

Endobronchial granular cell tumor: a case report


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ABSTRACT

Granular cell tumors (GCTs) are benign neoplasms that are most commonly found in the head and neck region. We present a case of endobronchial granular cell tumor presenting as hemoptysis in a 22-year-old African American female. Patient subsequently underwent a right upper and middle lobectomy, and upon histologic analysis was found to have GCT with borders impinging upon cartilage and adjacent peribronchial lymph nodes.

CASE REPORT

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The patient is a 22-year-old African American female who presented to the emergency room complaining of productive cough containing blood-streaked sputum, pleuritic chest pain, exertional dyspnea, without fevers or chills, of approximately five days duration. PA and lateral chest radiographs revealed rounded hilar prominence and upper lobe volume loss with associated patchy upper lobe density noted on the right (Fig. 1). CT of the chest was subsequently obtained revealing a soft tissue mass in the right hilar region measuring approximately 30 x 29 x 27 mm (Fig. 2). The soft tissue encased and narrowed the right upper lobe bronchus with incomplete atelectasis of the right upper lobe. Bronchiectatic changes of the posterior segment of the right upper lobe were also identified as well as multiple prominent mediastinal and hilar lymph nodes. Radiologic findings suggested a more chronic etiology as bronchiectasis was present and based on imaging characteristics, differential considerations included bronchial adenoma (carcinoid) and less likely lymphoma.

The patient was subsequently admitted for evaluation of tuberculosis, as it was the main clinical concern due to the

patient's presentation of blood streaked sputum. She had no significant past medical history. Vital signs and physical examination upon admission were within normal limits. The patient was placed on contact isolation and the infectious disease service was consulted.

During hospitalization, fiberoptic bronchoscopy with brushing and biopsy was performed by the admitting physician. Bronchoscopy revealed a mass at the posterior segment of the right upper lobe. Several cannulations and biopsies of the lungs were taken from the right upper lobe. The left lung was not visualized due to severe spasms. The right middle lobe and the right lower lobe showed no endobronchial lesions. Bronchial washings were negative for malignancy and were seen to contain benign and reactive bronchial cells, pulmonary macrophages, red blood cells, and leukocytes. The right upper lobe biopsy revealed granular cell tumor.

Thoracic surgery was consulted and the matter was discussed in detail with the patient and the family. It was felt that the patient was a candidate for thoracotomy for resection due to symptomatic obstruction of the right upper lobe

bronchus. At the time of surgery the right upper and middle lobes were completely atelectatic, with satisfactory ventilation of the right lower lobe. Upon visual inspection, the right hilar mass extended into the right upper lobe bronchus. The bronchus was opened, where there was noted to be a cream-colored tumor completely obstructing the orifice. A right upper lobectomy and right middle lobectomy with sleeve resection of the portion of the right main bronchus and reanastomosis of the right lower lobe to the right main bronchus was performed.

The specimen received included upper lobe bronchus, proximal bronchial stump, and right main bronchus and right upper and middle lobe lung. Microscopic examination demonstrated large polygonal cells with highly granular eosinophilic cytoplasm and central, small dark, uniform nuclei consistent with GCT (Fig. 3, Fig. 4). The frozen sections revealed endobronchial GCT with a pushing border that impinged upon the bronchial cartilage and impingement by direct extension upon included peribronchial lymph nodes (Fig. 5, Fig. 6). Eleven out of eleven peribronchial lymph nodes were negative for GCT. The remaining pulmonary parenchyma showed post-obstructive bronchopneumonia with edema, hemorrhage and focal foreign body giant cell reaction and benign pleura.

Immunohistochemically, the neoplastic cells expressed strong reactivity for S-100 protein and vimentin. Less than 10% staining within the lesional cells was present for Ki-67. Stains for CK20, pan keratin AE1/AE3, synaptophysin, smooth muscle actin, and CK7 were negative.

Based on the features described, diagnosis of a benign GCT tumor was rendered. Case was reviewed and diagnosis confirmed by an outside pathology consultant.

