European Journal of Radiology 83 (2014) 1470–1482

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Review

Multimodality imaging of cardiothoracic lymphoma

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ARTICLE INFO

Article history:
Received 24 December 2013
Received in revised form 2 April 2014
Accepted 9 May 2014

Keywords:
Lymphoma
Thoracic
Cardiac
CT
MRI
PET/CT

ABSTRACT

Lymphoma is the most common hematologic malignancy and represents approximately 5.3% of all cancers. The World Health Organization published a revised classification scheme in 2008 that groups lymphomas by cell type and molecular, cytogenetic, and phenotypic characteristics. Most lymphomas affect the thorax at some stage during the course of the disease. Affected structures within the chest may include the lungs, mediastinum, pleura, and chest wall, and lymphomas may originate from these sites as primary malignancies or secondarily involve these structures after arising from other intrathoracic or extrathoracic sources. Pulmonary lymphomas are classified into one of four types: primary pulmonary lymphoma, secondary pulmonary lymphoma, acquired immunodeficiency syndrome-related lymphoma, and post-transplantation lymphoproliferative disorders. Although pulmonary lymphomas may produce a myriad of diverse findings within the lungs, specific individual features or combinations of features can be used, in combination with secondary manifestations of the disease such as involvement of the mediastinum, pleura, and chest wall, to narrow the differential diagnosis. While findings of thoracic lymphoma may be evident on chest radiography, computed tomography has traditionally been the imaging modality used to evaluate the disease and effectively demonstrates the extent of intrathoracic involvement and the presence and extent of extrathoracic spread. However, additional modalities such as magnetic resonance imaging of the thorax and ^{18}F-FDG PET/CT have emerged in recent years and are complementary to CT in the evaluation of patients with lymphoma. Thoracic MRI is useful in assessing vascular, cardiac, and chest wall involvement, and PET/CT is more accurate in the overall staging of lymphoma than CT and can be used to evaluate treatment response.

1. Introduction

Lymphoma is the most common hematologic malignancy [1], arising from white blood cells in the blood, bone marrow, spleen, or other solid organs. Intrathoracic involvement is much more common in Hodgkin lymphoma (HL) than non-Hodgkin lymphoma (NHL) [2]. The most commonly involved sites within the chest include the lungs, mediastinum, pleura, and chest wall, and lymphomas may originate from these sites as primary malignancies or secondarily involve these structures after arising from other intrathoracic or extrathoracic sources. Recognition of the thoracic manifestations of lymphoma is necessary for accurate diagnosis of the disease, and key features can be identified on multiple modalities such as chest radiography, chest CT, thoracic MRI, and PET/CT.

In this article, we review the current classification system of pulmonary lymphomas and describe key radiologic features of cardiothoracic lymphoma across multiple imaging modalities.

2. Epidemiologic and clinical features

Lymphoma is the most common hematologic malignancy, representing approximately 5.3% of all cancers and 55.6% of all blood cancers [1]. The incidence of lymphoma in the United States is approximately 22.5 per 100,000 individuals [1].

Most lymphomas affect the thorax at some stage during the course of the disease, and thoracic involvement is much more common in HL than NHL [2]. One of the most important risk factors is immunosuppression resulting from medications such as

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http://dx.doi.org/10.1016/j.ejrad.2014.05.018
0720-048X/

chemotherapeutic agents or infections such as the human immunodeficiency virus (HIV) [3]. For all lymphomas, lymphadenopathy is the most common abnormality reported at the time of presentation. "B symptoms" such as fever, night sweats, and weight loss, as well as additional nonspecific symptoms such as fatigue, may be present [3]. However, in the setting of pulmonary lymphoma, it should be noted that patients may be asymptomatic or present with different symptoms or combinations of symptoms depending on the specific histologic type of pulmonary lymphoma and the extent of disease.

3. Classification

The World Health Organization (WHO) published its first classification scheme for lymphoma in 2001 [4], and subsequently released an updated edition in 2008 [5]. The WHO classification system groups lymphomas into categories based on cell type and additional characteristics such as molecular, cytogenetic, and phenotypic features [5]. In summary, lymphomas are grouped into 5 different categories: mature B-cell neoplasms, mature T-cell and NK neoplasms, HL, histiocytic and dendritic cell neoplasms, and post-transplantation lymphoproliferative disorder [5].

4. Pulmonary lymphoma

Pulmonary lymphoproliferative disorders may be classified into reactive/non-neoplastic lymphoid lesions and malignant pulmonary lymphoproliferative disorders. This article focuses on the latter, which have been divided into primary pulmonary lymphoma, secondary pulmonary lymphoma, and lymphomas affecting immunocompromised patients, specifically AIDS-related lymphoma (ARL) and post-transplantation lymphoproliferative disorder (PTLD).

