Nodular lymphoid hyperplasia of the lung: the role of positron emission tomography in diagnosis

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ÖZET

Akciğerin nodüler lenfoid hiperplazisi: Tanıda pozitron emisyon tomografinin rolü

Pulmoner nodüler lenfoid hiperplazi (NLH), akciğerde lokalize olan, soliter veya multipl nodüller veya lokalize infiltratlarla oluşan reaktif lenfoid proliferasyon olarak tanımlanır. Radyolojik görünümü genellikle soliter veya multipl nodüller şeklindedir. Fakat hava bronkogramları ve buzlu cam görünümü şeklinde de karşımıza çıkabilir. Hastalar genellikle asemptomatiktir. Lezyonlar çekilen akciğer grafisinde tesadüfen saptanır. Masif hemoptizi ve öksürük ile başvuran, 61 yaşındaki erkek hastada akciğerin kaviter lezyonu şeklinde gelişen NLH'li olgumuzu sunuyoruz. Lezyonda pozitif florodeoksiglukoz (FDG) tutulumu gözlendi. Bildiğimiz kadarıyla; bu hasta, pozitif FDG tutulumu gösteren, masif hemoptizi ve kaviter lezyon şeklinde literatürde sunulan tek olgudur.

Anahtar Kelimeler: *Hemoptizi, kaviter lezyon, PET, akciğerin nodüler lenfoid hiperplazisi.*

SUMMARY

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Pulmonary nodular lymphoid hyperplasia (NLH) is defined as reactive lymphoid proliferation forming solitary or multiple nodules or localized infiltrates localized in the lungs. Radiological presentations are generally solitary or multiple nodules, but air bronchograms and ground glass attenuation may be present. Patients mostly asymptomatic and the lesions were detected coincidentally on routine chest X-rays. We present a case of NLH with cavitary lesion arising in the lung of a 61 year-old man who admitted with cough and massive hemoptysis. The lesion had positive fluorodeoxyglucose (FDG) uptake. To our knowledge, this is the only patient reported in the literature presenting with massive hemoptysis and a cavitary lesion with positive FDG uptake.

Key Words: *Hemoptysis, cavitary lesion, PET, nodular lymphoid hyperplasia of the lung.*

Pulmonary nodular lymphoid hyperplasia (NLH) is defined as reactive lymphoid proliferation forming solitary or multiple nodules or localized infiltrates in the lungs. It is a very rare disorder which was first introduced by Kradin and Mark in 1983 (1). Its radiological findings are generally defined as discrete nodule(s), or ill-defined nodular opacities and air bronchograms. Occasionally, ground glass opacities may be present (2).

We present a case of NLH with cavitary lesion arising in the lung of a 61 year-old man. To the best of our knowledge, this is the first report of confirmed NLH presenting as a cavitary mass lesion with positive fluorodeoxyglucose (FDG) uptake.

CASE REPORT

A 61-year-old immunocompetent patient was admitted to our hospital with cough and hemoptysis in the last month. He was a heavy smoker without a history of tuberculosis. Physical examination was unremarkable. Chest X-ray demonstrated a mass located in the right middle zone. Thorax computerized tomography (CT) revealed a cavitary pulmonary mass localized to the superior segment of right lower lobe (Figure 1). In further evaluation of the patient with bronchoscopy, endobronchial lesion could not be detected. The histopathological assessments of bronchoalveolar lavage, brush and aspiration fluid were benign, and the smear was negative