DISCUSSION

Granular cell tumor (GCT) was initially described by Abrikossoff in 1926. Originally, it was thought to arise from myoblasts, hence its earlier name granular cell myoblastoma. Granular cell tumors are benign neoplasms that are most commonly found in the head and neck region [1, 2]. Granular cell tumors can occur in almost any organ. These tumors have been reported in various sites, but are most commonly seen in the skin, tongue, and breast [2, 3]. Approximately one-third to one-half of GCTs are found in the head and neck region, with the most tumors originating from the tongue [4]. They have been reported to occur synchronously in multiple organs and metachronously in a single organ [5]. Granular cell tumors of the lung are rare; 2-6% of GCTs occur in the lung, and of these, 90% are endobronchial [3,6]. There may be multiple endobronchial lesions in 4-10% of patients. Other organs may be also be involved by GCTs. Up to 13% of GCTs may be associated with a variety of other neoplasms of the lung, kidney and esophagus [6,7].

Computed tomography typically demonstrates a soft tissue endobronchial mass. GCT do not contain fat or calcification, which differentiates it from an endobronchial hamartoma, if

grossly visible. Intratumoral hemorrhage is not typical. Depending on the size of the endobronchial mass, there may be signs of distal pneumonia, atelectasis, mucoid impaction, bronchiectasis, and air trapping. Chest radiographs may be normal, have visible tumor, post-obstructive pneumonia or atelectasis. GCTs do not demonstrate FDG uptake on PET scan. On MR imaging GCTs are typically isointense to muscle on both T1 and T2 weighted images and demonstrate contrast enhancement.

The staining characteristics of GCT support the neuroectodermal origin of the neoplastic cell. Currently, the predominant opinion is that most GCTs are of Schwann cell origin [8]. It is thought that there is no difference in the incidence between male and females. Some papers however report an increase incidence in the female population [5, 8, 9]. Additionally, some report a higher incidence in African Americans [1, 8, 9].

Symptoms of GCTs can vary and are mostly determined by both the location of the tumor and its size. Centrally located tumors are more likely to cause symptoms due to their mechanical characteristics and make treatment necessary [5]. Dysphagia, pain, dyspnea, coughing, hemoptysis, and stridor may be present and are related to the location and size of the tumor [1, 10]. Based on size some may be amendable to conservative local excision, whereas large resections are justified for large tumors or if extensive damage to the lung parenchyma has occurred secondary to postobstructive pneumonia [7]. Complete resection is usually curative, although recurrences have been described.

Pulmonary GCTs are typically seen in the lower trachea and central bronchi down to the segmental level. They have the tendency to occur at bifurcation sites [3]. A case review presented by Maten Surgery [5] revealed a predilection for the upper lobe and the bronchus intermedius, however this has not been confirmed by others. This finding was present in our case presentation.

Grossly, GCTs are small, rounded, firm, mucosal covered masses and range in the size from 0.3-5.0 cm [1]. Diagnosis of GCT is through pathologic examination. Granular cell tumors are characterized for not being encapsulated and by having imprecise borders [1, 9]. This leads to their tendency of local invasion. Granular cell tumors may be found in lymph nodes by way of direct extension, a feature that should not be confused with lymph node metastasis. Microscopically tumor cells are polygonal or ovoid, with abundant eosinophilic and granular cytoplasm. Nuclei are small and hyperchromatic [5]. The hallmark of GCT is the granular appearance of the cytoplasm given by the periodic acid-Schiff positive and diastase-resistant granules [1, 11]. Most granular cell tumors stain positive for S-100, vimentin, neuron-specific enolase, NK1-C3, and CD68(KP-1). They stain negative for epithelial, endothelial, and smooth-muscle markers [2, 9, 11]. The benign behavior of GCTs is demonstrated by its occasional reactivity to KI-67 (MIB-1) and Bcl-2 [8].

Pseudoepitheliomatous epithelial hyperplasia appears on the mucosal layer in 50-65% of specimens [1, 3, 9]. Such

findings lead to confusion of squamous cell carcinoma when biopsy specimens are too superficial [1, 8, 9, 11]. For this reason pathologists are trained not to diagnose squamous cell carcinoma in the presence of granular cell tumor [3].

