

Transformation of MALT Lymphoma to Pure Plasma Cell Histology: Possible Association with Anti-CD20 Antibody Treatment

Noa Klein MD^{1*}, Avishay Elis MD^{1,4*}, Judith Radnay PhD², Ruth Zemer MSc³, Ami Klein PhD^{3,4} and Michael Lishner MD^{1,4}

¹Department of Internal Medicine, ²Cytohematology Laboratory and ³Molecular Biology Laboratory, Meir Medical Center, Kfar Saba, Israel

⁴Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

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Mucosa-associated lymphoid tissue lymphoma is a distinct subtype of non-Hodgkin's lymphoma that belongs to the group of marginal zone B cell lymphomas [1]. MALT lymphoma arises from lymphoid tissues that are exposed to persistent inflammatory stimulation, most commonly in the gastric mucosa, and has unique pathogenetic, histological and clinical features [1,2]. MALT lymphoma of the lung comprises 14% of the non-gastric primary sites and accounts for 70–80% of the primary lymphomas of the lung [1].

A prominent plasma cell component among MALT lymphoma cells is a well-known phenomenon called plasmacytic differentiation. It presents in up to 30% of patients with MALT lymphoma and its main differential diagnosis is extramedullary plasmacytoma [1,3]. However, transformation of MALT lymphoma to multiple myeloma or pure plasma cell histology is rare [2].

Since MALT lymphoma cells express CD20, the anti-CD20 antibody, rituximab, was recently introduced into chemotherapeutic regimens [2]. In this report we describe a patient with MALT lymphoma of the lung whose cytotoxic treatment regimen included rituximab

and who presented with a new pleural effusion rich in monoclonal pathological plasma cells. Data suggesting that the two neoplasms are clonally related are discussed, as is the possible association with rituximab treatment.

PATIENT DESCRIPTION

A 59 year old man was diagnosed with MALT lymphoma of the lung. The patient complained of abdominal pain and night sweats, but physical examination was unremarkable. Laboratory tests, including blood count, serum electrolytes, liver and kidney function tests, except for serum monoclonal immunoglobulin Mk (311 mg/dl), were all within the normal range. Chest X-ray and chest computed tomography revealed extensive consolidation with air bronchograms, involving most of the middle and lower lobes of the right lung and the lingula. Total body positron emission tomography-CT showed focally elevated uptake in the right lower and middle lobes of the lung and in the lingula area. Open lung biopsy revealed malignant low grade B cell lymphoma of MALT type, without plasmacytic differentiation. The tumor cells stained positively for CD20 and CD 79-9. Bone marrow aspiration and biopsy were normal.

Treatment consisted of the chemotherapeutic regimen R-COP (cyclophosphamide, prednisone, vincristine and rituximab). Just before the fourth course, the patient began to complain of cough

and shortness of breath. Physical examination revealed decreased breathing sounds over the right lung. All blood tests remained within the normal range, except for an increase of the serum monoclonal IgMk levels to 631 mg/dl and lactate dehydrogenase to 511 u/L. Repeat PET-CT showed no change in the primary tumor but demonstrated a new right pleural effusion with an elevated uptake of fluorodeoxyglucose. The fluid was aspirated and shown to be an exudate containing monoclonal pathological plasma cells. Recurrent bone marrow aspiration revealed 10% mature lymphocyte cells without any pathological plasma cells. Lytic lesions were not found on skeletal survey.

Gene rearrangement was obtained by polymerase chain reaction, followed by the differential fluorescence detection method of the heavy chains of the mononuclear cells. The results revealed that the heavy chains of the mononuclear cells isolated from the lung biopsy tissue at presentation and those isolated from the pleural fluid, bone marrow and peripheral blood during the reevaluation had the same band in the JH area. An additional band was found in the cells isolated from the pleural fluid [Figure].

The treatment with R-COP was discontinued. Eight months later the patient is asymptomatic while repeat chest X-rays revealed significant decrease in the amount of the pleural effusion.

