

Pulmonary manifestations of lymphoma: A pictorial essay

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Picture this by Jankharia, Mumbai, Maharashtra, India

ABSTRACT

Lymphomatous involvement of the lungs manifests in an infinite number of ways. Often there is a considerable overlap of the patterns of manifestations which comes as a diagnostic challenge to the radiologist. We retrospectively reviewed the pulmonary manifestations of biopsy proven cases of primary or secondary non-Hodgkin's lymphoma or Hodgkin's lymphoma. The patterns of lung involvement were then classified into broad categories which included large masses, mass like consolidation, nodules with or without cavitation, ground glass and lymphangitis/ perilymphatic pattern. This article illustrates the spectrum of CT manifestations of lung involvement in non-Hodgkin's lymphoma as well as Hodgkin's lymphoma.

KEY WORDS: biopsy, lymphoma, pulmonary

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Submitted: 06-May-2019 **Revised:** 18-Oct-2019 **Accepted:** 02-Nov-2019 **Published:** 04-May-2020

INTRODUCTION

Primary pulmonary lymphoma

“Primary pulmonary lymphoma represents a monoclonal lymphoid proliferation affecting the lungs in a patient with no detectable extra-thoracic lymphoma for at least 3 months after the initial diagnosis.”^[1]

Primary pulmonary lymphomas are rare and represent 0.5% of all primary lung neoplasms. The lymphoproliferative disorders that present with primary lung involvement include extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue origin (MALT lymphoma), diffuse large B-cell lymphoma (DLBCL), and lymphomatoid granulomatosis.^[1] Primary non-Hodgkin's lymphomas of the lung are a rare subtype of extranodal lymphomas that are usually low-grade B-cell types. These low-grade lymphomas originate from the MALT. The frequency of primary lymphomas arising in the

lung as the primary site is estimated to be <1% of all lymphomas.^[2]

Secondary pulmonary lymphoma

The incidence of pulmonary involvement in association with extrathoracic or diffuse lymphoma is more common than primary pulmonary lymphoma.^[3] Non-Hodgkin's lymphoma (NHL) is the most common type of lymphoma overall (80%–90% of all cases). It mainly consists of multiple mature B-cell subtypes such as follicular lymphoma and small lymphocytic lymphoma. Nearly half of the patients at their presentation have intrathoracic disease. Pulmonary parenchymal disease occurs in 24% of NHL, whereas Hodgkin's lymphoma (HL) which represents 10%–20% of all lymphoma cases has intrathoracic disease at presentation in 85% of cases.^[1]

In HL, pulmonary involvement is almost always associated with intrathoracic lymphadenopathy.

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How to cite this article: Angirish B, Sanghavi P, Jankharia B. Pulmonary manifestations of lymphoma: A pictorial essay. Lung India 2020;37:263-7.

Access this article online	
Quick Response Code: 	Website: www.lungindia.com
	DOI: 10.4103/lungindia.lungindia_200_19

However, this is not the case in NHL, wherein pulmonary involvement frequently occurs in the absence of mediastinal disease.^[1]

Overall, pulmonary parenchymal involvement with lymphoma has been reported as 3.7% for extranodal NHL and as 12% for HD.^[4,5]

METHODOLOGY

We retrospectively reviewed the pulmonary abnormalities in 18 biopsy-proven patients with primary, secondary, or recurrent NHL or HL on chest computed tomography (CT) examinations, seen at our institution with CT/positron emission tomography-CT scans over a period of 10 years. Out of our 18 biopsy-proven cases, 5 patients had secondary pulmonary involvement. The rest all were primary pulmonary lymphoma, though these are rare.

The images were evaluated to determine the morphological pattern of appearance, laterality, localization, number, size, presence of thoracic lymphadenopathy, and secondary/combined findings. Patients were included in the study if parenchymal involvement and other manifestations of lymphoma were recognized at initial diagnosis or during initial therapy (secondary lymphoma) or if pulmonary findings developed after a disease-free interval after therapy (recurrent lymphoma). Patients with pleural effusion or mediastinal manifestations were excluded from the study.