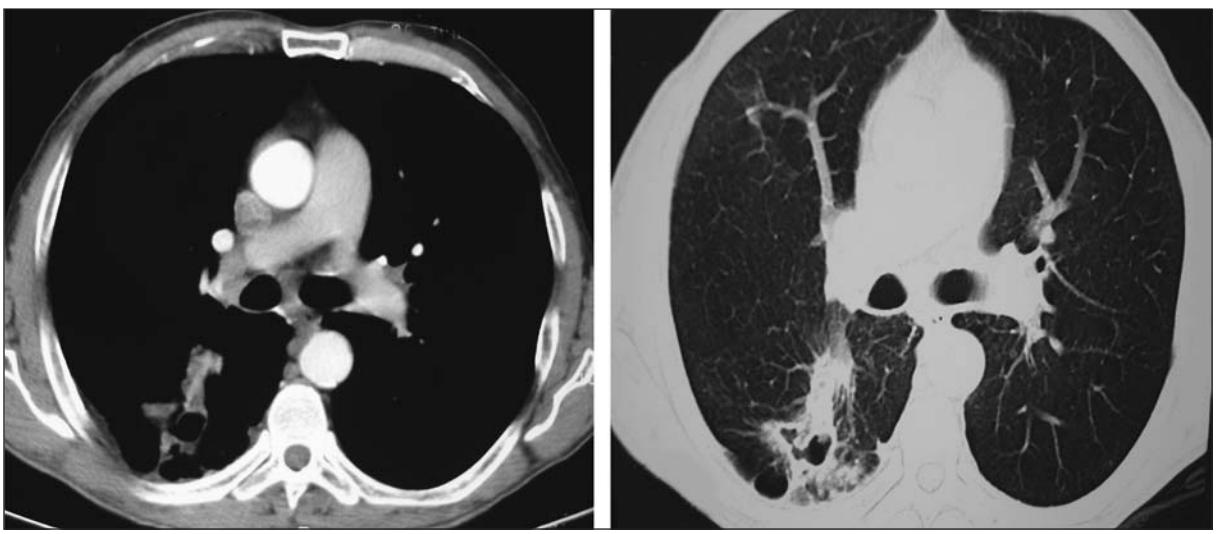

Figure 1. Thorax CT revealed a cavitary pulmonary mass localized to the superior segment of right lower lobe.

for tuberculosis. A second bronchoscopy to reach the diagnosis was uneventful. A transthoracic needle aspiration of the mass revealed lymphocytes and leucocytes without an evidence of malignancy. Regarding the high prevalence in our country, antituberculosis therapy was initiated although the smear was negative for tuberculosis. Four months later, he was referred from the local tuberculosis dispensary to our clinic with massive hemoptysis. Thorax CT demonstrated the same characteristics of the former lesion . Antituberculosis therapy was stopped, due to the negative cultures for sputum and bronchoscopic materials. Vasculitic syndromes such as Wegener's granulomatosis were suspected in the presence of an unidentified cavitary lesion. Myeloperoxidase and antiproteinase ANCA were negative. FDG-positron emission tomography (PET) standard uptake value was positive (SUV: 4.1), indicating malignancy or infection (Figure 2). There was not any pathological FDG uptake in the other parts of the body. An open lung biopsy confirmed the final diagnosis as NLH. The histologic examination was positive for CD3, CD20 and leukocyte common antigen (LCA) and negative for keratin (Figure 3). The patient was decided to be followed without resection. He is still stable with no exacerbation after the first year.

DISCUSSION

Pulmonary lymphoid lesions are inflammatory and reactive, which clinicians face difficulties in differential diagnosis of other reactive pathologies and malignancies. Formerly, nodular lymphoid proliferations were accepted as benign lesions, and Sultztein proposed the term "pseudolymphoma" to describe reactive localized masses of lymphoid tissue in the lung (3). However, it was shown that many of the pseudolymphomas were diagnosed as "mucosa associated lymphoid tissue lymphoma (MALT lymphoma)", and the impression emerged that most cases with pseudolymphomas could be classified as malignant lymphomas (4). The nomenclature was changed throughout the time. Kradin and Mark described the lesion as benign in 1983. And finally, World Health Organization (WHO) and International Association for the Study of Lung Cancer accepted the term NLH instead of pseudolyphoma in 1999 (5). A clinicopathological study by Abbondanzo et al. reevaluated 14 cases with NLH by using modern immunohistochemical and molecular techniques, and their findings reinforced that this entity could be classified as a subgroup among the reactive pulmonary lesions (6).

NLH shows a slight increase in female gender. Patients range from 19 to 65 though majority of them cumulate between ages 50 and 65. They are mostly asymptomatic, only one third of them present with symptoms like shortness of breath, cough and/or pleuritic chest pain (6).

In asymptomatic patients the lesions are detected coincidentally on routine chest X-rays. Radiographically NLH mostly presents as a solitary pulmonary nodule, though two or three nodules are found in %36 of patients (6). On CT the nodules are generally discrete, but ill defined nodular opacities may also be present. Nodules which are mostly located in the subpleural area may range from 0.6 to 6 cm (mean: 2.1 cm) in size, air bronchograms and ground glass attenuation are the other radiological presentations reported less frequently (2,6). Our patient was admitted to our hospital with hemoptysis and there was a cavitary lesion located in subpleural region. To the best of our knowledge, this is the only patient presenting with hemoptysis and a cavitary lesion reported in the literature.

