

# Relationship Between Follicular Lymphoma And Familial Mediterranean Fever

G Kadikoylu, I Yavasoglu, M Unubol, Z Bolaman

## Citation

G Kadikoylu, I Yavasoglu, M Unubol, Z Bolaman. *Relationship Between Follicular Lymphoma And Familial Mediterranean Fever*. The Internet Journal of Hematology. 2007 Volume 4 Number 2.

## Abstract

The genetic components and immunopathogenesis of lymphoma is still under debate. Familial Mediterranean Fever (FMF)-lymphoma was reported in one case (1). To our knowledge there is no notification about relationship between follicular lymphoma and FMF in literatures. Forty-four years old male case was referenced to the hematology clinic with complaints about 4 cm sized, non temperature increased swelling that progressively raised in three months on his left under arm. He did not describe any perspiration at night, itching, loss of weight. In his history he was diagnosed as FMF after complaints about abdominal pain attacks 6 years ago. He was treated with colchicine (1mg/day) during last 6 years and he was still under medication. In his family's history, his father died at 55 years old because of lung cancer and his mother had some clinic symptoms same as FMF. He was a 20 pocket/year smoker. In his physical examination he had bilateral axillary and inguinal multiple lymph nodes, hepatosplenomegaly. Spiral computed tomography of abdomen scan noticed that he had increased size lymph nodes (2cm) on paraaortic zone. In laboratory tests, LDH and hemoglobin levels were at normal limits. The biopsy of axillary lymph node marked as follicular lymphoma grade IIIA. According to Ann Arbor stage 3A, The International follicular lymphoma prognostic index (lymph node count and stage) patient was evaluated as 2. There was no infiltration in marrow examination. Rituximab-cyclophosphamide, doxorubicin, vincristine, prednisone were given as treatment to the patient. At this time, Reverse Dot Blot Hybridization and M694V heterozygote mutation were found out in tests made for FMF. The colchicine treatment let to continue 1mg/day. Pathogenesis of lymphoma was still undetermined.

The effects of genetic condition and immune system on FMF is well known. To our knowledge immune cells is not the

effect of the colchicine treatment. FMF is the most frequent hereditary inflammatory disease characterized by self-limited recurrent attacks of fever and serositis. It is transmitted in an autosomal recessive pattern and affects certain ethnic groups mainly Jews, Turks, Arabs, and Armenians. FMF is caused by mutations in MEFV gene, which encodes pyrin. This protein is expressed mainly in myeloid/monocytic cells and modulates IL-1beta processing, NF-kappaB activation, and apoptosis. A mutated pyrin probably results in uncontrolled inflammation (2). Pyrin deficient mice exhibit heightened sensitivity to endotoxin, excessive IL-1? production, and impaired monocyte apoptosis (3). Hereditary periodic fever syndromes such as hyper-IgD and periodic fever syndrome (HIDS), TNF-receptor-associated periodic syndrome (TRAPS), FMF are characterized by incapacitating attacks of fever and generalized inflammation. While the mutated genes for the major syndromes in this group are known, the pathogenesis remains unclear. HIDS (n=10) lymphocytes showed a decreased percentage of apoptosis during remission by both methods compared with controls, whereas no difference was observed in TRAPS (no=7) or FMFs (n=2) lymphocytes. This defective apoptosis of lymphocytes may be a central pathogenic mechanism in HIDS, since dysfunction of one of the inhibitory mechanisms to curtail the immunologic response could cause an unbridled generalized inflammation after a trivial stimulus (4). Lymphomas are a heterogeneous group of malignancies of B cells, T cells, and rarely natural killer cells that usually originate in the lymph nodes, but they may originate in any organ of the body. Approximately 90 percent of follicular lymphoma demonstrate the t(14,18)(q32, q21) involving rearrangement of the bcl-2 gene, leading to the constitute expression of the antiapoptotic bcl-2 protein. Variations in racial incidence, histology, and immunologic subtypes are found throughout

the world. Follicular lymphoma is more common North America and Western Europe. Contrary FMF, is commonly seen in Mediterranean region (3). We did not perform genetic analysis for the t(14,18). In conclusion, the effects of genetic condition and immune system in FMF may act acted in pathogenesis of lymphoma. Also, the possibility of a relationship in between lymphoma and FMF should be further evaluated with tests evaluating percentage of apoptosis of lymphocytes.

#### **CORRESPONDENCE TO**

Irfan Yavasoglu, Adnan Menderes University Medical Faculty, Division of Hematology, 09100 Aydin, Turkey. e-mail: dr\_yavas@yahoo.com Telephone: +90-256-2120020 Fax: +90-256-2146495

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**Author Information**

**Gurhan Kadikoylu**

Associate Professor, Internist, Hematologist, Division of Hematology, Adnan Menderes University Medical Faculty

**Irfan Yavasoglu**

Assistant Professor, Internist, Fellow in Hematology, Division of Hematology, Adnan Menderes University Medical Faculty

**Mustafa Unubol, MD**

Division of Hematology, Adnan Menderes University Medical Faculty

**Zahit Bolaman**

Professor, Internist, Hematologist, Division of Hematology, Adnan Menderes University Medical Faculty