Based on the predominant radiologic abnormalities, the lung lymphomas were categorized into five major patterns: (1) consolidation, (2) mass, (3) nodule, (4) ground-glass opacity (GGO), and (5) lymphangitis/perilymphatic. Area of consolidation was defined as homogeneous increase in pulmonary parenchymal attenuation obscuring the vessel margins and airway walls; mass was defined as rounded well-defined or moderately well-defined opacity >3 cm in maximum diameter; nodule was defined as rounded well-defined or moderately well-defined opacity ≤3 cm in maximum diameter; GGO was defined as a hazy increased attenuation of lung with preservation of bronchial and vascular margins. For every lung lesion identified, the presence of secondary associated features such as air bronchogram, bronchiectasis, calcification, and cavitation was also looked for. Other CT features, such as mediastinal lymphadenopathy, pleural effusions, and mosaic pattern, were also identified.^[6]

IMAGING PATTERNS

Masses

The pattern of CT findings of secondary pulmonary lymphoma consists of either solitary or multiple nodules, masses or mass-like consolidation, the masses usually ranging from 0.5 to 8 cm in diameter [Figure 1]. These large masses often have shaggy or ill-defined borders and are sometimes cavitary^[7] [Figure 2]. Cavitation is more

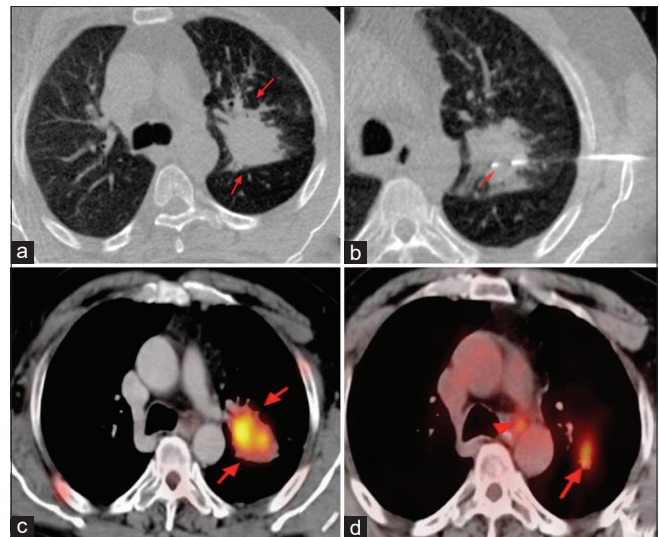


Figure 1: (a-d) Computed tomography (a) and computed tomography-guided biopsy (b) images of a 50-year-old patient presenting as a pulmonary mass (arrows) in the left upper lobe. Positron emission tomography/computed tomography (c and d) images show uptake in the mass (arrows) and aortopulmonary window region lymph node (arrowhead). Biopsy showed a primary pulmonary lymphoma-T-cell-rich B-cell non-Hodgkin's lymphoma

common in DLBCL, regardless of the immune status of the patient.^[1]

Primary pulmonary HL most commonly presents as single or multiple nodules with a predominantly seen upper lobe distribution.^[2] In a study by Lewis *et al.*, the most common finding with HL was mass or mass-like consolidation (seen in 80% of cases) whereas the most common finding observed with NHL was peribronchovascular interstitial thickening (seen in 69% of cases). Mediastinal lymph node enlargement was more commonly seen with HL (53%) than with NHL (19%)^[5] [Figure 3].

Nodules

In a study by Diederich *et al.*, pulmonary nodules were seen in 88% of cases of secondary pulmonary lymphoma. The nodules were multiple in number in 86% of cases and bilateral in distribution in 66% of cases [Figure 4]. Diffuse lung infiltration was seen in 27% of cases, and more than half of these patients showed nodules.^[7] The radiological differential of such multiple pulmonary nodules includes bronchogenic carcinoma, infections, and vasculitis.

Consolidation

The most commonly seen radiological appearance of primary NHL, particularly MALT lymphoma of the lung, is an area of opacification with poorly defined margins and air bronchograms seen within^[2] [Figures 5 and 6]. The localized area of consolidation seen in primary low-grade B-cell lymphoma may range from a small subsegmental area to an entire lobe, or less commonly, as multifocal and multilobar areas of consolidation.^[8,9] Such pulmonary parenchymal abnormalities show an indolent course, with slow growth

over a period of time.^[10] The bronchi traversing within such affected lung parenchyma may appear dilated or stretched and show a slightly narrowed lumen.^[11] A positive

