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Multicentric Castleman's disease of the lungs mimicking a multifocal adenocarcinoma

Authors: Ghaith Qsous¹, Wael Al-Qsous², Thomas Taylor³, Malcolm Will¹

1. Department of Thoracic Surgery, Edinburgh Royal Infirmary, Edinburgh

2. Department of Pathology, Western General Hospital, Edinburgh

3. Department of Radiology, Ninewells Hospital, Dundee

Correspondence to:

Dr Ghaith Qsous

Department of Thoracic Surgery, address, Edinburgh, EH4 2XU, UK.

Email: Ghaith.qsous@nhslothian.scot.nhs.uk

Tel: +447888166631

Summary:

A 76 year old woman presented with fever of unknown origin, night sweats and weight loss. She had no pulmonary symptoms. Investigations revealed bilateral ground glass lung lesions which were subsequently followed up with imaging. Two years later, a follow up CT scan revealed an increase in the size of the lesions which exhibited a more solid appearance. A diagnostic biopsy was difficult to perform and the patient underwent a left upper lobectomy for suspected primary lung malignancy. Histological examination showed lung involvement by Castleman's disease of plasma cell type which displayed a multifocal distribution. There was no evidence of nodal involvement. Following discussion at the Multidisciplinary Team meeting and correlation with radiology, a diagnosis of multicentric Castleman's disease of the lung was made.

Herein, we present an unusual case of multicentric Castleman's disease of the lung mimicking primary lung carcinoma. Our case highlights the importance of considering this entity in the differential diagnosis of multifocal lung lesions with a ground glass-like appearance to allow early diagnosis and management.

Background:

Lung nodules are common incidental findings with a wide differential diagnosis that includes infections, benign lesions and primary and secondary lung malignancies. Appropriate treatment depends on the exact nature of the lesion. In cases where reaching a definitive diagnosis is challenging, a multidisciplinary approach with input from various specialities, is essential to reach an appropriate management plan.

Castleman's disease (CD) is a relatively rare disorder characterised by proliferation of lymphoid tissue and can be localised (unicentric) or multicentric^{2,3,4}. It occurs most

commonly in adults but can also present in children. The most common clinical presentation is mediastinal lymph node enlargement. Lung involvement by Castleman's disease of the lung is rare and can pose a diagnostic challenge.

We describe a case of multicentric Castleman's disease primarily involving the lung with no evidence of nodal involvement which was clinically highly suspicious of a primary lung malignancy. Our case highlights the importance of considering this entity in the differential diagnosis of single and multifocal lung lesions especially those with a ground glass-like appearance.

Case Presentation:

A 76 years old lady, non smoker, who is known to have diverticular disease presented two years ago with fever of unknown origin, night sweats, weight loss, upper back pain and diarrhoea. She had no respiratory symptoms. Her blood tests showed high inflammatory markers with no other significant blood abnormality. The differential diagnoses included diverticular disease, discitis and osteomyelitis all of which were excluded by whole spine MRI and CT scans. However, an incidental finding on a chest CT was the presence of mixed ground-glass and soft tissue density in the left upper lobe of lung measuring 1.7 cm x 0.7 cm in addition to further separate small ground glass nodule anteriorly in the left upper lobe (Figure 1).

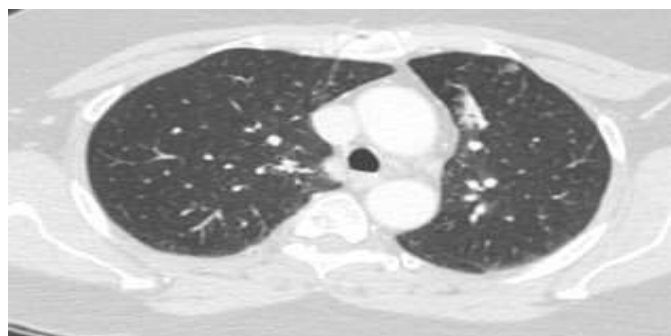


Fig. 1: CT scan shows mixed ground-glass and soft tissue density in the left upper lobe

Investigations:

Decision by multidisciplinary team was taken to follow up the lesion lesions with a chest CT scan which showed stability in the size of the lesions within the next 15 months. Accordingly, follow up continued with CT scan which was performed 2 years after her initial presentation. This showed a slight increase in the size of the left upper lobe nodule which now measured 17 x 10 mm (previously 17 x 7 mm) and it had an increased soft tissue component. The ground glass nodule anteriorly within the left upper lobe had increased from 5.5 mm to 8.5 mm (Figure 2). Further small ground glass nodules were now noted in the right lung.

