A Case with Extranodal Marginal Zone Non Hodgkin's Lymphoma of the Lung Diagnosed with Computed Tomography Guided Transthoracic Fine Needle Aspiration Biopsy

Bilgisayarlı Tomografi Kılavuzluğunda Transtorasik İnce İğne Aspirasyon Biyopsisi ile Akciğerin Ekstranodal Marjinal Zon Non Hodgkin Lenfoması Tanısı Alan Bir Olgu

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ABSTRACT Marginal zone lymphoma of the lung is a rare hereditary disease. We herein present a rare case with marginal zone lymphoma of the bronchus associated lymphoid tissue of the lung that was diagnosed by computed tomography guided transthoracic fine needle aspiration biopsy from the multiple pulmonary consolidations. Marginal zone lymphoma of the lung should be kept in mind for the differential diagnosis of the multiple pulmonary consolidations. Advanced biopsy techniques such as computed tomography guided transthoracic fine needle aspiration biopsy can be safely performed for the patients who were suspected lymphoma or malignancy of the lung. This technique also can provide adequate sample without more invasive surgery procedures such as open lung biopsy.

Key Words: Lymphoma, B-Cell, marginal zone; biopsy, fine-needle; lung diseases

ÖZET Marjinal zon lenfoma akciğerin nadir bir kalıtımsal hastalığıdır. Bu yazıda, multipl pulmoner konsolidasyon tanısı için bilgisayarlı tomografi kılavuzluğunda transtorasik ince iğne aspirasyon biyopsisi yapılarak akciğerin bronş ilişkili lenfoid dokusunun marjinal zon lenfoması tanısı alan nadir bir olgu sunuyoruz. Multipl pulmoner konsolidasyonların ayırıcı tanısında akciğerin marjinal zon lenfoması akılda tutulmalıdır. Akciğer malignitesi veya lenfomadan şüphelenilen hastalarda bilgisayarlı tomografi kılavuzluğunda transtorasik ince iğne aspirasyon biyopsisi güvenle kullanılabilir. Bu teknik ile açık akciğer biyopsisi gibi daha invaziv cerrahi işlemler olmadan da yeterli örnek sağlanabilir.

Anahtar Kelimeler: Lenfoma, B-hücreli, marjinal zon; biyopsi, ince-iğne; akciğer hastalıkları

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Primary pulmonary lymphoma (PPL) represents only 3-4% of extranodal non-Hodgkin's lymphoma (NHL) and 1% of NHL, and only 0.5% of primary pulmonary malignancies.[1,2]

Mucosa-associated lymphoid tissue (MALT) refers to lymphoid tissue located under the epithelia of the gastrointestinal, respiratory, and urogenital tracts, and their angles. MALT is located under the respiratory tract epithelia which is called bronchus associated lymphoid tissue (BALT).[3] BALT lymphoma is a rare extranodal low grade B-cell lymphoma.[1]

Marginal zone lymphoma (MZL) of the BALT, originating from the marginal zone and invading the bronchial epithelial tissue, is histopathologically characterized by a cellular infiltrate of lymphoid cells, with a pre-

dominance of smaller cell types. Lymphoepithelial lesion, another finding commonly observed in BALT lymphoma, are not specific and can also be seen in cases of reactive lymphoid hyperplasia. Accurate diagnosis depends on immunohistochemical staining findings.[1]

The most common computed tomography (CT) scan finding of MZL is a consolidation with air bronchograms caused by a cellular lymphocytic infiltrate expanding the interstitium and compressing the adjacent alveoli.[3] 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET) uptake in BALT lymphoma is usually mild and is not a factor that differentiates the lesion from the other pulmonary disorders including infection.[4] Treatment options are various, ranging from close observation to radiation, surgery or combination chemotherapy.[5]

MZL of the BALT is a relatively rare disease of the lung, so, clinical features, adequate treatment and the prognostic factors were not well defined.[6] Thus, the purpose of this article was to present the clinical features, radiological, cytologic and immunohistochemical staining findings of a case with MZL of the lung. Even though differential diagnosis is histologically challenging, especially when the sample size is small, CT guided transthoracic fine needle aspiration biopsy can provide adequate sample size.

CASE REPORT

A 63-year-old man was accepted to our clinic with cough and yellowish sputum, which had persisted for a year. He had used to smoke 60 pack/year fourteen years ago. The patient had not a history of comorbidity, environmental-occupational exposure, risk factors for human immunodeficiency virus (HIV) and drug use. He was in New York Heart Association functional class II. Respiratory and the other systems examination revealed normal findings and peripheral lymphadenopathy was not present.

On admission, laboratory tests including immune markers were at normal levels. Autoimmune diseases such as Sjögren's syndrome were excluded. Chest X-ray and thorax CT demonstrated consolidation in left upper zone and in mid-lower zones on bilateral lung fields (Figure 1). On 18F-FDG-PET scan, these left upper lobe (SUV:3.4) and mid-lower lobes lesions (SUV:4.3) showed pathological 18F-FDG uptake. There was no pathologic finding in the abdominal and pelvic CT examination.