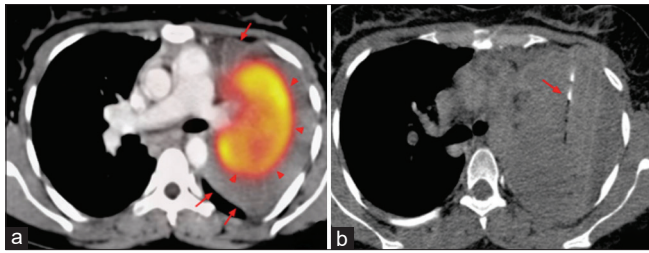


Figure 2: (a and b) Positron emission tomography/computed tomography (a) and computed tomography-guided biopsy (b) of a 27-year-old male patient presenting as a lung mass with a large homogeneous soft tissue density mass (arrows) in the left upper lobe encasing the left main pulmonary artery and abutting the pleura with fluorodeoxyglucose avid areas seen in the central part of the mass (arrowheads) which were targeted during the biopsy (b). Biopsy showed primary non-Hodgkin's lymphoma with a diffuse large B-cell phenotype

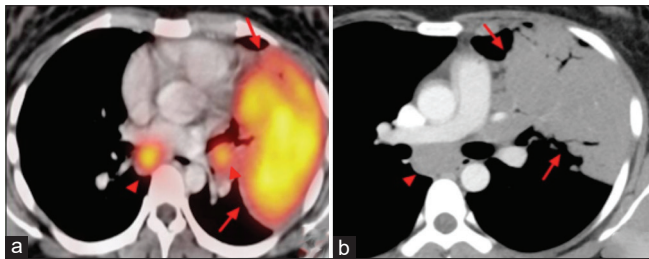


Figure 3: (a and b) Positron emission tomography/computed tomography (a) and computed tomography (b) images of a 27-year-old patient presenting with a large soft tissue mass in the superior lingula and the anterior segment of the left upper lobe (arrows) and mediastinal nodes (arrowheads). Biopsy was consistent with primary Hodgkin's lymphoma (lymphocyte rich)

“angiogram” sign, which consists of an “enhancing pulmonary vessel within a homogeneous area of consolidation,” and a halo of ground-glass attenuation at the margin of the lesion have also been reported in cases of MALT lymphoma, but these are nonspecific findings that can be seen in a number of other conditions as well, including bronchoalveolar cell carcinoma.^[1] The radiological differentials are organizing pneumonia and invasive mucinous adenocarcinoma.^[12]

Ground glass

GGO is the least common pattern of presentation of lung lymphoma^[6] [Figures 7 and 8]. Very limited literature is available for this pattern of presentation. Tokuyasu *et al.* reported two cases of lymphoma presenting as diffuse ground-glass opacities. The biopsy findings of these patients showed that the lymphoma cells were mainly infiltrating the bronchiolar walls and alveolar septa of the lungs, but were not seen in the alveolar spaces. These microscopic findings were an evidence of hematogenous spread of lymphoma cells. Thickening of the alveolar walls due to invasion by lymphoma cells, without involvement of the lymphatics, was also noted. These findings suggest that the pathological mechanism underlying bilateral diffuse GGO on chest CT is the spread of lymphoma cells mainly via the vascular rather than lymphatic pathways, a pattern known to occur but rare.^[13] The differential diagnosis of radiological patterns of diffuse ground-glass opacities is broad and includes infection, diffuse alveolar hemorrhage, and interstitial lung disease.

Lymphangitis/perilymphatic

Secondary pulmonary lymphomas are known to present most commonly as bronchovascular or lymphangitis-like patterns with thickening of bronchovascular bundles and interlobular septae as seen in 41% cases^[4] [Figures 9 and 10].

