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Multi-focal, multi-centric granular cell tumours: a management dilemma

Lokesh Yagnik[1], Hilman Harryanto[1], Mei Hui Eleanor Koay[2], Ben Dessauvagie[2] & Matthew Salamonsen[1]

[1]Department of Respiratory medicine, Fiona Stanley Hospital, Murdoch, WA, Australia.
[2]PathWest Laboratory Medicine WA, Fiona Stanley Hospital, Murdoch, WA, Australia.

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Correspondence
Lokesh Yagnik, Department of Respiratory Medicine, Fiona Stanley Hospital, 11 Robin-Warren drive, Murdoch, WA 6105, Australia. E-mail: lokesh.yagnik@health.wa.gov.au

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Abstract

Granular cell tumours (GCT) are uncommon, usually solitary tumours of neural/Schwann cell origin that occur at any site of the body, and typically run an indolent clinical course. Treatment by excision is recommended. Distant or nodal metastases are the only reliable signs of malignancy. We describe the case of a 47-year-old woman with a multi-focal, multi-centric GCT involving the pulmonary and gastrointestinal systems, highlighting the imaging and pathological features and the challenge faced in establishing its malignant potential.

Introduction

Granular cell tumours (GCT), are tumours of neural/Schwann cell origin that typically present as solitary lesions on skin and mucous membranes. Although they have been described in almost all body sites, there are less than 100 publications of GCT involving the pulmonary system [1]. We present an unusual case of GCT involving both the gastrointestinal and pulmonary systems, which raises the issue of multi-centric synchronous versus metastatic GCT.

Case Report

A 47-year-old, congenitally deaf woman presented with acute abdominal pain on a background of two weeks of non-productive cough and unintentional 5 kg weight loss over the previous six months. She was a smoker (30-pack per year history) with no other medical co-morbidities. She did not take any regular medication. A computed tomography (CT) of the abdomen showed right iliac fossa mass and bilateral pulmonary nodules in limited lung windows. Colonoscopic biopsies were performed for the caecal mass, but were non-diagnostic on histopathology assessment.

Computed tomography of the chest confirmed multiple (>5) bilateral broncho-centric pulmonary nodules (Fig. 1A). These were non-fluorodeoxyglucose (FDG) avid on positron emission tomography (PET) scan (Fig. 1B). There was no thoracic or extra-thoracic lymphadenopathy. The caecal mass showed a rim of calcification and low FDG activity. Bronchoscopy showed smooth, firm, white endobronchial tumours causing near complete obstruction of the right posterior basal and right upper lobe anterior sub-segments (Fig. 1C). Multiple endobronchial biopsies were performed of these two obstructing lesions followed by a right hemicolectomy as initial caecal biopsies were non-representative.

Histopathology of the pulmonary lesions demonstrated GCTs. The tumours were composed of spindled cells arranged in intersecting fascicles with abundant granular cytoplasm and uniform oval nuclei with smooth contours and fine, even chromatin and inconspicuous nucleoli (Fig. 2A–D). There were no mitoses. Apoptosis and necrosis were not seen. By immunohistochemistry, the tumour cells were strongly S100, inhibin and CD68 positive (Fig. 2E,F). The ki67 proliferative index was 2%. The right

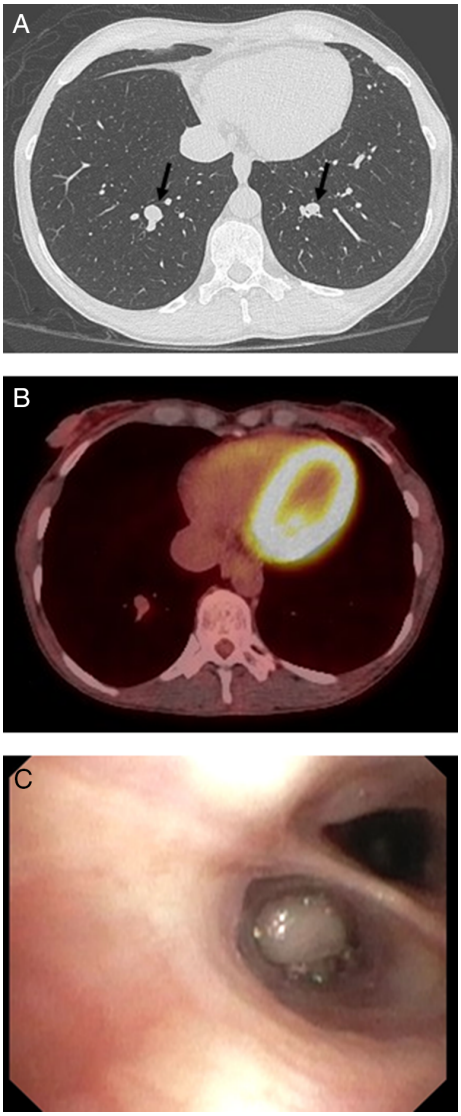

Figure 1. Imaging and bronchoscopic features. (A) Bilateral non-spiculated bronchocentric pulmonary nodules (arrows). (B) Low FDG avidity on PET imaging. (C) Smooth, firm white endobronchial tumours almost completely occluding the bronchus.

