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CASE SERIES

Granular cell tumour in tracheobronchial tree: Two case presentations with different outcomes

Dragana TEGELITJA[1-4], Golub SAMARDŽIJA[1,5], Bosiljka KRAJNOVIĆ[1,4], Milorad BIJELOVIĆ[2,4], Siniša MAKSIMOVIĆ [4,6], Dejan MILJKOVIĆ[4,7], Milan POPOVIĆ[7,8]*

[1]University of Novi Sad, Faculty of Medicine, Department of Pathology, Novi Sad, Serbia; [2] University of East Sarajevo Faculty of Medicine Foča, Foča, Republika Srpska, Bosnia and Herzegovina; [3]University of Banja Luka, Faculty of Medicine, Banja Luka, Republic of Srpska, Bosnia and Herzegovina; [4]Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica, Serbia; [5]Institute of Cardiovascular Diseases of Vojvodina, Sremska Kamenica, Serbia; [6]University of Novi Sad, Faculty of Medicine, Department of Surgery, Novi Sad, Serbia; [7]University of Novi Sad, Faculty of Medicine, Department of Histology and Embryology, Novi Sad, Serbia; [8]Oncology Institute of Vojvodina, Sremska Kamenica, Serbia.

Abstract

The lung's granular cell tumour (GCT) is a rare neoplasm originating from Schwann cells. GCT often grows in various sites and can be benign or malignant. Only 2-6% of GCTs occur in a tracheobronchial tree. We aim to present two cases of tracheobronchial GCT. A 68-year-old man had multiple endobronchial GCTs, while a 54-year-old woman had one endotracheal nodule of GCT. GCTs consist of submucosal infiltrates, round to oval cells, with abundant granular cytoplasm positive for S100 (2/2), NSE (2/2), and CD68 (2/2). One of the patients had a GCT on the right, treated by bronchoscopic extirpation and associated with acinic adenocarcinoma on the opposite side, which was diagnosed after the lobectomy on the right. Other patients had a tracheal GCT with fatal outcomes on the tenth day after the surgery due to the development of acute pulmonary oedema, which was confirmed at autopsy. Tracheobronchial GCT has a broad spectrum of clinicopathological symptoms and signs with different outcomes.

Keywords: granular cell tumour, trachea, bronchi, outcome.

INTRODUCTION

Granular cell tumours (GCTs) were initially thought to be of myogenic origin; however, based on the electron microscopic and immunohistochemical evidence, a neural origin has been proposed from Schwann cells.[1] GCT was first described in 1926. These tumours are reported in various sites, most frequently involving the tongue, and can be benign or malignant. Only 2-6% of GCTs occur in the tracheobronchial tree, presenting a broad spectrum of clinicopathological symptoms and signs.[2,3] When found in the lower respiratory tract, GCTs are called pulmonary GCTs (pGCTs).[4] The chest x-ray may show signs of pneumonia, mucoid impaction, atelectasis, and endobronchial tumour.[5] However, the definite diagnosis of GCTs is established by pathology or cytology.[5,6] Lung GCTs can be treated by bronchoscopic excision, laser therapy, or surgical resection, depending on the tumour size.[7,8]

We aim to present clinicopathological characteristics of two cases of GCT in the tracheobronchial tree with different outcomes.

CASE 1

A 68-year-old man, a former smoker who had hypertension, diabetes mellitus, and chronic obstructive disease, was admitted to our hospital complaining of progressive dyspnea, fever, and productive cough for the previous six days. The physical exam was unremarkable. The chest's computed tomography (CT) showed a cavitary mass within the left upper lobe measuring 19 × 16 mm. A bronchoscopy showed multiple

**Address for correspondence:* Milan POPOVIĆ. University of Novi Sad, Faculty of Medicine, Department of Histology and Embryology Hajduk Veljkova 3, 2100 Novi Sad, Serbia. Tel: +381216622890 (MP); E-mail: *milan.popovic@mf.uns.ac.rs* (MP)

polypoid yellow tumours, a few millimetres in diameter, on the right upper lobe bronchus. These tumours were treated by endoscopic resection. Histopathological examination showed a submucosal tumour composed of large polygonal cells with eosinophilic granular cytoplasm, which had prominent nucleoli, a low N/C ratio, and no necrosis. Tumour cells were separated by delicate fibrovascular stroma (Fig. 1a), and immunohistochemical staining demonstrated positivity for S100, neuron-specific enolase (NSE), and CD68. This confirmed the diagnosis of a granular cell tumour. After consultation with the thoracic surgery team, the patient also underwent an upper left lobectomy. The operation was successful, with no complications. A tumour described on CT was found in the upper lobe and pathohistologically confirmed as acinic adenocarcinoma (pT1cN0MX; IA3). Post-operatively, the patient was monitored by daily physical examinations and chest X-rays. The follow-up exams showed no recurrence or metastasis in the last seven months.