Because of the suspect of a pulmonary neoplasm, fiberoptic bronchoscopy was performed. The appearance of the tracheobronchial tree was normal. Bronchoalveolar lavage (BAL) was culture-negative and BAL content was consisted of 60% lymphocyte and 30% monocyte/macrophage. 64% of the lymphocyte cells was T-cell. The CD4/CD8 cells ratio was 0.5. The biopsies of bronchial mucosa were not diagnostic. These findings did not support any disease, so, CT guided transthoracic fine needle aspiration biopsy was performed to the pulmonary mass of the patient and the biopsy material was reported as consistent with MZL. CT guided transthoracic fine needle aspiration biopsy material was consisted of almost completely lymphoid tissue. The histological examination of hematoxylin-eosin-stained sections revealed atypical small lymphoid cells with mild nuclear irregularity (Figure 2). Immunohistochemically, atypical lymphoid cells were positive for CD20, bcl-2. Some plasma cells were positive for CD38. Tumor cells did not express CD3, CD23, bcl-6 and CD10 (Figure 3). Thus, the presence of MZL of the lung was con-

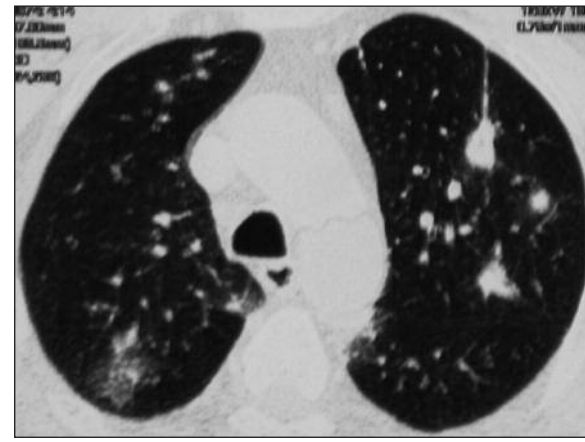

FIGURE 1: Multiple consolidation areas on thorax computed tomography on admission.

firmed pathologically. We planned to give chemotherapy treatment, but the patient rejected. So, "watch and wait" period started. There was no clinical and radiologic progression (Figure 4) for 3 years during his follow-up.

CONCLUSION

MZL of the lung is a rare disease and the its differential diagnosis is challenging. The most common CT scan findings of the MZL of the lung were initially reported as consolidation with air bronchograms caused by a cellular lymphocytic infiltrate expanding the interstitium and compressing the adjacent alveoli. However, later reports have suggested more diverse CT scan findings including airspace consolidation, nodules, ground-glass opacity and small centrilobular and branching nodules. In addition, multiple or bilateral distribution of the lesions is more common than focal distribution.[3] In this case, the patient's chest X-ray and thorax CT revealed the consolidation areas on lung field bilaterally.

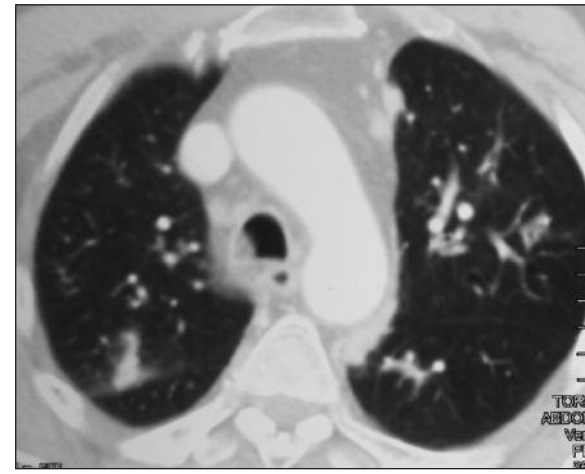

FIGURE 4: Multiple consolidation areas on thorax computed tomography after three years.

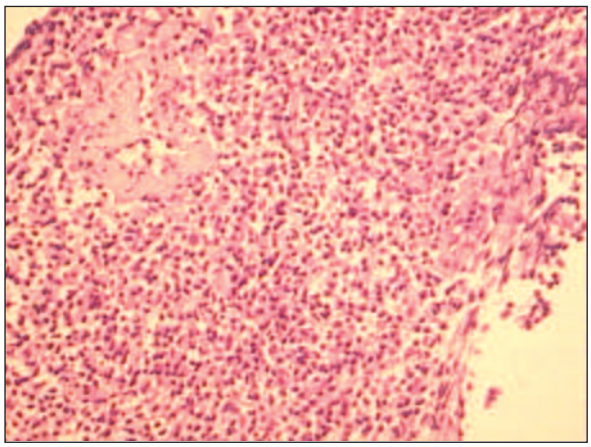

FIGURE 2: The appearance of histopathology of transthoracic fine needle aspiration biopsy specimen with hematoxylin-eosin (x20).
(See color figure at http://akcigerarsivi.turkiyeklinikleri.com/)

