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Case report

Pulmonary hyalinising granuloma: A rare cause of multiple lung nodules in lung cancer clinic

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ABSTRACT

Here we report a case of Pulmonary Hyalinising Granuloma (PHG) presenting with mild to moderate FDG positive nodules in an individual with a high risk of cancer. We explore the considerations in interpreting imaging findings and assess the benefits and risks of undertaking invasive investigations such as tissue biopsy. We highlight the importance of reaching an accurate diagnosis of this benign condition on our patients and their future outlook.

1. Introduction

When contemplating the presentation of an older patient with multiple lung masses on chest x-ray and a significant smoking history, metastatic cancer is often the primary differential. However, PHG a rare benign fibro-sclerosing disease first described by Engelman et al in 1977 [1] also presents with single or multiple lung masses. Patients with this condition can have vague chest symptoms or present incidentally with masses on a chest x-ray [2]. The nodules can differ in size and occasionally show calcification. They can have positive FDG uptake on Positive Emission Tomography (PET), often requiring further investigation.

The following case will explore further the considerations and challenges in coming to diagnose this rare, benign condition.

2. Case history

A 72-year-old lady presented to our clinic with a two month history of cough, shortness of breath and a monophonic wheeze. She was a smoker with a 55 year pack history and was diagnosed as having chronic obstructive pulmonary disease based on her symptoms, smoking history and obstructive spirometry (FEV1/FVC of 66%). In addition she had a background of hypertension and had a history of Bell's palsy.

She was referred to her local lung multidisciplinary team meeting under the cancer two week wait referral system by her general practitioner, who had noted bilateral upper and mid zone rounded opacities on chest radiography. Subsequent CT showed bilateral pulmonary nodules measuring up to 2cm in the upper and mid-zones, diffuse adrenal swelling and renal cysts (Fig. 1). In an effort to obtain a tissue diagnosis, she underwent a CT guided biopsy of a lesion in her left upper lobe. This procedure was complicated by a moderate apical pneumothorax and the findings were inconclusively reported as 'non-specific fibrosis and chronic inflammation'.

A PET-CT at this time showed multiple FDG avid nodules with maximum standardised uptake value (SUV) of 6.9 in both lungs (Fig. 2), alongside several FDG negative nodules in both lungs and an FDG avid portocaval nodule. No extra thoracic FDG avid primary was identified.

The multi-disciplinary meeting felt that in light of her PET-CT results, the most likely diagnosis was still malignancy. She was therefore referred for a right-sided VATS wedge resection in order to obtain a definitive tissue diagnosis.

The result showed a discrete nodule comprising bundles of hyalinising collagen interspersed by varying numbers of plasma cells, indicative of a pulmonary hyalinising granuloma (Fig. 3). Follow up CT scan at 4 months, continued to show stable disease. The patient was treated for airways disease and her symptoms remained stable.

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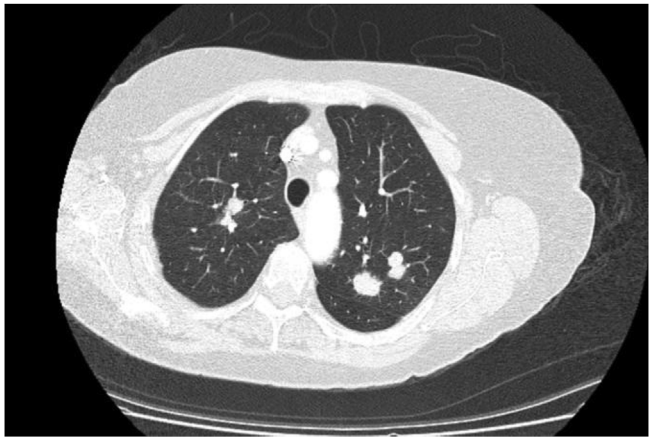

Fig. 1. CT image showing well circumscribed bilateral pulmonary nodules.

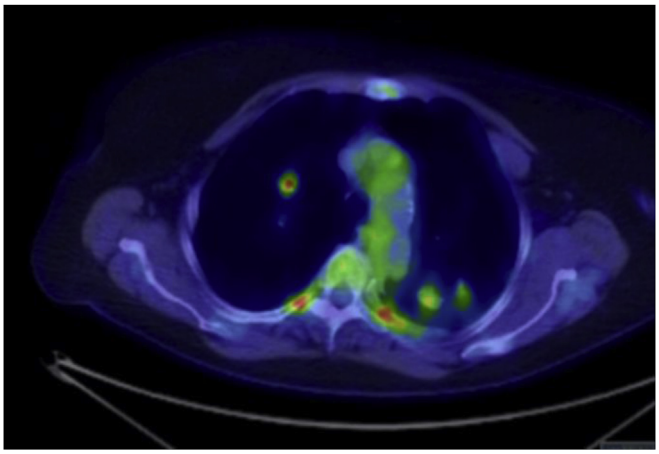

Fig. 2. PET- CT slice at the equivalent level showing bilateral FDG – avid pulmonary nodules.