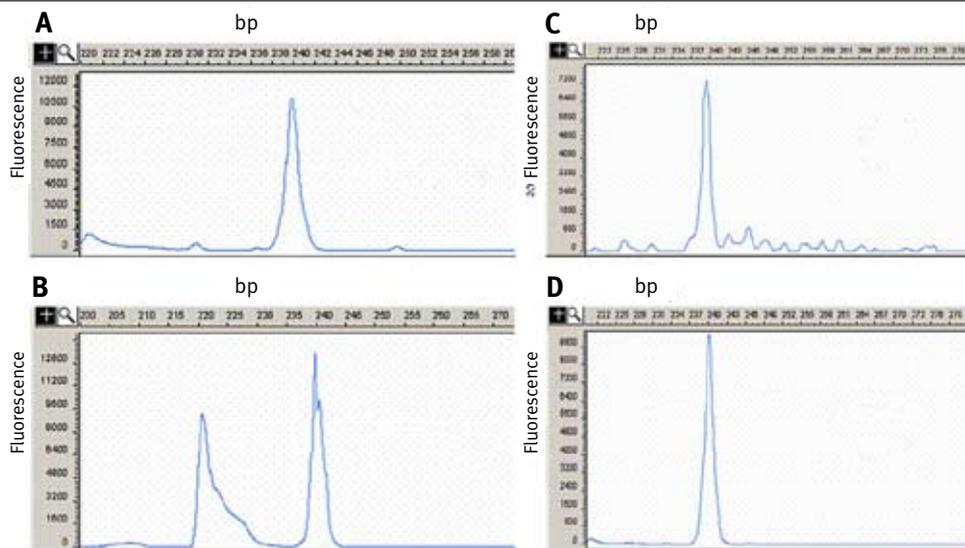
*The first two authors contributed equally to the study

MALT = mucosa-associated lymphoid tissue

PET-CT = positron emission tomography-computed tomography

Gene rearrangement results obtained by PCR followed by the differential fluorescence detection method. The following patient's specimens were investigated: **[A]** biopsy of lung (at presentation), **[B]** pleural effusion, **[C]** bone marrow, and **[D]** peripheral blood (during reevaluation).

The Fluorophor-conjugated PCR primers were of the conserved framework region (FR2 and FR3) of the immunoglobulin VH region and of the joining (J) region. The 240 bp peak, found in all four preparations, characterizes the same type of monoclonality in all. (The 220 bp peak, of the pleural effusion preparation, is not relevant since it is out of the frame of gene rearrangement peaks 230-280 bp.)



COMMENT

We describe a patient with MALT lymphoma of the lung who developed a new pleural effusion containing monoclonal pathological plasma cells during treatment with R-COP. The most important differential diagnosis of MALT lymphoma with extensive plasmacytic differentiation is extramedullary plasmacytoma. The latter is characterized by soft tissue infiltration of monoclonal plasma cells but, in contrast to multiple myeloma, there is no bone marrow plasmacytosis, bone destruction or evidence of anemia, hypercalcemia or impaired renal function [3].

MALT lymphoma with extensive plasmacytic differentiation has similar clinical and histological features to extramedullary plasmacytoma. Hussong et al. [4] reviewed the data of five patients with extramedullary plasmacytoma and two patients with MALT lymphoma. They concluded that extramedullary plasmacytoma and MALT lymphoma with extensive plasmacytic differentiation may represent the same disease. Tanimoto and collaborators [3] described a patient with MALT lymphoma of the rectum with extreme plasma cell differentiation. Nevertheless, transformation of MALT lymphoma into multiple myeloma or pure plasma cell histology is rare. Wohrer et al. [5]

reported a patient with retrobulbar MALT lymphoma who developed multiple myeloma. The authors found that despite the fact that both malignancies are derived from mature B cells, they had different immunophenotypic and molecular cytogenetic characteristics. They therefore concluded that the development of the two malignancies in the same patient was coincidental.

The pathophysiological involvement of rituximab in the transformation of MALT lymphoma into pure plasma cell histology is compelling. Woehrer and team [2] described a patient with MALT lymphoma of the lung and the stomach that transformed into a pure plasma cell tumor after treatment with rituximab. The authors assumed that the anti-CD20 antibody induced the histological changes on the primary MALT lymphoma by eradication of the CD20-positive cells and "overgrowth" of the CD20-negative plasmacellular component of the tumor. This hypothesis may be applied to our case. Furthermore, the results obtained from the PCR examination of our patient indicate that the MALT lymphoma cells and the plasma cells are clonally related. It may suggest that following the administration of rituximab the initial MALT lymphoma

evolved into a plasma cell neoplasm, and not that two separate B cell malignancies had developed in the same patient.

In conclusion, we describe a rare case of MALT lymphoma that was transformed into pure plasma cell histology. Our data suggest that the two neoplasms are clonally related. We hypothesize that treatment with rituximab may have induced these histological changes.

Correspondence:

Dr. M. Lishner

Head, Dept. of Medicine A, Meir Medical Center, Kfar Saba 44281, Israel

Phone: (972-9) 747-2516

Fax: (972-9) 746-0781

email: michaelz@cclalit.org.il

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PCR = polymerase chain reaction