The histological features of NLH are well defined. A well demarcated nodule contains a reactive germinal center, sheets of interfollicular mature plasma cells; well preserved mantle zones some containing Russell bodies without follicular colonization. Immunohistochemical findings reveal positivity for antibodies CD20, CD3, CD5, CD43 and CD45RA, and negative for BCl-1. The immunoglobulin light chain reactivity is polyclonal, whereas it is monoclonal in MALT lymphoma (6). The primary differential diagnosis of NLH should include MALT lymphoma. Primary non-Hodgkin's lymphoma in the lungs is very rare, and the most common is mucosa-associ-

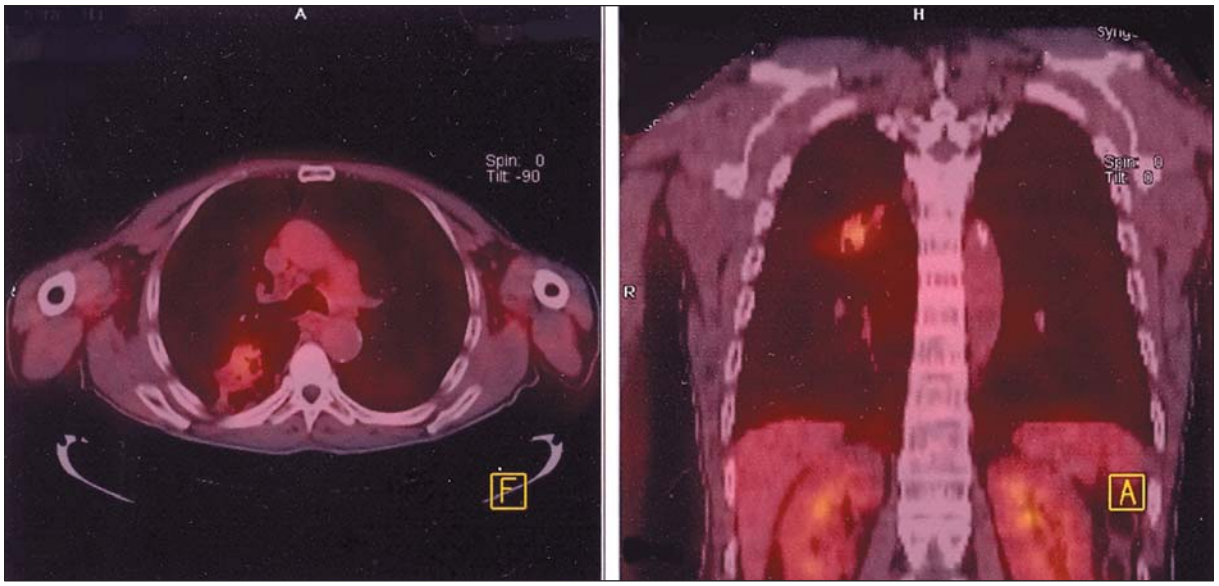

Figure 2. FDG-PET the lesion's standard uptake value was positive (SUV: 4.1).

