

Granular cell tumour of the bronchus: bronchoscopic and clinical features

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ABSTRACT Granular cell tumours are uncommon, generally benign neoplasms of uncertain origin that occasionally affect the tracheobronchial tree. Their incidence seems to be increasing, despite the fact that such tumours are rarely suspected on clinical grounds or bronchoscopic appearance. Here we describe three cases of endobronchial granular cell tumours, one of which regressed spontaneously after biopsy, and review previous accounts of their bronchoscopic and clinical features.

Before 1975 only 40 cases of endobronchial granular cell tumours had been reported. During the past 10 years, however, the number of reports has increased to more than 90. Although this increased reporting might reflect a real increase in the frequency of such tumours, the more widespread use of fiberoptic bronchoscopy, recognition of the subtle tracheobronchial abnormalities, and a more thorough elucidation of the tumour's pathological characteristics are probably contributing factors. Nevertheless, this diagnosis is rarely entertained when endobronchial abnormalities are found. Our report should alert the clinician and bronchoscopist to the incidence and features of these lesions.

Case reports

CASE 1

A 59 year old man was admitted after two days of producing purulent, blood streaked sputum. Two months previously he had been treated at another hospital for pneumonia in the upper lobe of the right lung. He had a history of cigarette smoking (40 pack years) and chronic obstructive pulmonary disease had been diagnosed previously. He reported having had brief, intermittent episodes of producing blood streaked sputum for several years before admission. Physical examination showed a healthy looking man with normal vital signs. There was mild finger clubbing and crackles were heard posteriorly at mid level

over the right lung. The remainder of the examination showed nothing remarkable. Fiberoptic bronchoscopy showed old blood within the tracheobronchial tree. Although no active bleeding was seen, a fourth generation bronchus of the right upper lobe was occluded by a small, lobulated, pale grey nodular tumour. Forceps biopsy yielded material with histological appearances of granular cell tumour. No other tracheobronchial lesions were noted, and the patient underwent surgical excision of the mass by lobectomy.

CASE 2

A 61 year old man, an alcoholic, was admitted to another hospital with pneumonia and atelectasis of the right upper lobe. Fiberoptic bronchoscopy showed normal appearances in the right upper lobe, but a small, pale, nodular tumour was found in the left mainstem bronchus. Biopsy yielded material with histological appearances consistent with granular cell tumour. No treatment was given at that time, and the patient was lost to follow up. Eight years later he was readmitted to hospital with left sided weakness and focal seizures. A mass was noted in the left upper lobe on chest radiography and computed tomography of the brain showed two nodules consistent with right parietal lobe metastatic disease. The patient was then transferred to our hospital for further management. No endobronchial lesions were found on repeat fiberoptic bronchoscopy, and biopsy at the normal appearing site of the previous granular cell tumour showed no residual tumour. Percutaneous needle biopsy of the pulmonary mass yielded material with histological features of large cell carcinoma of the lung.

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CASE 3

A 48 year old man was admitted for evaluation of a mass in the upper lobe of the right lung. He reported a 9 kg weight loss during the previous four months and a three month history of cough productive of scant whitish sputum. Chest radiography showed a 6.5 cm mass occupying the upper lobe of the right lung, but no mediastinal tumour was evident. Bronchoscopy showed features of extrinsic compression but no endobronchial obstruction. In the posterior basal segment of the right lung, however, there was a nodular, pale, grey lobulated lesion 0.5 cm in diameter. Forceps biopsy material had appearances consistent with granular cell tumour. No other lesions were found, and the patient's right lung was later removed. The surgical specimen included a lesion with appearances characteristic of granular cell tumour and large cell carcinoma of the right upper lobe (figure).

Discussion

Abrikossoff in 1926 was the first to describe granular cell tumour in a series of five patients with tumours of the tongue.¹ Since that first description, nearly 1000



Resected specimen from case 3: A pale, nodular, discrete lesion (1 × 1 cm) is evident in the right lower lobe segmental bronchus. (Divisions on the scale are 5 mm).

cases have been reported, of which only 6% (range 0–10%) affected the tracheobronchial tree.^{2–6} Although the histogenesis of this tumour remains controversial, it is no longer generally believed to originate from muscle cells; the original term “myoblastoma” has been replaced by the descriptive “granular cell tumour.” Recent histochemical⁷ and electron microscopic^{8,9} studies have lent support to a neuroectodermal origin of the granular cells, which may resemble Schwann cells undergoing Wallerian degeneration.