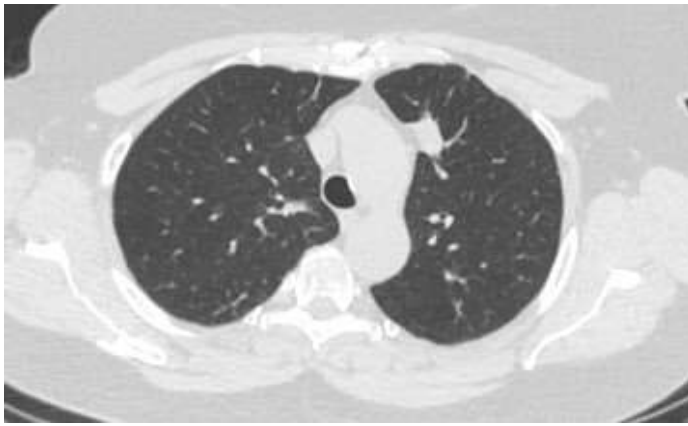


Fig. 2: Left upper lobe nodule.

A PET CT scan was performed and the nodule on the medial aspect of the anterior segment of left upper lobe, showed increased FDG uptake (SUVmax - 4.8 g/ml) (Mediastinal Blood Pool SUV max 3.2g/ml) (Fig.3 , Fig 4). The 5 mm peripheral nodule in the anterior segment of left upper lobe did not show any FDG uptake (Figures 5a and 5b), but at 8mm is at the borderline of sensitivity for this scanner

Unfortunately, due to the location of the larger lesion near the vessels it was not possible to do bronchoscopic or percutaneous biopsy. The Herder score was calculated at 81% risk of malignancy.

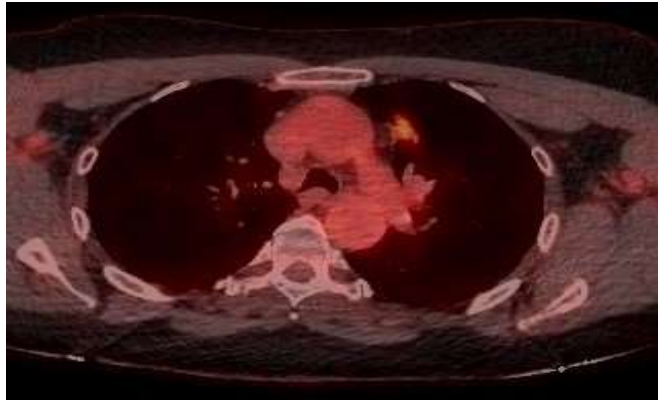


Fig. 3 : PET scan shows the nodule on the medial aspect of the anterior segment of left upper lobe with high FDG uptake.

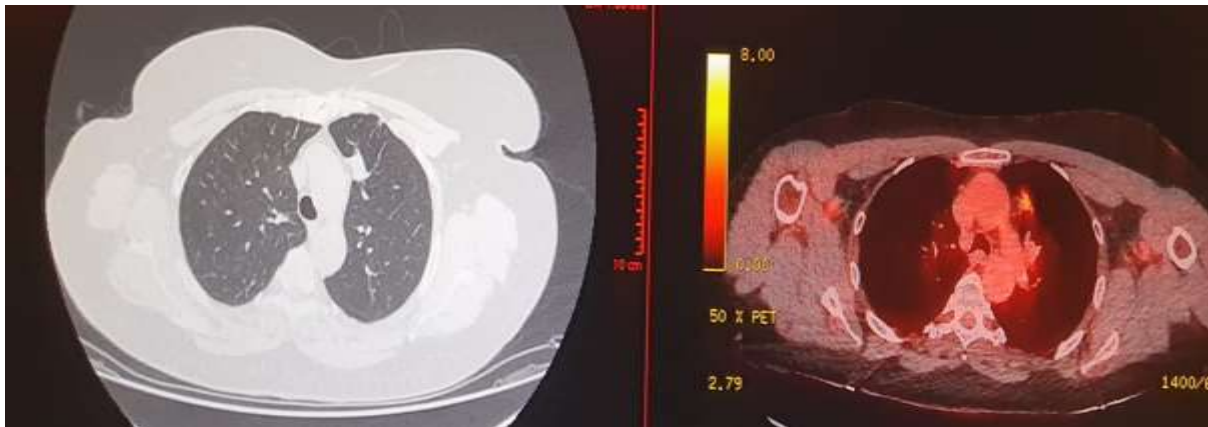


Fig. 4 : CT and PET scan for the main lesion in left upper lobe.

