuse strong aberrant immunoexpression for synaptophysin, initially construed as carcinoid. Focal synaptophysin expression has been described in few gastric GTs, and a nasal GT. Diligent histomorphological examination and careful selection of IHC panel helps in clinching the diagnosis. Complete resection is the standard treatment of modality.

Keywords Glomus tumor · Synaptophysin · Trachea

Introduction

Glomus tumors (GTs) are uncommon benign tumors, that account for < 2% of all soft tissue tumors. They usually occur within the dermis or subcutis of distal extremities. Primary tracheal GTs are rare, and to date less than 40 cases of tracheal GT have been reported. They usually present as a polypoidal submucosal mass, clinically simulating a carcinoid tumor, which is a malignant entity with metastatic potential.

Histomorphologically, GTs show nests of uniform round cells around branching vascular channels, similar to a carcinoid [1, 2]; however, carcinoid can be distinguished by diffuse immunoexpression of CK and neuroendocrine markers

(synaptophysin and chromogranin). Thus, an aberrant synaptophysin expression in GT can prompt an erroneous diagnosis of carcinoid. Synaptophysin expression has never been reported in tracheal GT, and has been seen focally in few gastric GTs [3–5]. We here present a case of tracheal GT with diffuse and strong synaptophysin expression.

Case Report

A 44-year-old male with no significant past or family history presented with complaints of recurrent cough with hemoptysis and hematemesis for one month, for which he was hospitalized and one unit of blood transfused. Fibreoptic bronchoscopy revealed a polypoidal lesion in the trachea (Fig. 1), while upper gastro-intestinal endoscopy was normal.

On further evaluation computed tomographic (CT) scan of thoracic region also showed a large intraluminal enhancing polypoidal lesion in trachea measuring 14 × 10 mm at T3-vertebral level, causing partial luminal compromise (Fig. 2). CT thorax also showed subtle ground glass haziness involving medial segment of right middle lobe and the basi-segment of left lower lobe. CT angiogram of abdomen showed no significant abnormality.

Per-operatively a sessile polyp with base in membranous trachea was seen, around 5 cm from vocal cord (4th

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Fig. 1 Bronchoscopy image showing polypoid tracheal lesion causing luminal compromise; inset shows the gross specimen of tracheal ring with luminal polypoid growth.

to 5th ring of trachea). In view of bleeding on touch, a wide local excision of the polyp was done along with 4th tracheal ring. The gross specimen received comprised of tracheal ring measuring 2 cm in diameter, with a polypoid growth

protruding in the lumen with surface hemorrhage, measuring $17 \times 10 \times 10$ mm (inset Fig. 1).

Microscopic examination depicted polyp with partially ulcerated stratified squamous mucosa devoid of any dysplasia, with an underlying tumor lying over the submucosal tracheo-bronchial glands, splaying the trachealis muscle with no destructive invasion. The tumor cells were arranged in lobular and alveolar pattern separated by fine fibro-vascular septa, with a striking perivascular pattern. The tumor cells were monomorphic round with fine chromatin, inconspicuous nucleoli, and moderate amount of eosinophilic cytoplasm. Mitotic activity was $\sim 1\text{--}2/10\text{hpf}$, and there was no necrosis (Fig. 3).

The histomorphological differential diagnosis included a typical carcinoid, paraganglioma and glomus tumor. Immunohistochemistry (IHC) was performed for confirmation, which revealed a surprising cytokeratin (CK) negativity with diffuse and strong synaptophysin positivity. On further IHC, tumor cells were also diffusely positive for smooth muscle actin (SMA), smooth muscle myosin heavy chain (SMMH), and focally for desmin, while were negative for chromogranin and epithelial membrane antigen (EMA) (Fig. 4). CK and chromogranin negativity ruled out the possibility of carcinoid and paraganglioma, while positive SMA and SMMH immunoexpression provided a tangible evidence to suggest a final diagnosis of GT of trachea.

Post-operative period was uneventful with speedy recovery, and patient is free of any symptoms after a post-operative follow-up of 12 months.