Granular cell tumours are usually small, firm, solitary, non-encapsulated nodules with no distinguishing external features. The histological appearance is characteristic and consists of nests and sheets of large, distinctly bordered ovoid and polygonal cells that contain a finely granular, eosinophilic cytoplasm. These granules apparently are lysosomal structures.¹⁰ The nuclei are usually small and uniform, and tend to be pyknotic and centrally located. The cells are arranged in small clusters delineated by basement membrane material. Myelinated nerve bundles, often arranged in concentric whorls and surrounded by granular cells, are seen in about half of the cases.

At bronchoscopy most lesions have been found within the trachea or a mainstem bronchus, 47% on the right side, 42% on the left, and 15% within the trachea or carina (table 1). The tumour has most often been described as a solitary, discrete endobronchial nodular mass, usually pale pink, grey, or yellow, but may also resemble an infiltrating carcinoma (table 2). The lesions reported had a mean diameter of 1.6 cm, with a wide range of 0.4–6.5 cm. Although complete occlusion of the bronchial lumen by the tumour is unusual, peribronchial invasion may lead to considerable endobronchial narrowing. Full thickness invasion of the bronchial wall has been reported in about 40% of affected patients and should be suspected in large infiltrating lesions. Small polypoid or pedunculated tumours are unlikely to have extensive submucosal invasion. At the time of bronchoscopy 18% of patients have had multiple intrapulmonary lesions identified and 7% have had simultaneous extrapulmonary lesions, most frequently at subcutaneous sites. Metachronous lesions at different sites within the tracheobronchial tree have been reported in two patients.^{11,12} Because the tumour is covered only by a thin layer of bronchial epithelium, results of forceps biopsy have been almost invariably positive. Diagnostic cytopathological examination of bronchial washings is, however, unusual, and has been reported in only three patients.^{13–15} Squamous metaplasia of the overlying respiratory epithelium is found in about half of patients, and may occasionally resemble squamous cell carcinoma. Nevertheless, a squamous cell carcinoma overlying a granular cell

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Table 1 Tracheobronchial distribution of 82 granular cell tumours^{4-6 11-19 24-39}

Location	No (%)
Trachea and main carina	13 (15)
Right lung	
Main bronchus	11 (13)
Upper lobe bronchus	11 (13)
Bronchus intermedius	4 (5)
Lower lobe bronchus	6 (7)
Segmental bronchus	2 (2)
Left lung	
Main bronchus	8 (10)
Upper lobe bronchus	7 (8)
Lower lobe bronchus	12 (14)
Segmental bronchus	4 (5)
Other	4 (5)

Table 2 Bronchoscopic appearances of 93 granular cell tumours^{4-6 11-19 24-39}

Description	No (%)
Discrete endobronchial tumour	37 (40)
Infiltrating mass lesion	12 (13)
Raised plaque like, mucosal thickening	12 (13)
Others	5 (5)
Not seen at bronchoscopy	5 (5)
Not described	22 (24)

tumour has been reported only once, and that was on the vulva.¹⁶

Clinically, most patients have presented with recurrent or unresolved pulmonary infiltrates related to bronchial obstruction (table 3). The mean duration of symptoms from onset to diagnosis has been 11.2 months, varying with the presenting complaint: from one day in a case of haemoptysis to seven years with recurrent pneumonia. Twelve per cent of cases presented with an asymptomatic lung nodule or mass, and in 13% the tumour was discovered only incidentally at bronchoscopy performed for another indication, as in our second and third patients. Occasionally, endobronchial granular cell tumours have been found unexpectedly during evaluation of suspected bronchogenic carcinoma, but there is no clear relationship to lung cancer. Constitutional complaints are uncommon with granular cell tumours, and only 10% of patients have been reported to have lost weight.