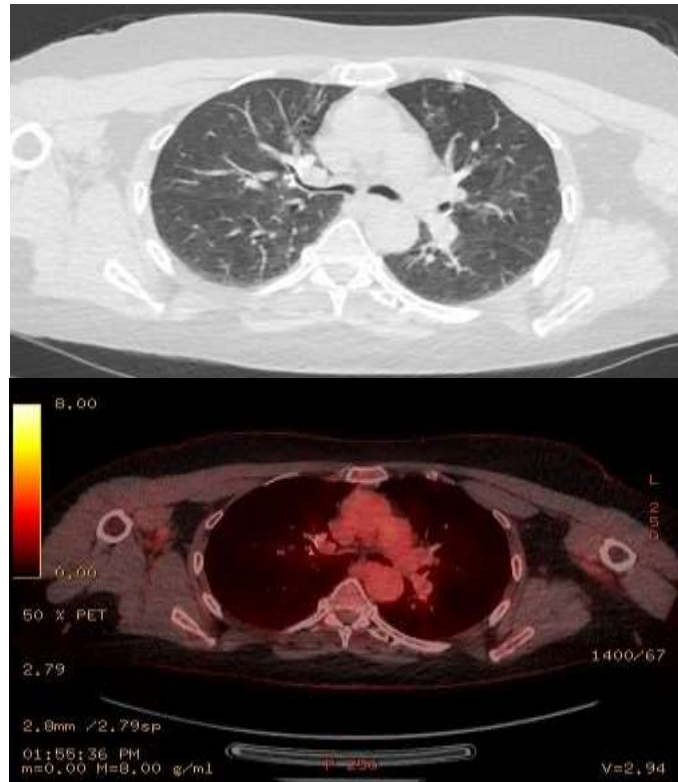


Fig.5 a,b: 5 mm peripheral nodule in the anterior segment of left upper lobe did not show any FDG uptake.

Differential Diagnoses:

Differential diagnosis included primary lung cancer, secondary lung metastasis, lymphoma and a benign lesion. The case was discussed in the multidisciplinary team and taking in consideration increasing the size of the nodules, transforming from ground glass to solid lesion and increased the uptake on the PET scan differential diagnosis was toward primary malignant pathology of the lung.

Treatment:

As there was high suspicion of malignancy the plan was to proceed for surgery as minimal invasive lung resection +- frozen section.

A video-assisted thoracoscopy (VATS) left upper lobectomy was performed and the patient recovered well without any postsurgical complications. The specimen was sent for histopathological examination.

Outcome:

Histological examination of the lobectomy specimen showed multifocal infiltration of the lung parenchyma by a dense infiltrate that consisted of numerous numerous reactive lymphoid follicles with prominent germinal centres in addition to many rather atretic looking follicles (Figure 4A). The interfollicular areas contained sheets of mature looking plasma cells with frequent Russell bodies also noted (Figure 4B). Immunohistochemistry showed the follicles exhibited a normal immunophenotype being negative for BCL2 (Figure 4C). The plasma cells in the interfollicular areas were highlighted with MUM1 and displayed a polytypic pattern of staining with kappa and lambda immunohistochemistry (Figures 4E, 4F). There was no evidence of an EBV or HHV8 infection. The appearances were consistent with multifocal lung involvement by Castleman's disease of plasma cell type. Examination of the recovered lymph nodes showed non-specific reactive change with no evidence of involvement by Castleman's disease.

Following the histological diagnosis, the findings were correlated with imaging which showed bilateral lung involvement and, therefore, a final diagnosis of multicentric Castleman's disease was made.

Later on the case was discussed on the lung MDT and they recommended long term follow up with the local haematology team and no need for further adjuvant treatment.

