Primary Marginal Zone Lymphoma of the Lung and Organizing Pneumonia: A Diagnostic Challenge

Tal Corina Sela MD[1]*, Ofrat Beyar Katz MD[1]*, Tamar Tadmor MD[2], Jacob Bejar MD[3] and Elad Schiff MD[1]

[1]Departments of Internal Medicine, [2]Hematology, and [3]Pathology, Bnai Zion Medical Center, Haifa, Israel

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Organizing pneumonia (OP) may be cryptogenic or secondary to another condition. We present a patient with a clinical course, imaging, and histological characteristics suggestive of OP. However, systemic presentation led to pursue the correct diagnosis of pulmonary marginal zone lymphoma. The distinction between OP and pulmonary marginal zone lymphoma is discussed and reviewed.

PATIENT DESCRIPTION

A 65 year old woman presented to the emergency room with fever, which had lasted for 3 weeks, associated with a cough for the past 6 months accompanied by non-specific symptoms, including lack of energy and malaise. She reported active smoking and was otherwise healthy.

On admission, she was pale and mild bilateral wheezing was evident. Laboratory results were normal, except for anemia (Hb-9.5 g/dl), with no vitamin deficiencies, a faintly positive Coombs test, elevated inflammatory markers (ferritin 467 ng/ml; C-reactive protein [CRP] 50.8 mg/L), and mildly elevated liver enzymes. Vast blood cultures and serology were negative. Computed tomography (CT) scans of the chest, abdomen, and pelvis showed bilateral pulmonary alveolar opacities and modest hepatosplenomegaly (liver 20 cm, spleen 14 cm). Bone marrow biopsy showed one epithelioid granuloma without monoclonality. Bronchoalveolar lavage was normal, including infection panels. Transbronchial biopsy results were compatible with OP.

Due to systemic findings, a confident diagnosis of cryptogenic OP could not be established. Video-assisted thoracoscopic surgery (VATS), including a biopsy, was performed, which revealed histological findings consistent with the diagnosis of pulmonary extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT). Treatment with corticosteroids and rituximab was initiated with good response. At the time of this writing, the patient was in complete clinical and laboratorial remission and follow-up positron emission tomography (PET)-CT revealed resolution of lungs opacities.

COMMENT

Primary pulmonary lymphoma (PPL) accounts for 3–4% of all extranodal non-Hodgkin's lymphoma and only 0.5–1% of primary pulmonary malignancies [1]. The most common form of PPL is MALT lymphoma, which is a low-grade indolent subtype [1,2] thought to be associated with chronic antigenic stimulation [1,2]. It belongs to the category of marginal zone lymphomas (MZL) [1].

A significant proportion of patients are asymptomatic prior to diagnosis [1,2]. Among symptomatic patients, pulmonary symptoms are the most common [1,2]. Physical examination and radiological findings are usually non-specific and may vary [1,2].

The final diagnosis is based on histopathological findings [1]. Biopsy taken by bronchoscopy usually yields a small-sized specimen, which might show inflammation and could miss the underlying lymphoma [2]. Accordingly, although associated with a higher risk of complication, and sometimes difficult to perform, the recommended method for establishing the diagnosis is via surgical biopsy [2].

The optimal therapy for pulmonary MALT lymphoma has yet to be established, but for disseminated cases in which resection is less favorable, systemic non-aggressive therapy is usually preferred due to the indolent nature of the disease [1,3].

In this report, we describe a patient who presented with systemic and respiratory symptoms, and our initial difficulty in establishing a correct diagnosis. OP was still considered, even after a transbronchial lung biopsy. OP can be idiopathic (cryptogenic) or can occur in association with other diseases [4]. Table 1 summarizes the differences between pulmonary MALT lymphoma and OP. Due to the systemic presentation of the disease, the correct diagnosis could only be determined by further surgical procedures. The histologic specimen obtained by VATS was still intriguing, possibly due to overlapping OP modifying the histologic picture of pulmonary MZL.

CONCLUSIONS

Diagnosis of pulmonary MALT lymphoma is sometimes challenging and requires an invasive approach including lung biopsy. The treating physician should be aware of the differential diagnosis in cases where lymphoma and OP may present simultaneously or overlap, thereby masking the correct diagnosis.

