The Many Faces of Pulmonary Lymphoma: Pearls and Pitfalls

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Learning objectives

To illustrate typical patterns of pulmonary involvement in subtypes of aggressive and indolent lymphoma on CT and FDG PET-CT.

To demonstrate atypical patterns of pulmonary involvement where lymphoma mimics other pathologies.

To discuss investigation of solitary pulmonary lesions, with emphasis on overlap of appearances between lymphoma and bronchial carcinoma and the importance of biopsy.

Pulmonary Post Transplant Proliferative Disorder (PTLD) will be discussed as a diagnosis which should be considered in patients following solid organ transplant.
Background

Pulmonary involvement in lymphoma is most commonly seen in the context of disseminated nodal and extranodal disease. The most common lymphoma subtypes comprising Hodgkin Lymphoma (HL), Diffuse Large B Cell Lymphoma (DLBCL) and Marginal Zone Lymphoma (MZL) often demonstrate typical radiological features and patterns of distribution.

However, pulmonary lymphoma can present with disease confined to, or predominantly within the thorax. This has been previously described in the literature, particularly for MALT$^{1,2}$. In these cases, differentiation from other malignancies or benign processes can be difficult. This is particularly problematic when the presenting radiological abnormality is a solitary pulmonary mass, as the appearances are indistinguishable from a bronchogenic malignancy. As the treatment of these two disease entities is very different, biopsy of solitary lesions must be undertaken wherever possible to ensure optimal patient management.

Post transplant lymphoproliferative disease is a condition which occurs in patients following solid organ transplant. It is related to immunosuppression and EBV infection and occurs in around 5-10% of lung and cardiac transplant patients, often in the first 1-2 years following transplant$^{3}$. 
Findings and procedure details

A cohort of 150 patients with a histological diagnosis of lymphoma who underwent CT between 2008-2012 were reviewed. 31 of these patients also had a FDG PET CT scan. We found that there were imaging features that had greater association with certain subsets of lymphoma.

Three subsets of lymphoma demonstrate distinctive disease patterns with pulmonary involvement.

**Hodgkin Lymphoma**

- Bulky mediastinal and hilar lymph nodes with contiguous infiltration into the lung parenchyma. Fig. 1 on page 7 Fig. 2 on page 7 Fig. 3 on page 8
- Lung nodules usually discrete and well defined, sometimes with cavitation Fig. 4 on page 9
- Extrathoracic disease less common
- High intensity FDG uptake on PET CT Fig. 5 on page 10

**DLBCL**

- Multiple lung nodules which can be either well defined or irregular Fig. 6 on page 11
- Extrathoracic nodal and extranodal disease common
- High intensity FDG uptake on PET CT Fig. 7 on page 12

**Marginal Zone Lymphoma**

- Often multifocal with mixed interstitial and airspace components Fig. 8 on page 13 Fig. 9 on page 14 Fig. 10 on page 15
- Variable FDG uptake on PET CT

**Atypical patterns of Pulmonary Lymphoma Mimicking other Pathology**

**Solitary Pulmonary Nodule/ Mass**

Of the 31 PET CT cases reviewed, 14 were performed to stage a potential lung cancer and the diagnosis of lymphoma was only reached following resection or biopsy.
Lymphoma presenting as a solitary pulmonary nodule or mass generally shows high intensity FDG uptake on PET-CT and is indistinguishable from primary bronchial carcinoma Fig. 11 on page 16 Fig. 12 on page 17 Fig. 15 on page 20. Lung nodules with low to intermediate FDG uptake and those with air bronchograms have very similar appearances to bronchial adenocarcinoma Fig. 13 on page 18 Fig. 14 on page 19. In our series, marginal zone lymphoma was the most common mimic of a peripheral lung cancer.