CASE 2

A 54-year-old woman, a smoker, had hypertension and intramural uterine leiomyoma treated with a hysterectomy nine years ago. The patient suffered from a chronic cough and stridor for the previous two months. The pulmonary function test indicated upper airway obstruction. The tracheal tumour measuring 30 × 14 × 29 mm was seen on the chest CT (Fig. 1b). A bronchoscopy was performed, and a polypoid and whitish Narrow-Band Imaging (NBI)-negative coloured tumour obstructing 10% was seen in the distal third of the trachea. Histologically, the tumour was built from clusters of oval cells with eosinophilic, finely granular cytoplasm and small nuclei, with no pleomorphism and no mitosis, separated by delicate fibrovascular stroma (Fig. 1c). Immunohistochemically, tumour cells were S-100 (Fig. 1d), CD68 (Fig. 1e), and NSE (Fig. 1f), and diagnosis of GCT was confirmed. The patient was admitted to the surgery department to operate on this tracheal tumour. She underwent sternotomy and resection of 35 mm of the trachea. The resection margins of a benign tumour were positive, and the trachea was resected to a length of 5 mm with laryngotracheal anastomosis. Secondary bleeding (500 ml for 15 min) developed on the tenth day after the surgery. An emergency bronchoscopy was performed, and anastomotic dehiscence with hematoma was seen. Resternotomy with extra-anatomical bypass was performed from the proximal brachiocephalic truncus to the proximal part of the right common carotid artery. However, there was a fatal outcome due to the development of acute pulmonary oedema, which was confirmed at the autopsy.

DISCUSSION

Pulmonary GCT is a sporadic bronchus tumour. The histogenesis of GCT is unknown, although most studies suggest a peripheral nerve sheath origin.[8] Our immunohistochemical results with positive staining for antibodies to S100 (2/2), CD68 (2/2), and NSE (2/2) are consistent with this concept. Pulmonary GCT has been reported to be associated with genetic mutations in PTPN11 as part of LEOPARD syndrome9 and many other neoplasms (malignant melanoma, thyroid carcinomas, and lung carcinoma).[4,6,10] The coexistence of pulmonary GCT with malignant neoplasms was noticed in our first case. Acinic adenocarcinoma, diagnosed after the left lobectomy, was associated with multiple GCTs, which were seen and resected bronchoscopically in the upper right lobe. Five thousand one hundred eighty-one titles appeared when Houcine *et al*. searched the PubMed database and found the terms "granular cell tumour" and "granular cell myoblastoma". This review analysed 50 case reports and 5 case series for clinicopathologic characteristics in 120 cases. Pulmonary GCT was described in the bronchus (94, 78.3%), trachea (15, 12.5%), and lung (11, 9.1%). The right lung was more percent affected than the left one (42.5 vs. 31.6).[11,12] In our case, GCT has been reported in the right lung.

Pulmonary GCTs predominantly affect adults in the fourth to sixth decades of life, with a median of 45 years and a low incidence in children and adolescents.[13-17] Our patient is the oldest individual reported in the literature, to our knowledge. About half of the patients have a positive smoking history.[18] Similar to those results, one patient was a smoker, and one was a non-smoker.

Common symptoms at presentation include haemoptysis (17%), chronic cough (13%), chest pain (6%) and unexplained dyspnea (3%).[19] The symptoms depend on the size and location of the tumour. In both our cases, cough was the dominant symptom. In case 2, the tumour caused endoluminal obstruction and stridor.

Grossly, GCTs are not encapsulated, polypoid, or nodular but are tan-yellow and firm, mucosal-