Correspondence
Dr. T.C. Sela
Dept. Internal Medicine, Bnai Zion Medical Center
Haifa 38041, Israel
email: Tal200390@gmail.com

Table 1. Characteristic features of bronchiolar associated lymphoid tissue lymphoma and cryptogenic organizing pneumonia

		Cryptogenic organizing pneumonia [4,5]		PPL of MALT type [1-3]	
Epidemiology	Age at onset, years	50–60		50–70	
	Gender	No clear gender predisposition		No clear gender predisposition	
	Smoking as a risk factor	No		Yes	
Presentation	Symptoms	Short duration, usually ‹ 3 months		Mostly asymptomatic	
		Respiratory Non-productive cough, dyspnea with exertion	**Non-respiratory** Fever and malaise, weight loss	**Respiratory** Cough, dyspnea, chest pain, hemoptysis	**Non-respiratory** B symptoms: fever, weight loss, night sweats, fatigue
	Signs in physical examination	Inspiratory crackles, wheezing (rare), clubbing (rare)		Crackles, wheezing (rare)	
Imaging studies	X-ray	Diffuse not homogeneous bilateral, often migratory, alveolar opacities, mostly bases of lungs		Alveolar opacities, air bronchogram, alveolar masses, interstitial infiltrates (rare), atelectasis (rare), pleural effusion (rare), nodules (rare)	
	CT scan	Ground glass pattern		Small nodules, dilated bronchi, hilar/mediastinal adenopathy	
Pulmonary function tests		Normal or restrictive pattern		Usually normal, obstructive/restrictive pattern, low PaO_2	
Bronchoalveolar lavage		High lymphocyte count		Lymphocytic alveolitis, mostly CD20+B-cells	
Pathology		Inflammation in alveoli and bronchioles, Masson bodies, bronchial occlusion due to inflammation		Centrocyte-like cells, monocytoid cells, small lymphocytes, plasmacytic, reactive follicles: large germinal centers, mature plasma cells (rare), macrophages (rare), blastic cells (rare), amyloid deposits (rare) Cells are positive for B-cell associated antigens: CD19, 20, 21, 22, 35, 79a Cells are negative for B-cell associated antigens: CD5, 10, 23 Mono-clonality evident by: • Light chain restriction (Kappa or Lambda) by IHC or FACS • IgH gene rearrangements	
Treatment		Corticosteroids, steroid sparing agents (mostly azathioprine), cytotoxic agents (mostly cyclophosphamide)		Corticosteroids, anti CD20 biologic therapy, immunochemotherapy	
Prognosis		Complete recovery in about ⅔ of patients, persistent/relapse disease in about ⅓ of patients		Usually an indolent, chronic disease, good overall survival, high remission rate	

CD = cluster of differentiation, CRP = C-reactive protein, CT = computed tomography, ESR = erythrocytes sedimentation rate, FACS = fluorescence activated cell sorting, IgH = immunoglobulin heavy chain, IgM = immunoglobulin M, IHC = immunohistochemistry, MALT = mucosa-associated lymphoid tissue, PPL = primary pulmonary lymphoma

References

1. Cadranel J, Wislez M, Antoine M. Primary pulmonary lymphoma. *Eur Respir J* 2002; 20 (3): 750-62.
2. Ahmed S, Siddiqui AK, Rai KR. Low-grade B-cell bronchial associated lymphoid tissue (BALT) lymphoma. *Cancer Invest* 2002; 20 (7-8): 1059-68.
3. Oh SY, Kim WS, Kim JS, et al. Pulmonary marginal zone B-cell lymphoma of MALT type--what is a prognostic factor and which is the optimal treatment, operation, or chemotherapy? Consortium for Improving Survival of Lymphoma (CISL) study. *Ann Hematol* 2010; 89 (6): 563-8
4. Schlesinger C, Koss MN. The organizing pneumonias: an update and review. *Curr Opin Pulm Med* 2005; 11 (5): 422-30.
5. King TE Jr, Mortenson RL. Cryptogenic organizing pneumonitis. The North American experience. *Chest* 1992;102 (1 Suppl): 8S-13S.

Capsule

Association between inflammatory back pain characteristics and magnetic resonance imaging findings in the spine and sacroiliac joints

Arubak et al. investigated the association between magnetic resonance imaging (MRI) findings at the sacroiliac (SI) joints and vertebral endplates and pain characteristics assumed to be indicative of axial inflammation. Patients ages 18–40 years with persistent low back pain referred to an outpatient spine clinic participated in the study, including an unknown proportion of axial spondyloarthritis patients. Data included an MRI of the spine and SI joints and self-reported responses to questions covering the Calin, Berlin, Assessment of Spondyloarthritis International Society, and Bailly inflammatory back pain (IBP) definitions. Of the 1020 included patients, 53% were women, and the median age was 33 years. Positive associations were found between the SI joint MRI findings and pain characteristics, odds ratios ranging from 1.4 to 2.7. SI joint bone marrow edema (BME) was associated with morning stiffness > 60 minutes, and SI joint erosions with the Calin, Berlin, and Bailly IBP definitions, alternating buttock pain, and good response to nonsteroidal anti-inflammatory drugs. SI joint fatty marrow deposition (FMD) was associated with insidious onset, and SI joint sclerosis with pain at night. In addition, the spinal MRI changes were associated with IBP, odds ratios ranging from 1.4 to 2.0. Vertebral endplate BME was associated with morning stiffness and vertebral endplate FMD with the Calin and Bailly IBP definitions, was connected with improvement with exercise, morning stiffness › 30 minutes, and pain worst in the morning.

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