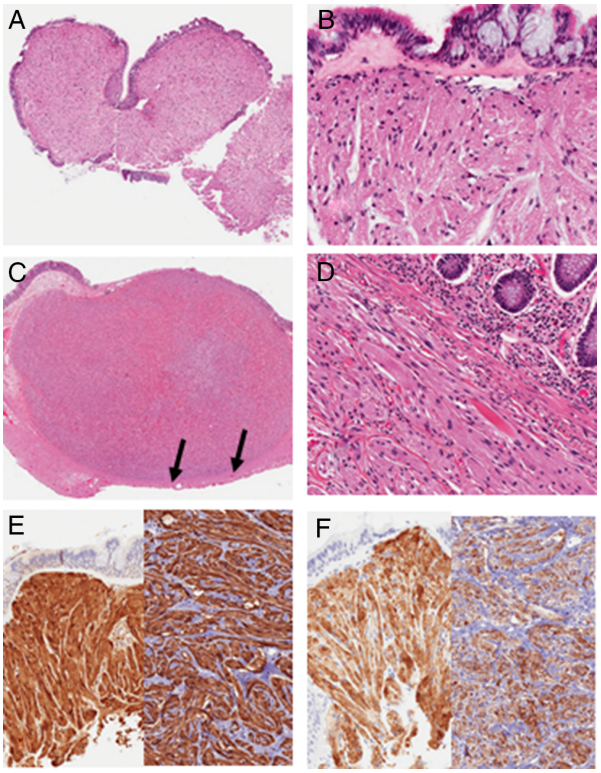

Figure 2. Pathological findings. (A) Low power (×4) H&E micrograph showing a submucosal pulmonary nodule. (B) At high power (×20) the tumour is composed of spindled cells with abundant granular cytoplasm and bland nuclei. (C) Low power (×0.5) H&E micrograph showing a caecal submucosal tumour pushing into the muscularis propria (arrows) with erosion of the overlying mucosa. (D) At high power (×20) the constituent cells are of similar appearances to those of the lung tumour. (E,F) Both tumours (lung, left; colon, right) express s100 (E), and inhibin (F) by immunohistochemistry (×10).

hemicolectomy demonstrated a 24 mm, submucosal caecal tumour, abutting both the overlying mucosa and underlying serosa. The morphologic and immunophenotypic features were similar to the pulmonary lesions (Fig. 2E,F). It was not possible, by pathology alone, to conclusively determine whether the pulmonary nodules were synchronous primaries (synchronous with the caecum, thereby representing multi-focal, multi-centric tumour) or metastatic from the caecum.

Given the history of congenital deafness, and a known association between multi-focal GCT and certain genetic syndromes such as LEOPARD syndrome, a full assessment was performed by a clinical geneticist. As no syndromic features were identified, further genetic testing was not performed.

She has shown no clinical or radiological signs of progression during nine months of surveillance imaging; however, further surveillance is planned.

Discussion

Granular cell tumours are an uncommon entity of neural/Schwann cell origin. They typically present as a solitary lesion in skin or mucous membranes. They commonly occur in the head and neck and aerodigestive tract but have been reported in almost any site of the body. Rare multi-centric presentations have also been described [2]. While most tumours have a benign clinical course, malignant behaviour of GCTs, manifesting as local infiltration and/or distant metastasis has been seen in 1–2% of cases.

Histological features are not a reliable predictor of malignant behaviour. Evidence of metastasis is the only definite feature of malignancy.

Case series data suggest a female preponderance. They are also more common in African-American people [3]. Up to 8% of GCTs are familial and syndromic associates are seen in about a third of cases including PTPN11 mutation associated genetic syndromes, Noonan syndrome, LEOPARD syndrome, PTEN hamartoma tumour syndrome, and neurofibromatosis 1 [2]. Most GCTs are asymptomatic with clinical manifestations due to local mass effects, such as pruritus and radicular pain in cutaneous lesions, cough, wheezing and haemoptysis in pulmonary lesions, dysphagia in oesophageal lesions, and constipation or diarrhoea in gastrointestinal lesions [4]. They are difficult to diagnose on imaging alone and often require multimodality imaging [CT, ultrasound, magnetic resonance imaging (MRI), and PET scans] [4].

Based on case reports, wide local excision is the recommended treatment for both primary and metastatic disease. Treatment with local radiation therapy, chemotherapy and pazopanib in the metastatic setting has also been described with limited success [2].

In our case it was difficult to definitively distinguish metastatic tumours from multi-centric/synchronous “benign” tumours. Both tumours had low FDG uptake on PET scan where some studies have shown that malignant GCTs are usually intensely FDG avid [5]. On imaging, the caecal lesion was larger than the pulmonary lesions and was calcified, the latter often a sign of chronicity. Histopathological features at both sites were indistinguishable and no overt malignant features were observed. Specifically, there was no evidence of local nodal metastasis in the mesenteric lymph nodes sampled in the hemicolectomy specimen. Thoracic nodes were not sampled.

Given the size and calcification of the caecal lesion, the pattern of tumour distribution (single large caecal lesion, multiple small pulmonary lesions), the infrequency of multiple synchronous GCTs and lack of an identifiable genetic syndrome in the patient, a primary caecal tumour, with metastasis to the lung was ultimately the favoured diagnosis.

In summary, our case report describes the presentation, imaging characteristics and histopathological findings of the rarely encountered multi-focal, multi-centric GCT and highlights the diagnostic dilemma in establishing their malignant potential.

Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

References

1. Radic P, and Brcic L. 2017. Pulmonary granular cell tumours: case presentations and literature review. Scott. Med. J. 62(2):70–73.
2. Machado I, Cruz J, Lavernia J, et al. 2016. Solitary, multiple, benign, atypical, or malignant: the "granular cell tumor" puzzle. Virchows Arch. 468(5):527–538.
3. Khansur T, Balducci L, and Tavassoli M. 1987. Granular cell tumor. Clinical spectrum of the benign and malignant entity. Cancer 60:220–222.
4. Xu GQ, Chen HT, Xu CF, et al. 2012. Esophageal granular cell tumors: report of 9 cases and a literature review. World J. Gastroenterol. 18(47):7118–7121.
5. Akahane K, Kato K, Ogiso S, et al. 2015. Malignant granular cell tumor of the breast: case report and literature review. Breast Cancer 22(3):317–323.