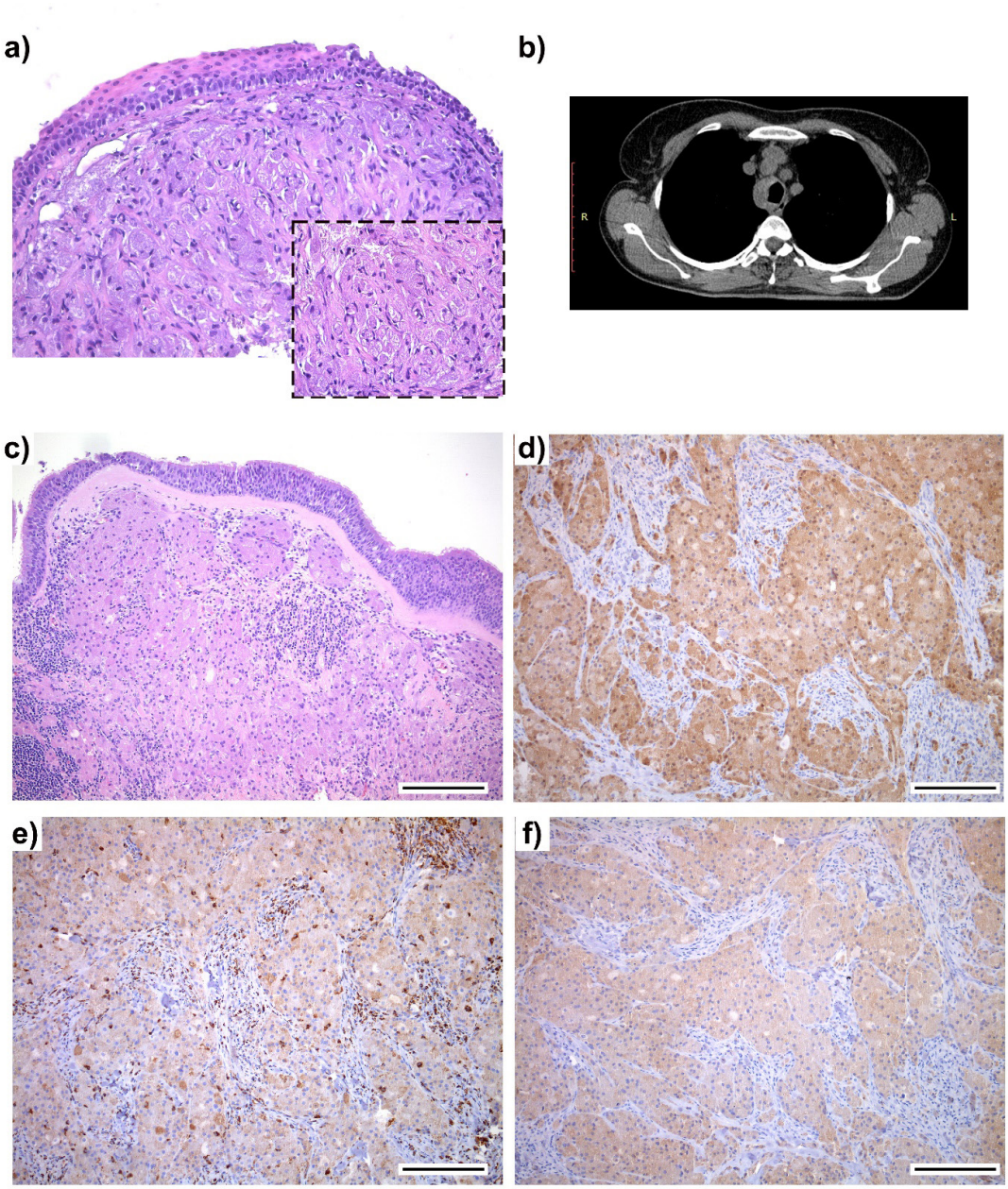

FIG. 1. Granular cell tumour: a) Histological microphotograph of an endobronchial granular cell tumour, haematoxylin and eosin (H&E) stain, ×20 (inset ×40). b) CT scan indicating the presence of a tracheal tumour. c) Histopathological microphotograph of the granular cell tumour depicting groups of cells with abundant granular cytoplasm, H&E stain, ×10, scale bar 200 µm. d) Immunostained microphotograph demonstrating that the tumour cells were positive for S-100, ×20, scale bar 100 µm. e) Immunostained microphotograph indicating that the tumour cells were positive for CD68, ×20, scale bar 100 µm; f) Immunostained microphotograph showing that the tumour cells were positive for neuron-specific enolase (NSE), ×20, scale bar 100 µm.

covered masses ranging from 0.3 to 8cm.[4,18] However, the definite diagnosis of GCT is based on the cytomorphological and histological features.[20]

The fine needle aspiration smears revealed moderate to high cellularity of singly lying and clustered uniform polygonal cells with low N/C ratio, granular, cytoplasm, and eccentrically placed round nuclei without necrosis or mitoses. Histologically, clusters of cells were separated by a delicate fibrovascular stroma.[20,21] According to the Fanburg-Smith criteria, the most common pulmonary GCTs were benign (117, 97.5%). They had a recurrence rate of 2 to 8% when resection margins had no tumour and increased to 20% when the resection margins of a GCT were positive for tumour infiltration.[18,22] Malignant GCTs account for only 1 to 2% of all cases of GCT.[23] They are usually >5 cm in diameter, with spindling of the tumour cells, the presence of vesicular nuclei with prominent nucleoli, increased mitotic rate (>2 mitoses/10 high-power fields at 200× magnification), a high nuclear-to-cytoplasm (N/C) ratio, pleomorphism, and necrosis. The malignant GCT is diagnosed when three or more criteria are fulfilled: an immunohistochemical panel, increased p53 expression, and an elevated nuclear proliferative index. Most patients die within 2–5 years after the diagnosis.[2,6] In our cases, the tumour sizes were 0.3 and 3 cm. The previous histological criteria did not fulfil the criteria for malignant GCT; thus, a benign GCT diagnosis was established.

Differential diagnoses include benign or malignant tumours. A large panel of immunohistochemical stains is sometimes needed. Morphological and immunohistochemical features correlate with the diagnosis of granular cell tumour.[5,6,18]

Granular cell tumours fail to respond to radiotherapy and chemotherapy. Tumours <1.0 cm in diameter may be treated by bronchoscopic extirpation, laser therapy, or sleeve resection. However, tumours with a diameter greater than 1 cm are treated by surgical resection, but tumour recurrence has been reported. Therefore, a follow-up once a year for a minimum of 5 years is recommended.[5,24]

CONCLUSION

We report two patients (a woman aged 54 and a man aged 68 years old) diagnosed with benign GCTs in the tracheal and bronchial tree. They were managed by bronchoscopic extirpation and surgical resection, with negative margins, without any progression at the follow-up in one case and a lethal outcome in the second case.

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