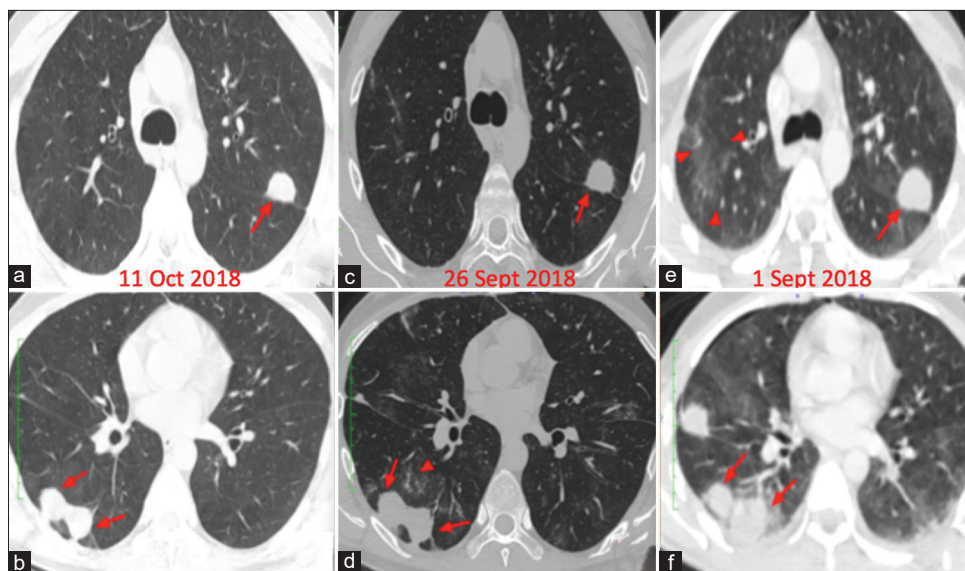


Figure 4: (a-f) Biopsy-proven case of secondary non-Hodgkin's lymphoma (diffuse large B-cell lymphoma). Close follow-up images of a 26-year-old male who presented with multiple lung nodules (arrows) and ground-glass opacities (arrowheads). On treatment, there was regression of the ground-glass opacities (arrowheads) seen in both the upper and lower lobes with mild reduction in the nodules (arrows)

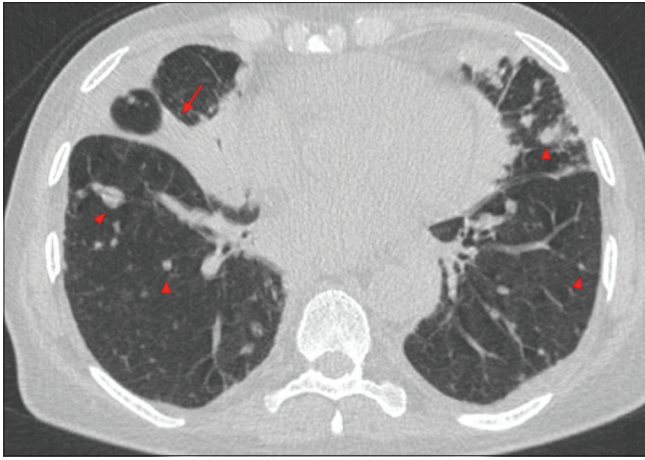


Figure 5: A 67-year-old patient presenting with patchy consolidation (arrow) and nodules (arrowheads) in both lungs. Biopsy showed secondary pulmonary lymphoma – high-grade (diffuse large B-cell lymphoma) non-Hodgkin’s lymphoma

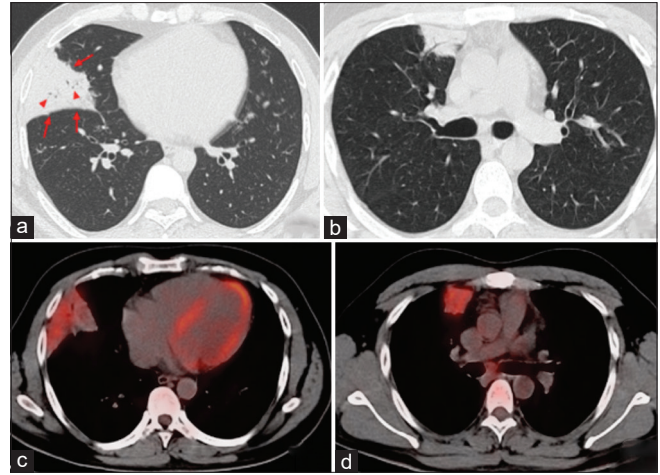


Figure 6: (a-d) Computed tomography (a and b) and positron emission tomography/computed tomography (c and d) of a 29-year-old male presenting with nonresolving consolidation (arrows) with air bronchograms (arrowheads) in the right middle lobe and the anterior segment of the right upper lobe (B and D). Biopsy showed primary low-grade B-cell non-Hodgkin’s lymphoma of follicle cell type