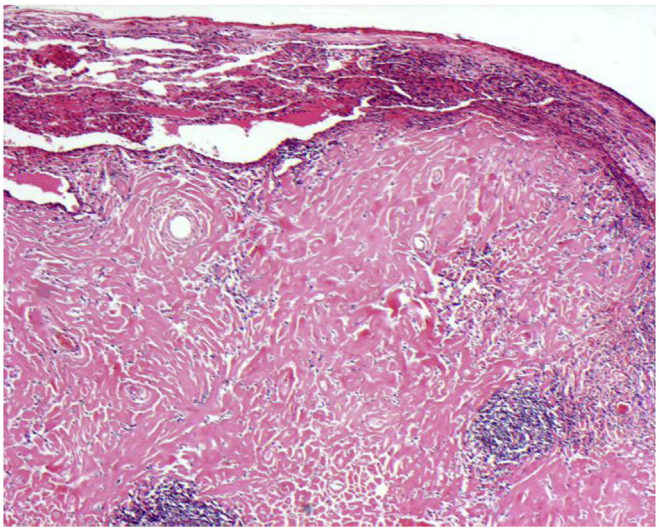

Fig. 3. A pulmonary hyalinising granuloma comprising of a well circumscribed mass made up of thick collagen bundles interspersed by a patchy non-specific chronic inflammatory cell infiltrate (H&E stain, x40).

3. Discussion

PHG has been described in 15–77 [3,4] year olds with no clear sex or race predilection. Presenting symptoms are non-specific such as cough, chest pain, breathlessness and fever, it is present incidentally in 25% of patients [3]. The exact aetiology is so far unknown, but there have been associations with fungal, mycobacterial infections [5] and immune mediated phenomena as there are reports of patients with raised anti-nuclear, anti-globulin and rheumatoid factor [3,5]. There is also a consideration that it might be related to other fibro-sclerosing conditions such as sclerosing mediastinitis, retroperitoneal fibrosis and sclerosing cholangitis [2].

PHG is often found as solitary or multiple opacities with the appearances of pulmonary malignancy or infection on chest radiography and CT scanning, Where there are multiple randomly distributed pulmonary nodules as in this case, the differential is broad including; malignancy (metastatic or primary), infection (tuberculosis, histioplasmosis, septic emboli and fungal infections), autoimmune causes (rheumatoid arthritis, Granulomatosis with polyangiitis) and granulomatous disease (sarcoidosis, lymphatoid granulomatosis and plasma cell granuloma) [5,6].

Multidisciplinary teams are a vital part of deciding the best approach in these complex cases. Twenty-five percent of high-risk individuals screened for lung cancer will have an abnormal chest CT [7]. Though FDG-PET does give useful information, the next confirming step is often to seek tissue diagnosis. The options are often CT- guided (sensitivity of 0.81–0.97 [7]) or trans-bronchial biopsy (sensitivity 0.70 [7]). Pneumothorax, as occurred in this case, occurs at a higher rate of 15% in CT-guided versus 1.6% in trans-bronchial biopsies. However CT guided biopsies are associated with a lower cost and a third of the rate of subsequently requiring VATs wedge resection where the initial biopsy is non-diagnostic [7].

A recent systematic review suggests FDG-PET has a pooled sensitivity of 0.82 (95% CI, 0.76–0.87) and specificity 0.81 (95% CI, 0.66–0.90) in differentiating malignant from benign nodules [6]. This patient had an SUV of 6.9, SUV is a measure which reduces variability introduced by patient size and the amount of FDG uptake [8]. SUV thresholds are not widely accepted as they have huge variability due to situational, physiological and biological sources of error, for example differences in renal function, compliance with fasting pre-procedure, accuracy of weight measurement and biological differences in tracer uptake (which can amount to 10% variability) [8]. A high SUV should not be used in isolation as a marker of malignancy but rather its value lies in interpreting SUV comparatively where follow up scans are performed, or where a patient has biopsy proven malignancy and the clinician seeks to asses response to treatment [8].

FDG-PET can be falsely positive, as occurred in this case. PHG, amongst several non-cancerous entities, can only be diagnosed on histological basis. PHG is a benign disease with a good prognosis [5] . There are reports of the use of corticosteroids and resections, however there is no definitive treatment for PHG [4,5]. Most commonly active monitoring with imaging is all that is necessary, as occurred in this patient who remains stable with the disease. Hence, if an alternative diagnosis to malignancy is not supported by preliminary assessment in cases with suspected lung cancer, a histological diagnosis must be sought.

4. Conclusion

PHG is a rare diagnosis, not well known among generalists. Radiological presentation such as this in an individual with high risk of malignancy, based on age and smoking history, could be mistaken for metastatic cancer. These patient could endure significant anxiety and there is the potential for them being denied lifesaving treatment such as a critical care bed if they presents through the emergency route. We stress the importance of lung multidisciplinary team involvement, however there are limitations to this approach in that cancer MDTs tend to be looking for malignancy and as a consequence, do not always fully investigate for other differentials such autoimmune, infectious and granulomatous pathologies.

With increasing confidence in imaging techniques, it is important to take care that positive FDG uptake on PET scan should not dissuade from seeking definitive tissue diagnosis as long as the patient is fit for the procedure. In this case, after an image guided biopsy failed to provide a firm diagnosis, the decision to proceed to VATs wedge resection ultimately is what confirmed the diagnosis. It showed the characteristic concentric hyaline lamellae with perivascular chronic inflammatory cells [1], reassuring the patient and giving them a positive future outlook.

Conflict of interest statement

The authors whose names are listed immediately below certify that they have no affiliations with or involvement in any organisation or entity with any financial or other interest in the subject matter or materials discussed in this case report.

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