Discussion:

Castleman's disease is a rare lymphoproliferative disease that can affect single (unicentric) or multiple (multicentric) lymph nodes. Mainly there are two pathologic types; hyaline-vascular and plasma cell type.⁵ The cause of Castleman's disease is unknown, for example, the plasma-cell type could be a reaction to chronic infection. However, no bacteria or such organisms could be isolated.² The hyaline-vascular type may originate from an antigen stimulus involving a lymph node containing abnormal plasmacytoid monocytes.⁶

Castleman's disease most commonly affects young males and children. Common sites affected include neck, mediastinum, abdomen and rarely the retroperitoneum.⁶ Lung involvement is a very rare presentation of CD. The typical appearance on a CT scan is an enhancing mediastinal nodal mass mimicking lymphoma, thymoma, or neurogenic tumor.³ Patients with Castleman's disease are often asymptomatic or has non-specific symptoms such as fever, weight loss, diarrhea, anemia.⁷ This presents a challenge in making the diagnose of CD particularly as the finding imaging are hard to discriminate from lung malignancy. The treatment of unicentric Castleman's disease is usually with surgery or radiotherapy while multicentric disease usually treated with chemotherapy and/or steroids.²

Yeh et. al reported a case of 42 year old male patient who presented with chronic cough and a CT scan showed 4.5 cm x 3 cm mass located in the left upper lobe. The patient underwent surgery due to concern of malignancy. Final pathology showed hyaline-vascular lymph node hyperplasia, compatible with Castleman's disease.² Luo et. Al described 48 cases of intrathoracic Castleman's disease over 20 years. Of these, only 3 cases were confined as unicentric and underwent surgery. On the other hand, all multicentric CD treated with chemotherapy or observation depends on the severity of the symptoms but no one was treated as therapeutic resection.⁴

Incidental findings of lung nodules are common and pose diagnostic challenge due to wide differential of benign or malignant diseases. The multidisciplinary team approach is skeletal to guide treatment of these nodules. Surgical resection is frequently required when biopsy is not possible and confirms diagnosis as well as being the recommended treatment.

Learning Points:

- Castleman's disease of the lungs is very rare and therefore can pose a diagnostic challenge.
- Castleman's disease should be considered as a rare cause of multifocal lung lesions, including those with ground glass appearance.
- Multidisciplinary team discussions are essential in approaching difficult lung lesions to allow early diagnosis and management.

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Figures and legends:

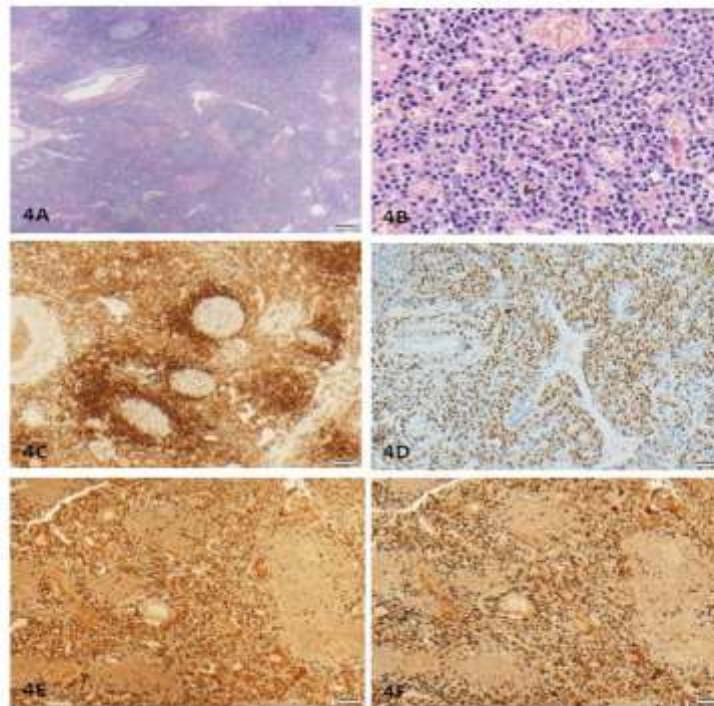


Figure 4A: Histological examination showed infiltration of the lung by an infiltrate that included reactive follicles in addition to atretic follicles (H&E x 4). **Figure 4B:** The interfollicular areas contained sheets of plasma cells including Russell bodies (H&E X 20). **Figures 4C:** The follicles were negative for BCL2 (H&E X 4). **Figures 4D, 4E and 4F:** The plasma cells stained positively for MUM1 and were polytypic with kappa and lambda immunostains (H&E X 4).