Treatment modality of choice is dependent on whether or not there is invasion of the tracheal wall and should be evaluated by high-resolution computed tomography or magnetic resonance imaging [5]. Differentiation of GCTs from other carcinomas on the basis of imaging findings is not possible. Differential considerations include carcinoid, malignant endobronchial tumors such as bronchioloalveolar carcinoma, endobronchial metastases, fibroepithelial polyp, hamartoma, mucus plugs, adenoid cystic carcinoma, mucoepidermoid carcinoma and lipoma. Granular cell tumors fail to respond to radiotherapy and chemotherapy; wide local excision of these tumors is the treatment of choice [9,11]. Resection margins must be generous due to local tumor infiltration [1]. The slow growth rate of GCTs makes follow-up of once a year for at least 5 years to detect recurrences necessary [5].

Malignant degeneration occurs in 1-3% of all GCTs [1, 4]. Malignant GCTs appear pathologically similar to nonmalignant GCTs except for the occasional presence of nuclear pleomorphism [1, 11]. Malignant GCT tend to be larger than 4 cm at initial presentation and demonstrate rapid growth; the only distinguishing factor may be the presence of metastasis [4, 11]. Malignant GCT has a poor outcome, as most patients die within 2-5 years after diagnosis [1].

TEACHING POINT

Granular cell tumors (GCT) are rare benign neoplasms of neuroectoderm in origin that most frequently occur in the head and neck region. Differentiation of GCTs from other carcinomas on the basis of imaging findings is not possible. Based on the infiltrative behavior of the tumor, complete resection is recommended.