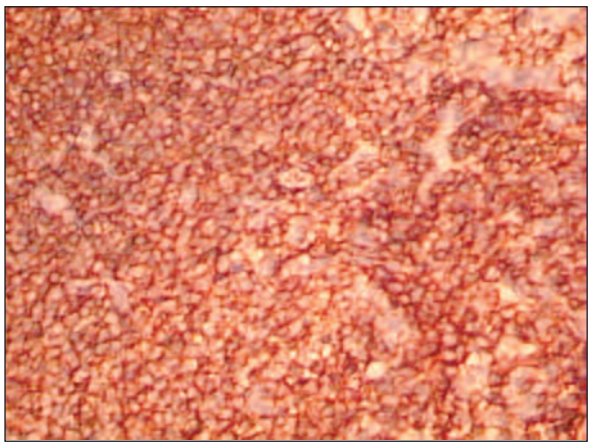

FIGURE 3: The appearance of immunohistopathology of transthoracic fine needle aspiration biopsy specimen; atypical lymphoid cells show CD20 immune positivity (x20).
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The diagnosis of the BALT lymphoma is based on histological examination of surgical samples or bronchial, transbronchial or transthoracic biopsy material. The diagnostic yield of bronchial, and especially transbronchial biopsy is higher when it targets visible endobronchial lesions or radiographic abnormalities. However, the absence of specific signs in most of these samples as in our case, necessitates further diagnostic investigations. Histologically, especially when the sample is small, the main difficulty is distinguishing BALT lymphoma from diffuse lymphoid hyperplasia or interstitial lymphoid pneumonia (ILP), and follicular bronchitis (FB). BAL's value for the positive diagnosis of PPL is inadequately discussed in the literature. BAL appears to be particularly valuable if it shows lymphocytic alveolitis (lymphocytes >20% of total cells), which is found 60% lymphocyte in our patients.[2] The final diagnosis of our patient's was confirmed by CT guided transthoracic fine

needle aspiration biopsy and immunohistochemical analysis. Fine needle aspiration biopsy sample was enough for histological examination. This emphasizes the importance of further investigation in the histological diagnosis of lung lesions before more invasive surgical procedures.

MZL diagnosis based on a lymphoepithelial lesion showing lymphoid cell migration from the marginal zone to the bronchiolar epithelium.[2] The immunophenotype of intraepithelial lymphocytes in BALT lymphoma and reactive lymphoid hyperplasia is different. The presence of a monotonous population of CD20-positive intraepithelial lymphocytes supports a diagnosis of BALT lymphoma. Immunohistochemically, BALT lymphoma shows the CD5-, CD10-, CD23- immunophenotypes.[7] In our case CT guided transthoracic fine needle aspiration biopsy material was consisted of almost completely lymphoid tissue. It was composed of atypical small lymphoid cells with mild nuclear irregularity. Immunohistochemically, atypical lymphoid cells were positive for CD20. Tumor cells were negative for CD23 and CD10. This findings supported diagnosis of the MZL of the BALT.

BALT lymphomas have been associated with Sjögren's syndrome, dysgammaglobulinemia, amyloid deposits, collagen vascular diseases, *Helicobacter pylori* infection and HIV.[8,9] Our case had no history of comorbidity, environmental-occupational exposure, risk factors for human immunodeficiency virus and drug use. All immune markers were at normal level and so, collagen vascular diseases and Sjögren's syndrome were excluded. The other MZL associated situations (dysgammaglobulinemia, amyloid deposits, *Helicobacter pylori* infection) also were not determined.

18F-FDG PET is used to evaluate glucose metabolism in lung lesions. Due to increased metabolism, malignant tissues typically demonstrate higher FDG uptake than benign lesions and normal tissues. Because of the MZL of BALT's indolent growth, less FDG uptake is expected.[4] In this case, on 18F-FDG-PET scan, these left upper lobe (SUV:3.4) and mid-lower lobes lesions (SUV:4.3) showed pathological FDG uptake as similar to a few previous cases.[10]

In our case, any primary lung cancer was diagnosed from specimens of the fiberoptic bronchoscopy or CT guided transthoracic fine needle aspiration biopsy. Any extrathoracic lymphadenopathy and findings of extrathoracic malignancy on FDG-PET was present.

The outcome of BALT lymphoma is generally favourable in most series, with a 5 year survival rate of >80% and a median survival time of >10 years.[2] A "watch and wait" strategy is widely accepted for stable, asymptomatic patients and patients with low tumour mass. Surgery may be proposed for symptomatic patients who have localised BALT lymphoma. When a chemotherapy treatment is to be suggested, chlorambucil-based chemotherapy is preferred.[5] Our patient is in our follow up without medical therapy for three years with a good prognosis.

We herein report a relatively rare pulmonary malignancy case diagnosed as MZL of the lung. We thought that the possibility of MZL should be kept in mind when multiple pulmonary concolidations, masses and nodules exists and in such cases the further investigation is needed. Advanced biopsy techniques such as CT-guided transthoracic fine needle aspiration biopsy can be safely performed for these cases. Also, adequate sample can be obtained by this method before more invasive surgical prosedures. The patient is still our under follow up program without progression of the disease or a second malignancy for three years.

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