FDG PET-CT characteristics of solitary pulmonary nodules

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<tr>
<th>Lymphoma subtype</th>
<th>Number of cases</th>
<th>SUV range (average)</th>
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<tbody>
<tr>
<td>MZL</td>
<td>10</td>
<td>2.5- 12.4 (6.2)</td>
</tr>
<tr>
<td>FL</td>
<td>1</td>
<td>3.4</td>
</tr>
<tr>
<td>DLBCL</td>
<td>3</td>
<td>16.0- 27.2 (22.4)</td>
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Radiological Patterns of Lymphoma Mimicking other Pathologies

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<thead>
<tr>
<th>Radiological Pulmonary Abnormality</th>
<th>Lymphoma Mimic</th>
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<tr>
<td>Cavitating nodules with groundglass halo</td>
<td>Invasive aspergillosis Fig. 17 on page 22 Fig. 18 on page 23 Fig. 19 on page 24</td>
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<tr>
<td>Interstitial thickening</td>
<td>Interstitial pneumonia or lymphangitis Fig. 20 on page 25 Fig. 21 on page 26 Fig. 22 on page 27</td>
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<tr>
<td>Peripheral wedge shaped consolidation</td>
<td>Infection or bronchial adenocarcinoma Fig. 16 on page 21 Fig. 17 on page 22</td>
</tr>
<tr>
<td>Multiple nodules</td>
<td>Metastases from other malignancy Fig. 6 on page 11 Fig. 7 on page 12</td>
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Post Transplant Proliferative Disorder

Post transplant lymphoproliferative disease is a condition which occurs in patients following solid organ transplant and is related to immunosuppression and EBV infection. It occurs in around 5-10% of lung and cardiac transplant patients, most often in the first 1-2 years following transplant.
PTLD is classified as either polymorphic or monomorphic. Polymorphic PTLD commonly responds to a reduction in immunosuppressive therapy. Monomorphic PTLD is most often Non Hodgkins Lymphoma of B cell origin with DLBCL being the most common histological type, response to a reduction in immunosuppressive therapy is less likely and treatment with chemotherapy and/or monoclonal antibody is often required. Prognosis is variable but often poor.

Imaging usually shows solid masses within the allograft, often with hilar and mediastinal lymphadenopathy. The tumours are typically highly FDG avid on PET-CT. Fig. 23 on page 28 Fig. 24 on page 29
Fig. 1: Fig 1-3. 21 year old male patient with newly diagnosed HL with bulky mediastinal lymphadenopathy and chest wall invasion with sternal destruction. There is direct infiltration of the left lung from the hilum and mediastinum, with contiguous lung nodules containing air bronchograms. Tumour nodules involve the pleura anteriorly and there is a small right pleural effusion. The tumour shows high intensity FDG uptake.

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Fig. 2: Fig 1-3. 21 year old male patient with newly diagnosed HL with bulky mediastinal lymphadenopathy and chest wall invasion with sternal destruction. There is direct infiltration of the left lung from the hilum and mediastinum, with contiguous lung nodules containing air bronchograms. Tumour nodules involve the pleura anteriorly and there is a small right pleural effusion. The tumour shows high intensity FDG uptake.

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**Fig. 3:** Fig 1-3. 21 year old male patient with newly diagnosed HL with bulky mediastinal lymphadenopathy and chest wall invasion with sternal destruction. There is direct infiltration of the left lung from the hilum and mediastinum, with contiguous lung nodules containing air bronchograms. Tumour nodules involve the pleura anteriorly and there is a small right pleural effusion. The tumour shows high intensity FDG uptake.

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**Fig. 4:** Figs 4 & 5. CT and FDG PET-CT images in a 19 year old female with newly diagnosed Hodgkin's disease. There are well defined rounded cavitating lung nodules which show high intensity FDG uptake. The patient also had bulky mediastinal and hilar lymphadenopathy with direct infiltration of the perihilar lung parenchyma (not shown). There are small pericardial and left pleural effusions.

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Fig. 5: Figs 4 & 5. CT and FDG PET-CT images in a 19 year old female with newly diagnosed Hodgkin's disease. There are well defined rounded cavitating lung nodules which show high intensity FDG uptake. The patient also had bulky mediastinal and hilar lymphadenopathy with direct infiltration of the perihilar lung parenchyma (not shown). There are small pericardial and left pleural effusions.