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FIGURES

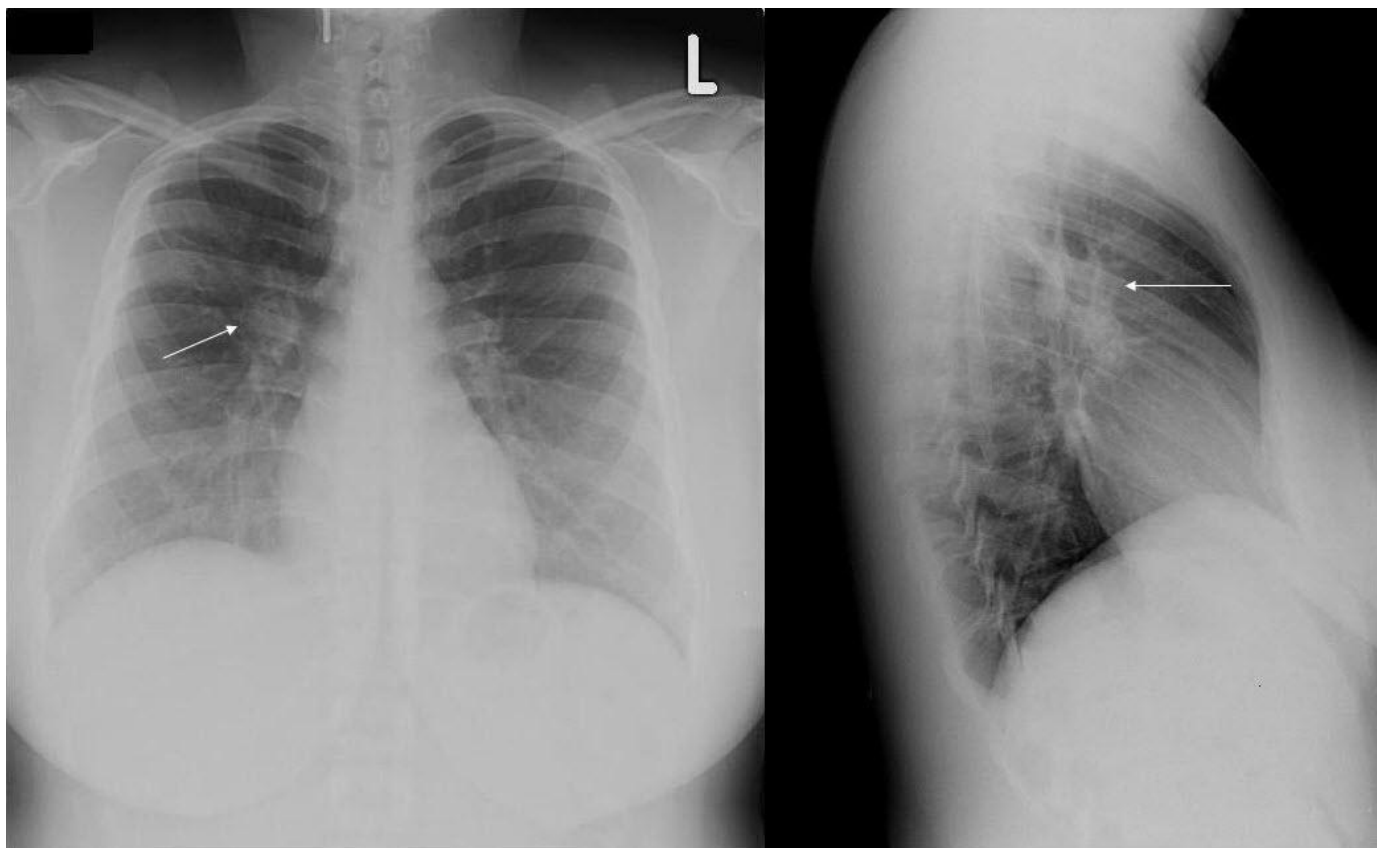


Figure 1: 22-year-old female diagnosed with endobronchial granular cell tumor. PA and lateral chest radiographs, arrow points to a rounded right hilar prominence and volume loss in the right upper lobe with associated patchy right upper lobe density.



Figure 2: 22-year-old female diagnosed with endobronchial granular cell tumor. Axial (left image) and coronal (right image) contrast-enhanced CT images of the chest (GE brand scanner, 40 mA, 120 kV, obtained at 2.5 mm slice thickness, after administration of 90 mL of Optiview iodinated intravenous contrast). Arrow points to a soft tissue mass in the right hilar region measuring approximately 30 x 29 x 27 mm. The soft tissue encases and narrows the right upper lobe bronchus with incomplete atelectasis of this lobe and with bronchiectatic changes in its the posterior segment.

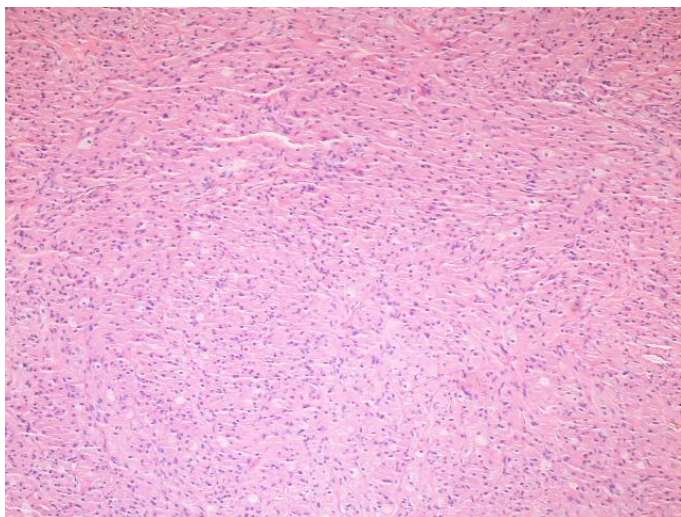


Figure 3: 22-year-old female diagnosed with endobronchial granular cell tumor. Granular cell tumor (10x magnification) stained with periodic acid-schiff. Large polygonal cells with highly granular eosinophilic cytoplasm and central, small, dark, uniform nuclei.

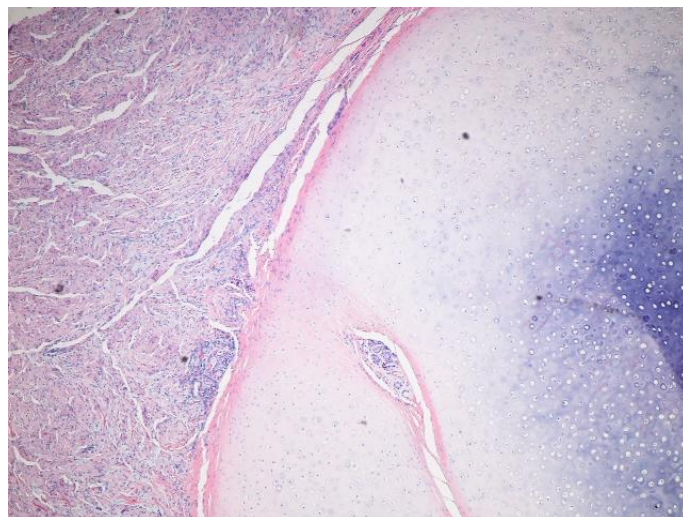


Figure 5: 22-year-old female diagnosed with endobronchial granular cell tumor. Granular cell tumor (40x magnification) stained with periodic acid-schiff infiltrating up to the bronchial cartilage.