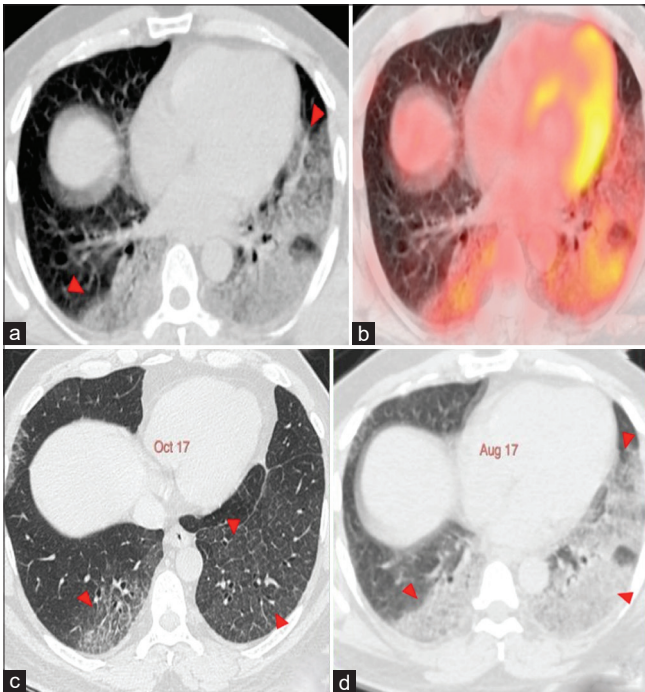


Figure 7: (A-D) Primary non-Hodgkin’s lymphoma (follicular type). Computed tomography scan (a) shows diffuse ground-glass opacities in the superior segments of both lower lobes (arrows). Note the absence of lung nodules and mass-like areas of consolidation. Positron emission tomography-computed tomography (b) shows fluorodeoxyglucose uptake in the areas of ground-glass opacities. Subsequent follow-up (c and d) on treatment shows significant resolution of the ground glass

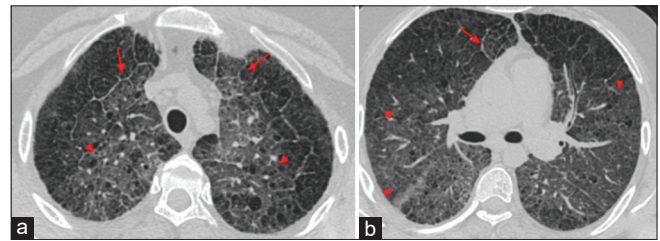


Figure 8: (a and b) A 27-year-old male presented with diffuse ground-glass opacities (arrowheads) and interlobular septal thickening (arrows). Biopsy showed primary non-Hodgkin’s lymphoma (diffuse large B-cell phenotype) of the lungs

Table 1: Summary of various pulmonary presentations of lymphoma

Pattern	Key radiological features
Masses	Solitary or multiple nodules, masses or mass-like consolidation, the masses usually ranging from 0.5 to 8 cm in diameter. Some masses may show cavitation
Consolidation	Area of opacification with poorly defined margins and air bronchograms seen within. Subsegmental to lobar involvement.
Ground glass	Rare, Bilateral diffuse ground-glass opacities.
Lymphangitis/ perilymphatic	Thickening of bronchovascular bundles and interlobular septae

These findings can be convincingly explained on the basis of the anatomy of the lymphatic system in the lungs. One typical method of spread of pulmonary lymphoma is along the lymphatics, most commonly in the form of retrograde spread of tumor seen directly from involved hilar or mediastinal nodes. However, parenchymal involvement can also result from antegrade spread from multiple foci. Hematogenous spread of

lymphoma is believed to be rare but is known to occur.^[5] These interstitial patterns consisting of perilymphatic nodules, septal, and peribronchovascular thickening can appear identical to those seen with lymphangitic carcinomatosis or sarcoidosis.^[12]

Pleural involvement

Primary pleural lymphoma is rare and presents often as two subtypes: primary effusion lymphoma or

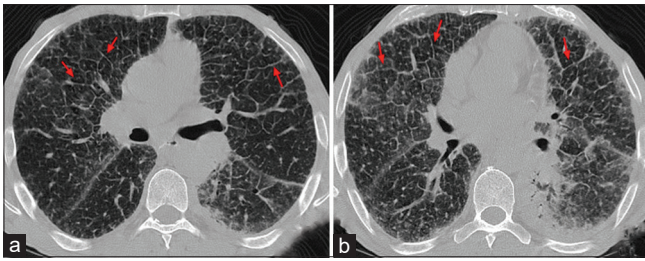


Figure 9: (a and b) Biopsy-proven case of primary non-Hodgkin's lymphoma of large B-cell phenotype showing perilymphatic pattern of spread seen as septal thickening (arrows)

pyothorax-associated lymphoma. Secondary pleural NHL may arise through hematogenous or lymphatic dissemination or by direct extension from pulmonary or nodal disease. Extrinsic lymphatic or venous compression by enlarged mediastinal lymph nodes may cause benign transudative effusion, which is more commonly seen in Hodgkin's disease.^[12] Pleural effusion is a common finding in patients with NHL, with a incidence of 16%–20%. Among them, 60% account for DLBCL lymphoma.^[12,14] Pleural involvement in lymphoma has a diverse presentation; however, pleural effusions were not the focus of this retrospective review.