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**Fig. 6:** Figs 6 & 7. CT and coronal fused FDG PET-CT images in a 69 year old female who presented with multiple lung nodules. CT guided lung biopsy showed diffuse large B-cell NHL. CT showed multiple well defined rounded solid nodules of varying size throughout both lungs. The nodules show high intensity FDG uptake. There was no lymphadenopathy and small right renal nodules were the only other site of disease (seen on the coronal PET-CT image).

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Fig. 7: Figs 6 & 7. CT and coronal fused FDG PET-CT images in a 69 year old female who presented with multiple lung nodules. CT guided lung biopsy showed diffuse large B-cell NHL. CT showed multiple well defined rounded solid nodules of varying size throughout both lungs. The nodules show high intensity FDG uptake. There was no lymphadenopathy and small right renal nodules were the only other site of disease (seen on the coronal PET-CT image).

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**Fig. 8:** Figs 8 & 9. Pulmonary MALT lymphoma in a 70 year old male presenting with multiple lung masses. The lesions are predominantly peripheral and wedge shaped with prominent air bronchograms. There is also basal subpleural interstitial thickening which is likely to be due to interstitial pneumonia, MALT lymphoma may cause similar interstitial shadowing, but is less likely in this case due to it's diffuse nature. A smooth right posterior pleural mass is also likely to be due to lymphoma.
Fig. 9: Figs 8 & 9. Pulmonary MALT lymphoma in a 70 year old male presenting with multiple lung masses. The lesions are predominantly peripheral and wedge shaped with prominent air bronchograms. There is also basal subpleural interstitial thickening which is likely to be due to interstitial pneumonia, MALT lymphoma may cause similar interstitial shadowing, but is less likely in this case due to it's diffuse nature. A smooth right posterior pleural mass is also likely to be due to lymphoma.

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Fig. 10: CT in a 46 year old male with MALT lymphoma. There are several areas of poorly defined interstitial shadowing within both lungs. The patient also had diffuse pleural thickening, a longstanding right hydropneumothorax and round atelectasis at the bases (not shown).

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Fig. 11: Figs 11 & 12. Pulmonary lymphoma in a 77 year old male, presenting as a solitary pulmonary nodule. The nodule is solid and well defined. FDG PET-CT showed very high intensity uptake (SUV max 27). The nodule was resected and histology showed diffuse large B-cell NHL. Bilateral subpleural interstitial fibrosis was longstanding and related to asbestos exposure.

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Fig. 12: Figs 11 & 12. Pulmonary lymphoma in a 77 year old male, presenting as a solitary pulmonary nodule. The nodule is solid and well defined. FDG PET-CT showed very high intensity uptake (SUV max 27). The nodule was resected and histology showed diffuse large B-cell NHL. Bilateral subpleural interstitial fibrosis was longstanding and related to asbestos exposure.

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Fig. 13: Figs 13 & 14. Pulmonary lymphoma presenting as a solitary pulmonary nodule in a 60 year old female. The nodule is well defined with a lobulated contour and shows only low to intermediate intensity FDG uptake (SUV max 3.0). Biopsy showed MALT lymphoma.

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**Fig. 14:** Figs 13 & 14. Pulmonary lymphoma presenting as a solitary pulmonary nodule in a 60 year old female. The nodule is well defined with a lobulated contour and shows only low to intermediate intensity FDG uptake (SUV max 3.0). Biopsy showed MALT lymphoma.

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Fig. 15: Fig 15. Left lung mass in an 86 year old male with follicular lymphoma and possible transformation. The mass is well defined with a low density centre and mimics a bronchial carcinoma. There is also mediastinal lymphadenopathy and a slightly enlarged left axillary node.

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Fig. 16: Pulmonary lymphoma mimicking infection in a 64 year old female with follicular NHL. CT shows widespread bilateral perihilar and basal airspace shadowing with air bronchograms. The differential diagnosis of this appearance is broad, but in a non acutely unwell patient includes pulmonary lymphoma and bronchial adenocarcinoma.