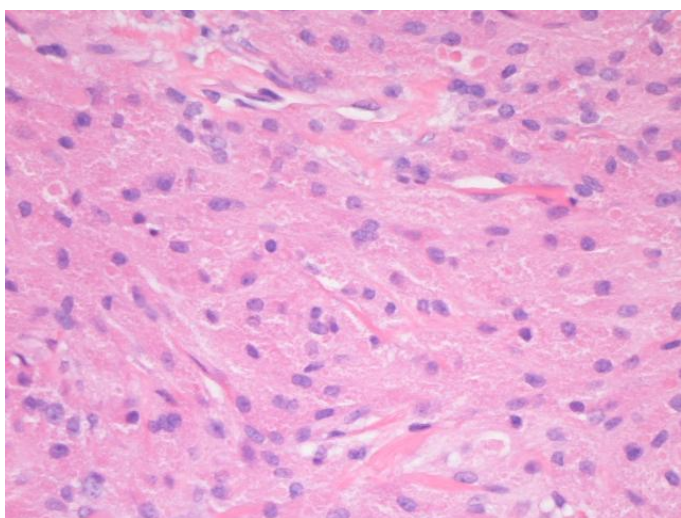


Figure 4: 22-year-old female diagnosed with endobronchial granular cell tumor. Granular cell tumor (40x magnification) stained with periodic acid-schiff. The cytoplasm contains innumerable fine cytoplasmic granules as well as scattered large eosinophilic globules.

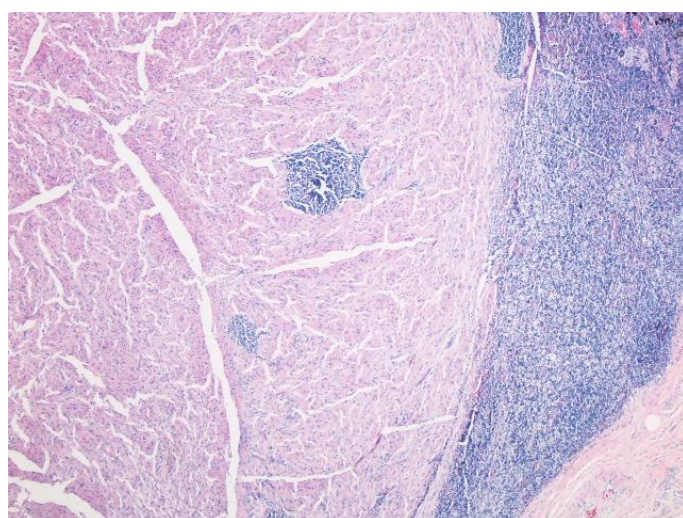


Figure 6: 22-year-old female diagnosed with endobronchial granular cell tumor. Granular cell tumor (40x magnification) stained with periodic acid-schiff compressing on pulmonary interstitial lymphoid tissue.