Fig. 2 Axial and Sagittal computed tomographic (CT) scan images reveal polypoid lesion (white arrow) in trachea at T3 vertebral level, with luminal compromise

Fig. 3 Photomicrograph images showing a lobulated tumor in the membranous wall of trachea (a), nests of tumor cells seen lying under the metaplastic squamous mucosal (b), perivascular arrangement of

tumor cells around dilated vessels (c), and monomorphic tumor cells exhibiting round nuclei with fine chromatin, inconspicuous nucleoli, and moderate eosinophilic cytoplasm (d)

Discussion

Glomus tumors account for < 2% of all soft tissue tumors, typically seen within the dermis or subcutis of distal extremities, particularly the subungual space, hand, wrist and foot [1–3]. They very rarely occur in deep soft tissue and visceral organs, where glomus bodies are absent, and unlike cutaneous GT they are painless [3, 6]. Most of the visceral GT occur in the gastro-intestinal tract, especially the stomach [6]. Rare cases have also been reported in penis, bladder, mediastinum, nerve, bone and lung. Multiple lesions may be seen in 10% cases, and most are seen in young adults, but may occur at any age [2].

GT are benign tumors originating from modified perivascular smooth muscle cells (glomus cells) around arteriovenous anastomosis, which are responsible for thermoregulation [1–3].

Primary GTs of thoracic region are rare, and the glomus bodies are thought to be absent in thorax. Intrathoracic extracutaneous GTs have been reported in trachea, esophagus and lung [1]. Tracheal GTs arise in submucosa

of trachea, and are usually polypoidal, clinically and radiologically resembling a carcinoid [3, 4].

To date, less than 40 tracheal GTs have been reported, first being described by Hussarek and Reider in 1950 [7]. Venegas et al reviewed the literature of these 40 cases, and observed that in all cases tumor arose from the membranous wall of trachea, which shows increased density of mucous glands and vessels. The mean age was 51 years (range 10–83 years), with 60% occurring in males, and a mean size of 2.0 cm (range 1.2–3.0 cm). Of these 24%, 22% and 54% were in proximal, middle and distal trachea, respectively. Most of these underwent open resection (67.5% cases) while others had endoscopic resection, and of all 40 cases only 2 cases (5%) displayed malignant histology [1].

As seen in our case, GTs show characteristic nests of small, uniform, round cells surrounded by basal lamina around branching vascular channels, with variable hyaline and myxoid change, and 75% are solid tumors [1, 2]. Occasional cases show oncocytic or epithelioid change [2]. Morphologic differentials of GT include carcinoid, vascular tumors (hemangiopericytoma & hemangioendothelioma), and paraganglioma [3, 4].

Fig. 4 Immunohistochemistry showing cytokeratin (CK) negative tumor with adjacent positive glands and mucosa (a), and diffuse strong positive expression for synaptophysin (b), smooth muscle actin (SMA) (c), and smooth muscle myosin heavy chain (SMMH) (d)

Immunophenotypically, they express vimentin, SMA, desmin (variably), caldesmon, calponin and CD34, and are negative for CK, neuroendocrine markers, CD31, S-100 and C-Kit [1]. The presented case showed strong synaptophysin expression. This almost led to the erroneous diagnosis of carcinoid, which is a low grade neuroendocrine tumor with metastatic potential. Lack of CD31 excluded the vascular tumors, and chromogranin negativity ruled out possibility of paraganglioma.

Synaptophysin expression has not been seen in GTs of extremities [6], and none of the reported tracheal GT have shown synaptophysin expression till date. However, few gastric GTs have shown focal synaptophysin expression [4]. In a study, approximately 10% of gastric GTs showed focal to diffuse synaptophysin expression [5]. A single case of sinonasal tract GT among 40 reported, has also shown strong and diffuse synaptophysin expression, without any neuroendocrine differentiation [6].

Multiple familial GT, with autosomal dominant inheritance, are associated with inactivating mutations in glomulin gene (GLMN) and neurofibromatosis type I (NFI). [2]. Given the potential for occult malignancy and the symptomatic presentation of lesions, resection is the standard

of care. Endoscopic resection is a more common modality than open resection; however, survival is similar in both the approaches [1].

Conclusion

To conclude, GT of trachea are rare benign tumor which simulate carcinoid on clinical, radiological and histomorphological examination. A judicious IHC panel helps to resolve the differentials. Complete resection is the standard treatment modality with complete cure from symptoms, and negligible risk of recurrence.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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