4.1. Primary pulmonary lymphoma

Primary pulmonary lymphoma is rare, representing less than 1% of malignant pulmonary neoplasms [6], less than 1% of all malignant lymphomas [7], and 3.6% of extranodal lymphomas [8]. The diagnostic criteria for primary pulmonary lymphoma include involvement of the lung, lobar, or primary bronchus, with or without mediastinal lymphadenopathy, but without evidence of extrathoracic lymphoma for at least 3 months following the initial diagnosis [9]. NHL represents 80% of primary pulmonary lymphomas, and the most common type is mucosa-associated lymphoid tissue (MALT) lymphoma. Patients with MALT lymphoma are typically asymptomatic and the prognosis is good. Diffuse large B-cell lymphoma (DLBCL) is the other major histology of primary pulmonary lymphoma, and is frequently seen in immunocompromised patients. In contrast to MALT lymphoma, these patients are usually symptomatic and may present with dyspnea, fever, and/or weight loss, and the prognosis is poor [10].

MALT lymphomas demonstrate a wide variety of findings on CT. Single or multiple pulmonary nodules (Fig. 1) or foci of consolidation are present in 70% of cases [10] (Fig. 2). These findings tend to be multiple and bilateral, as well as peribronchovascular in distribution, which can result in airway dilatation [10]. Hilar and/or mediastinal lymphadenoapthy is present in 30% of cases [10]. DLBCL usually manifests as solitary or multiple pulmonary nodules or masses, frequently with cavitation [10] (Fig. 3).

When primary pulmonary lymphoma manifests as pulmonary nodules, the differential diagnosis should include benign entities such as non-calcified granulomas, pulmonary infection such as fungal pneumonia and septic emboli, and vasculitides such as granulomatosis with polyangiitis. Malignant etiologies such as metastatic disease should be suspected in the setting of a known malignancy and multiple pulmonary nodules. In the setting of a solitary pulmonary nodule or mass, primary lung cancer must be included in the differential diagnosis. When consolidation is the predominant feature of primary pulmonary lymphoma, the differential diagnosis should include benign etiologies such as pneumonia, organizing pneumonia, and pulmonary hemorrhage. In the setting of non-resolving consolidation, low-grade pulmonary adenocarcinoma should be considered.

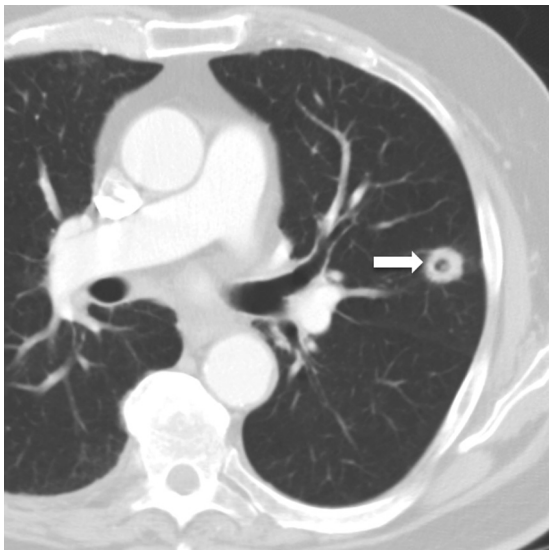

Fig. 1. Axial contrast-material enhanced CT image of a 37-year-old man demonstrates a solitary solid nodule with central cavitation (arrow) in the left upper lobe. CT-guided biopsy revealed MALT lymphoma.

4.2. Secondary pulmonary lymphoma

Secondary pulmonary lymphoma is much more common than primary pulmonary lymphoma. NHL represents 80–90% of all cases of secondary pulmonary lymphoma with nearly 50% of patients presenting with thoracic involvement and 24% with pulmonary parenchymal disease [11]. HL represents 10–15% of all cases of secondary pulmonary lymphoma with nearly 85% of patients presenting with thoracic involvement and 38% with pulmonary parenchymal disease [11].

The imaging findings in secondary pulmonary lymphoma are extremely variable, as a wide variety of primary lymphomas may secondarily involve the lung parenchyma. Three distinct patterns of pulmonary disease have been described: lymphangitic, nodular, and alveolar [12]. Overall, lymphadenopathy is the most frequent intrathoracic manifestation of secondary pulmonary lymphoma. Mass-like consolidation (Fig. 4) and interstitial thickening (Fig. 5) are the most common pulmonary manifestations of NHL and HL, respectively [13]. Pulmonary nodules measuring less than 1 cm, alveolar opacities, and pleural abnormalities such as nodules and effusions are seen in equal frequency in NHL and HL [13]. Air bronchograms are somewhat more prevalent in NHL (61%) than HL (47%) [10]. Pulmonary parenchymal disease in HL is almost always associated with hilar and/or mediastinal lymphadenopathy, whereas isolated pulmonary involvement in NHL may occur [10].

The most common pulmonary manifestations of secondary pulmonary lymphoma, specifically mass-like consolidation in HL and interstitial thickening in NHL, are nonspecific and can be seen in a wide variety of disease processes other than pulmonary lymphoma. When consolidation is the predominant feature of secondary pulmonary lymphoma, the differential diagnosis should