	CT	x-ray	PET
Granular cell tumor	Endobronchial soft tissue mass which is typically well defined. Depending on size may show signs of distal pneumonia, atelectasis, mucoid impaction, bronchiectasis, and air trapping.	Chest radiographs can be normal, have visible tumor, post-obstructive pneumonia/atelectasis.	No FDG uptake
Malignant endobronchial tumors: Bronchioloalveolar Carcinoma >95%	Chronic peripheral consolidations with associated nodules and ground-glass opacities. Enhancing, branching, pulmonary vessels within low attenuation consolidation, known as the CT angiogram sign.	Typically presents as an unresolving consolidation.	FDG avid
Carcinoid	Thoracic carcinoid most commonly found in within the bronchial lumen, but can also be partially encased in the bronchial wall, creating an iceberg growth pattern. Demonstrate marked homogenous early contrast enhancement, as it is highly vascular. Post-obstructive findings may be present if lesion is large enough to obstruct the bronchus.	Chest radiographs can be normal, have visible tumor, post-obstructive pneumonia/atelectasis	Variable, may show only mild to moderate FDG avidity
Endobronchial Metastases: breast, renal, colorectal, sarcoma, cervix	Can have central necrosis and contrast enhancement. Depending on size may show signs of distal pneumonia, atelectasis, mucoid impaction, bronchiectasis and air trapping. Typical multiple lesions which may be endobronchial and parenchymal in location, as opposed to a single endobronchial lesion.	Chest radiographs can be normal, have visible tumor, post-obstructive pneumonia/atelectasis. Typically present with multiple lung nodules as opposed to a single endobronchial lesion.	FDG avid
Fibroepithelial polyp	Endobronchial soft tissue mass which is typically well defined. Depending on size may show signs of distal pneumonia, atelectasis, mucoid impaction, bronchiectasis and air trapping.	Chest radiographs can be normal or demonstrate post-obstructive pneumonia/atelectasis	No FDG uptake
Hamartoma	Round, well-defined lesions. Demonstration of fat and calcifications within the lesion is diagnostic. Can appear as nonspecific soft tissue mass on CT. Slow growing and can cause post-obstructive changes.	Normal chest. May present as a calcified nodule or signs of bronchial obstruction if the lesion large enough.	No FDG uptake
Mucus plugs	Endobronchial secretions which are low density in appearance and demonstrate no contrast enhancement. May cause bronchial obstruction with signs of distal pneumonia, atelectasis, mucoid impaction, bronchiectasis and air trapping.	Chest radiographs can be normal or demonstrate post-obstructive pneumonia/atelectasis. Findings typically resolve with clearing of secretions.	No FDG uptake
Adenoid cystic carcinoma	Demonstrates a well defined soft tissue intraluminal mass that infiltrates the airway wall and the surrounding mediastinal fat. Can present with circumferential wall thickening and stenosis. May cause bronchial obstruction with signs of distal pneumonia, atelectasis, mucoid impaction, bronchiectasis and air trapping.	Chest radiographs are typically normal.	No FDG uptake
Mucoepithelioid carcinoma	Shows the same pattern as bronchial carcinoid tumors, presenting as an endobronchial mass, but contrast enhancement is typically mild.	Chest radiographs can be normal or demonstrate post-obstructive pneumonia/atelectasis.	No FDG uptake
Lipoma	Pedunculated endobronchial mass arising which is fat density without any calcification. Bronchial obstruction if frequent leading to post-obstructive pneumonia/atelectasis.	Chest radiographs can be normal or demonstrate post-obstructive pneumonia/atelectasis.	No FDG uptake

Table 1: Differential diagnosis table of endobronchial lesions

Etiology	Neuroectoderm
Incidence	Exact incidence of granular cell tumors (GCTs) unknown, 2-6% of GCTs occur in the lung, 90% of which are endobronchial.
Gender ratio	M=F, although some reports indicate a female predominance
Age predilection	None known
Risk factors	None known.
Treatment	Surgical excision
Prognosis	Complete resection is usually curative, although recurrences have been reported. Malignant degeneration seen in 1-3% of GCTs. Malignant GCT has a poor outcome, as most patients die within 2-5 years after diagnosis.
Findings on Imaging	CT demonstrates a soft tissue endobronchial mass. Depending on size may show signs of distal pneumonia, atelectasis, mucoid impaction, bronchiectasis, and air trapping. Chest radiographs can be normal, have visible tumor, post-obstructive pneumonia/atelectasis. Absence of air-bronchograms strongly suggest endobronchial lesion as the cause of atelectasis.

Table 2: Summary table of granular cell tumor

ABBREVIATIONS

- CT: Computed tomography
- FDG: Fluorodeoxyglucose
- GCT: granular cell tumor
- MRI: Magnetic resonance imaging
- PET: Positron emission tomography

KEYWORDS

Granular cell tumor, endobronchial

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