Haemoptysis has been recorded in 25% of cases. Bleeding is usually minor, but massive haemoptysis has been reported.¹⁷ In most patients the mechanism for haemoptysis is largely unknown. Granular cell tumours rarely penetrate the bronchial mucosa, are not densely vascular, and have not been reported to erode bronchial vessels. Nevertheless, manipulation of the tumour can result in appreciable haemorrhage.^{18 19} None of our patients was bleeding at

Table 3 Presenting clinical and radiographic features of tracheobronchial granular cell tumours: information from 68 cases^{4-6 11-19 24-39}

Feature	No (%)
Haemoptysis	17 (25)
Recurrent pneumonia	17 (25)
Persisting pulmonary infiltrate, atelectasis	14 (20)
Chronic cough	13 (19)
Incidental bronchoscopy finding	10 (15)
Asymptomatic lung nodule or mass	8 (12)
Bronchiectasis or abscess	6 (9)
Unexplained chest pain	6 (9)
Normal chest radiograph	4 (6)
Unexplained dyspnoea	3 (4)

the time of bronchoscopy, and the bleeding resulting from forceps biopsy of their tumours was minimal. Including the present report (case 1), only three patients have been reported as having presented with haemoptysis and a normal chest radiograph.^{20 21}

Although most tumours grow slowly, frequently remaining unchanged radiographically for years, an occasional granular cell tumour has acted malignantly, giving rise to regional lymphatic and distant metastases.²⁰⁻²³ None of the malignant granular cell tumours, which have been reported in only 26 patients, was of bronchial origin. Half of the malignant tumours, however, metastasised to the lungs and, like other haematogenously disseminated neoplasms, metastatic granular cell tumours have also presented as extrabronchial peripheral pulmonary nodules.

Treatment of patients with endobronchial granular cell tumours has not been clearly defined. Difficulties in selecting the optimum therapeutic approach arise from uncertainties about their natural history and, because no study comparing the various alternatives has been reported, therapeutic decisions necessarily derive from anecdotal reports. Current therapeutic options include surgical resection, endoscopic removal, fulguration, and laser photocoagulation. Overall, surgical excision of the tumour mass has resulted in the highest cure rate. Of 20 surgically treated patients with long term follow up (mean 3.3 years, range 4 months to 12 years), only one was reported to have had symptomatic recurrence. Yet the optimum extent of surgery remains unclear. Most authors agree that when postobstructive parenchymal damage has occurred, segmental or lobar resection is indicated; in fact, such resection has been the most frequently used approach. When local resection of the mass is anatomically feasible, however, sleeve resection is considered to be the procedure of choice.

Less invasive therapeutic alternatives have also met with some degree of success. Endoscopic resection (n = 13), fulguration (n = 2), and laser photo-

coagulation (n = 4) have been reported in 19 patients,^{11 18 19 24-38} 10 of whom remained symptom free at follow up. There were six (32%) documented recurrences—at 3 months, 5 months, 15 months, 2.5 years, 3 years, and 6 years. In three patients follow up information was not available.

Factors affecting tumour recurrence after treatment have not been fully identified, but Daniel and associates³⁹ noted that the likelihood of successful bronchoscopic removal is related to tumour size. Only the larger tumours (1–2 cm) recur, and full thickness invasion of the bronchial wall is found only when tumours exceed 8 mm in diameter. Thus smaller neoplasms may be treated by endobronchial resection, whereas larger tumours would require a broader surgical approach. Lack *et al*² found a 25% recurrence rate in incompletely excised extrapulmonary lesions. Because of the slow growth rate of these tumours, treatment should not be considered successful until completion of at least two years of follow up, which has been the mean time for recurrence.

Extended symptom free intervals have also been observed in some untreated patients. Of seven untreated patients, four remained symptom free after two years. Spontaneous resolution, however, has been documented in only one previous case. Although spontaneous resolution of the tumour after transbronchoscopic biopsy was likely in our second case, the lesion might have been completely excised by the forceps at the time of biopsy. Thus in selected patients with multiple lesions, in patients in whom a small tumour is detected incidentally, or when thoracotomy presents high risks, reasonable alternatives are endoscopic laser photocoagulation, fulguration, and observation alone, all with periodic endoscopic surveillance.

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