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Fig. 17: Figs 17 & 18. Pulmonary lymphoma mimicking fungal infection. CT images in a 56 year old man with a long history of MALT lymphoma. There were multiple peripheral wedge shaped opacities in both lungs with a left upper lobe lesion showing cavitation with a central ball and air crescent sign. The lung lesions showed 'halos' of ground-glass shadowing. The appearances were considered typical of invasive aspergillosis and the patient was treated with antifungal therapy, but unfortunately deteriorated and died. Post mortem showed multiple lung deposits of MALT lymphoma with no evidence of fungal infection.

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Fig. 18: Figs 17 & 18. Pulmonary lymphoma mimicking fungal infection. CT images in a 56 year old man with a long history of MALT lymphoma. There were multiple peripheral wedge shaped opacities in both lungs with a left upper lobe lesion showing cavitation with a central ball and air crescent sign. The lung lesions showed 'halos' of ground glass shadowing. The appearances were considered typical of invasive aspergillosis and the patient was treated with antifungal therapy, but unfortunately deteriorated and died. Post mortem showed multiple lung deposits of MALT lymphoma with no evidence of fungal infection.

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Fig. 19: Pulmonary lymphoma mimicking fungal infection in an 83 year old female presenting with multiple lung nodules. Several of the nodules were irregular with a predominant airspace component and with a prominent ground glass halo, mimicking invasive aspergillosis. CT guided lung biopsy showed MALT lymphoma.
**Fig. 20:** Figs 20-22. Pulmonary lymphoma mimicking interstitial pneumonia in a 69 year old patient with Mantle Cell NHL. Earlier CT (Fig 20) showed areas of subpleural interstitial shadowing anteriorly within both lungs which were felt likely to represent interstitial pneumonia. However, on follow up 6 months later these had enlarged and formed masses with an airspace pattern. FDG PET-CT (Fig 21) showed high intensity FDG uptake within the lesions. CT guided biopsy showed Mantle Cell NHL.

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Fig. 21: Figs 20-22. Pulmonary lymphoma mimicking interstitial pneumonia in a 69 year old patient with Mantle Cell NHL. Earlier CT (Fig 20) showed areas of subpleural interstitial shadowing anteriorly within both lungs which were felt likely to represent interstitial pneumonia. However, on follow up 6 months later these had enlarged and formed masses with an airspace pattern. FDG PET-CT (Fig 21) showed high intensity FDG uptake within the lesions. CT guided biopsy showed Mantle Cell NHL.

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**Fig. 22:** Figs 20-22. Pulmonary lymphoma mimicking interstitial pneumonia in a 69 year old patient with Mantle Cell NHL. Earlier CT (Fig 20) showed areas of subpleural interstitial shadowing anteriorly within both lungs which were felt likely to represent interstitial pneumonia. However, on follow up 6 months later these had enlarged and formed masses with an airspace pattern. FDG PET-CT (Fig 21) showed high intensity FDG uptake within the lesions. CT guided biopsy showed Mantle Cell NHL.

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Fig. 23: Fig 23. Post transplant lymphoproliferative disease (diffuse large B-cell lymphoma) in a 54 year old female presenting 13 months following bilateral lung transplant for alpha 1 anti-trypsin deficiency. CT shows a discrete right hilar mass with contiguous lower paratracheal lymphadenopathy.

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Fig. 24: Fig 24. Post transplant lymphoproliferative disease (diffuse large B-cell lymphoma), in a 61 year old man 4 months following double lung transplant for alpha 1 anti-trypsin deficiency. CT shows large bilateral hilar and mediastinal nodes and multiple well defined rounded cavitating lung nodules.

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Conclusion

Radiologists should recognise the diverse patterns of pulmonary involvement with lymphoma and the overlap of appearances with other malignancies, inflammatory processes and infective pathologies.

Lymphoma presenting as a solitary pulmonary lesion is indistinguishable from primary bronchial carcinoma and biopsy is vital to ensure correct management.
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