The various presentations of pulmonary lymphoma are summarized in Table 1.

SUMMARY

The pulmonary manifestations of lymphoma are varied and can be a diagnostic challenge at times. These presentations can mimic a variety of disease patterns and lymphoma should be placed high among the differential diagnoses. A coordinated clinical and radiological approach should be followed and an aggressive workup should be done. Similarly, any new lung lesion in a known or treated case of lymphoma should be viewed with suspicion for disease spread or recurrence.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

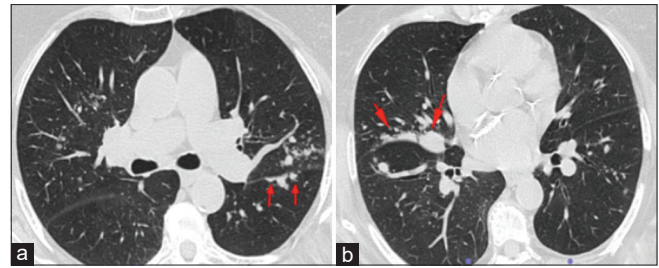


Figure 10: (a and b) Secondary non-Hodgkin's lymphoma in a known case of Sjogren's syndrome, showing perilymphatic pattern of distribution of lung nodules. Biopsy shows extranodal marginal zone lymphoma (arrows)

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Hare SS, Souza CA, Bain G, Seely JM, Frcpc, Gomes MM, et al. The radiological spectrum of pulmonary lymphoproliferative disease. *Br J Radiol* 2012;85:848-64.
- Lee KS, Kim Y, Primack SL. Imaging of pulmonary lymphomas. *AJR Am J Roentgenol* 1997;168:339-45.
- Mentzer SJ, Reilly JJ, Skarin AT, Sugarbaker DJ. Patterns of lung involvement by malignant lymphoma. *Surgery* 1993;113:507-14.
- Fujimoto Y, Nomura K, Shimizu D, Okuda T, Yoshida N, Matsumoto Y, et al. Pulmonary relapse of non-Hodgkin's lymphoma in bilateral upper lobes. *Intern Med* 2006;45:971-3.
- Lewis ER, Caskey CI, Fishman EK. Lymphoma of the lung: CT findings in 31 patients. *AJR Am J Roentgenol* 1991;156:711-4.
- Austin JH, Müller NL, Friedman PJ, Hansell DM, Naidich DP, Remy-Jardin M, et al. Glossary of terms for CT of the lungs: Recommendations of the nomenclature committee of the Fleischner Society. *Radiology* 1996;200:327-31.
- Diederich S, Link TM, Zühlsdorf H, Steinmeyer E, Wormanns D, Heindel W, et al. Pulmonary manifestations of Hodgkin's disease: Radiographic and CT findings. *Eur Radiol* 2001;11:2295-305.
- Bosanko CM, Korobkin M, Fantone JC, Rubin SB, Lynch JP. Lobar primary pulmonary lymphoma: CT findings. *J Comput Assist Tomogr* 1991;15:679-82.
- O'Donnell PG, Jackson SA, Tung KT, Hassan B, Wilkins B, Mead GM, et al. Radiological appearances of lymphomas arising from mucosa-associated lymphoid tissue (MALT) in the lung. *Clin Radiol* 1998;53:258-63.
- Au V, Leung AN. Radiologic manifestations of lymphoma in the thorax. *AJR Am J Roentgenol* 1997;168:93-8.
- King LJ, Padley SP, Wotherspoon AC, Nicholson AG. Pulmonary MALT lymphoma: Imaging findings in 24 cases. *Eur Radiol* 2000;10:1932-8.
- Bligh MP, Borgaonkar JN, Burrell SC, MacDonald DA, Manos D. Spectrum of CT findings in thoracic extranodal non-Hodgkin lymphoma. *Radiographics* 2017;37:439-61.
- Tokuyasu H, Harada T, Watanabe E, Touge H, Kawasaki Y, Endo A, et al. Non-Hodgkin's lymphoma accompanied by pulmonary involvement with diffuse ground-glass opacity on chest CT: A report of 2 cases. *Intern Med* 2009;48:105-9.
- Choy CF, Lee S. Pleural Lymphoma. *J Bronchol Int Pulmonol* 2016;23:146-8.