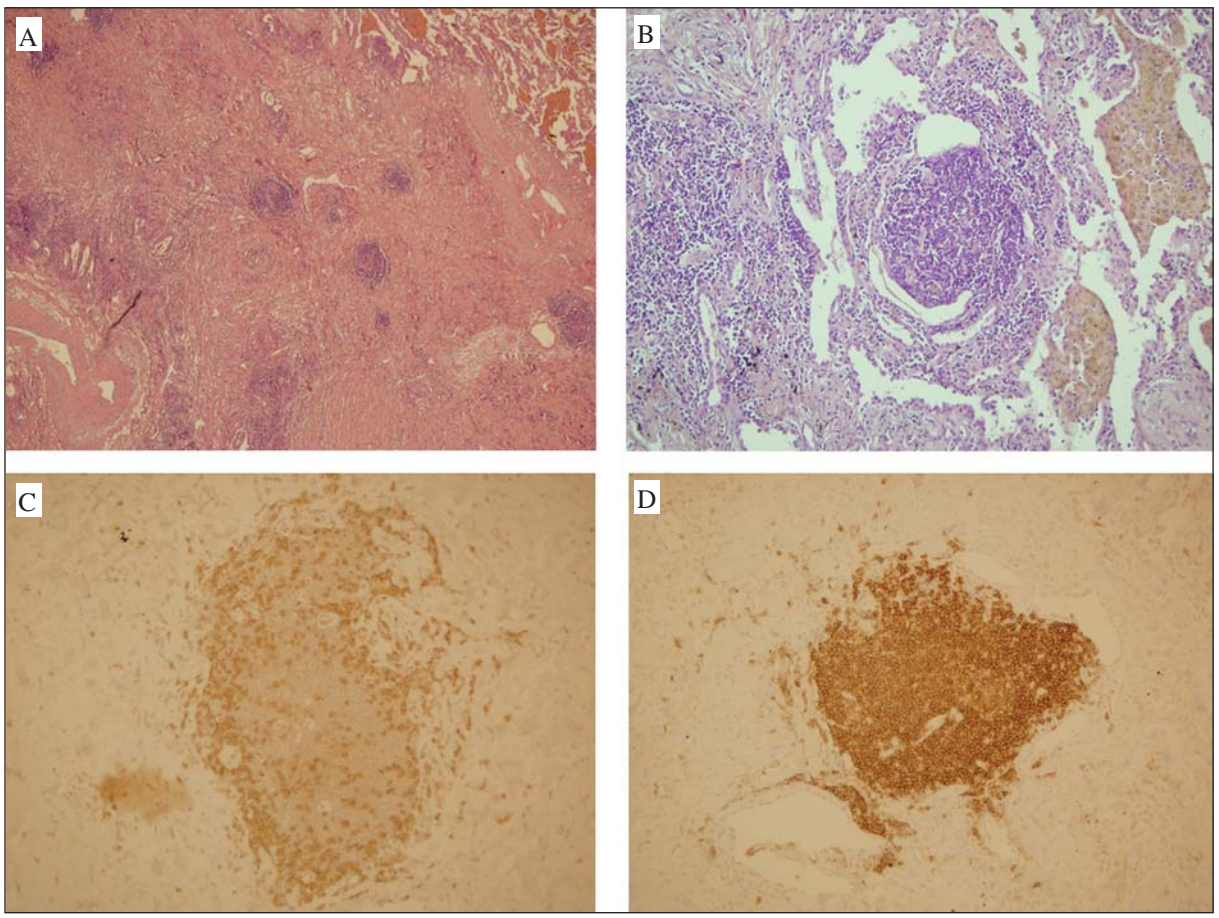

Figure 3. A. Multiple lymphoid clusters in sclerotic ground (HE x4) B. Nodular lymphoid hyperplasia with hematoxylen eosin staining (HE x20) C. CD3 positivity in nodular lymphoid hyperplasia (CD3 x20) D. CD20 positivity in nodular lymphoid hyperplasia (CD20 x20).

ated lymphoid tissue lymphoma (MALToma), that arises from bronchial mucossa-associated lymphoid tissue. The appearance of MALT lymphoma on chest X-ray is highly heterogeneous. It may be a mass, single or multiple nodules or even a pleural effusion, or it may have a bronchiectasis-like appearance (7). Preoperative diagnosis is mostly difficult and it can be made only by pathological examination. Regarding our case, which presented with hemoptysis and a cavitary mass lesion, the differential diagnosis should include malignancies, vasculitic syndromes and tuberculosis.

PET has become very popular in diagnosing lung cancer, and it is reported to have a sensitivity of 79-89%, a specificity of 82-92%, positive predictive value of 40-100%, and a negative predictive value of 75-100% (8-10). PET scanning using injected 18F-fluorodeoxyglucose provides visual and quantitative information for the rate at which glucose is taken up by the lung. The CT scan gives highly accurate density and anatomic information to locate areas of inflammation seen on the PET scan, increasing the accuracy of the interpretation. With regard to organ involvement, PET/CT and contrast-enhanced CT are found to have a sensitivity of, 88% and 50%, and a specificity of 100% and 90%, respectively. Regarding the exclusion of disease, some reporters have concluded that the, PET/CT performed significantly better than contrast-enhanced CT (11). Recently, it has been reported that PET/CT appears to provide relevant information in the staging, therapy and also monitoring of patients with MALT lymphoma (12). PET has shown to be positive in this case. To best of our knowledge, it is the first case with nodular lymphoid hyperplasia with positive FDG uptake.

Although there is no standardized treatment for NLH, resection of the lesion has been suggested. The prognosis is excellent; no recurrence has been detected in patients followed up to 6 years (6). Our patient is also in good clinical condition with no symptoms, and the lesion is stable after one year.

In conclusion; nodular lymphoid hyperplasia, though very rare, should be kept in mind in the differential diagnosis of the cavitary mass lesions with positive FDG uptake.

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