

Letters to the Editor

Editöre Mektuplar

Lipid disorders in Familial Mediterranean Fever patients: Is inflammation the only cause?

Dear Editor,

We read the article about the relationship between lipid indices and Familial Mediterranean Fever (FMF) reported by Çakırca et al. with great interest. The lipid indices of FMF patients were compared with healthy counterparts and it was reported that the high-density lipoprotein (HDL) level was lower in FMF patients than in healthy controls, and as a result, the atherogenic lipid indices are worse in FMF patients. A chronic inflammatory state was suggested as the underlying mechanism for this difference.^[1]

Erythrocyte sedimentation rate, CRP, and fibrinogen are all inflammatory indices, and these parameters were assessed only in FMF patients and not evaluated in the healthy counterparts. Thrombocytosis is a well-known characteristic of chronic systemic inflammation and the thrombocyte counts were similar between the 2 groups. Therefore, according to these findings, we think that it is difficult to say the 2 groups are significantly different according to inflammatory state.

Secondary amyloidosis occurs as a consequence of overproduction and extracellular deposition of serum amyloid A protein (SAA); it is a well-known complication of FMF. The incidence in FMF patients is 8.6%.^[2] SAA is synthesized from the liver with the induction of inflammatory cytokines, including interleukin (IL)-1, IL-6 and tumor necrosis factor alpha. SAA binds to HDL and replaces it with apolipoprotein A. Increased SAA levels are associated with de-

creased HDL levels.^[3] Cengiz et al.^[4] reported that renal amyloidosis had deleterious effects on the lipid profile independent of inflammatory state. HDL levels were significantly lower in patients with renal amyloidosis than in patients with chronic renal failure due to other causes, while the values of low-density lipoprotein, lipoprotein a, triglycerides, and total cholesterol levels were higher in renal amyloidosis patients.

To conclude, chronic inflammation most certainly has important effects on the lipid profile in FMF patients, but in our opinion, patients should be evaluated for renal amyloidosis, as it is a frequent complication of FMF and is associated with dyslipidemia.

✉ Yusuf Ziya Şener, M.D., ✉ Metin Okşul, M.D.,
✉ Gül Sinem Kılıç, M.D.

Department of Cardiology, Hacettepe University
Faculty of Medicine, Ankara, Turkey

e-mail: yzsener@yahoo.com.tr

doi: 10.5543/tkda.2018.44389

Conflict of interest: None declared.

References

1. Çakırca G, Çelik MM. Lipid profile and atherogenic indices and their association with platelet indices in familial Mediterranean fever. *Turk Kardiyol Dern Ars* 2018;46:184–90.
2. Alghamdi M. Familial Mediterranean fever, review of the literature. *Clin Rheumatol* 2017;36:1707–13.
3. Westermark GT, Fändrich M, Westermark P. AA amyloidosis: pathogenesis and targeted therapy. *Annu Rev Pathol* 2015;10:321–44.
4. Cengiz K, Bakan A, Yılmaz H. Lipoprotein abnormalities in patients with secondary renal amyloidosis. *Int Urol Nephrol* 2001;32:615–9.

**Authors reply**

Dear Editor,

We thank the authors for their important comments on our article. Familial Mediterranean fever (FMF) is a chronic inflammatory disease that is the result of a mutation of the MEFV gene. Mutation of the MEFV gene leads to a loss of pyrin function and results in uncontrolled inflammation.^[1] In our study, we found that high-density lipoprotein (HDL) levels in FMF patients were lower than those of the control group. This finding was consistent with previous studies.^[2,3] We also

found a negative correlation between HDL and C-reactive protein (CRP) in the FMF group. Hence, based on the results of this study, we think that low HDL levels may be associated with the inflammatory process of FMF. Similarly, Candan et al.^[2] reported that low grade inflammation caused by MEFV mutations may be responsible for this low HDL level in FMF. In our study, the absence of erythrocyte sedimentation rate, CRP and fibrinogen level values for the control group may be a limitation of the study. However, the controls were healthy individuals who presented at the hospital for a check-up and did not have any disease.

In addition, the white blood cell count ($\times 10^3/\mu\text{l}$), an inflammatory marker, was higher in FMF patients when compared with the controls (7.61 ± 2.08 vs. 6.95 ± 1.31 ; $p=0.039$) (these data were not provided in the study article). Thrombocytosis is defined as an abnormally elevated platelet count. Makay et al.^[4] found that platelet numbers were higher than normal ($>400 \times 10^3/\mu\text{L}$) in 8 of 48 patients during an FMF attack and 6 of 63 patients at a time without an attack. In other studies, there were no cases with a blood platelet count higher than $400 \times 10^3/\mu\text{L}$ in FMF groups.^[5,6] The literature data on platelet count in FMF are conflicting, with some studies reporting an elevated blood level of platelets in FMF,^[4,5] while other studies have demonstrated either no difference in platelet count between control and FMF groups,^[6,7] i.e., similar to our data, or a lower platelet count in patients with FMF.^[8] Therefore, given these findings, we think that platelet count may not precisely reflect inflammation in FMF.

Amyloidosis is the most serious complication of FMF disease and leads to organ dysfunction, most prominently in the kidneys. For this reason, FMF patients are checked regularly. FMF patients with amyloidosis were excluded from our study.

✉ Gökhan Çakırca, M.D., ✉ Muhammet Murat Çelik, M.D

¹Department of Biochemistry, Şanlıurfa Mehmet Akif İnan Training and Research Hospital, Şanlıurfa, Turkey.

Where is the missing piece of the puzzle? Failed device therapy in patients with left ventricular assist device

Dear Editor,

We read the article by Çay et al.^[1] titled “Prolonged ventricular fibrillation in a patient with left ventricular assist device” recently published in the journal with great interest. The authors reported the case of a 50-year-old male who was admitted to the emergency department (ED) following 6 device discharges of 35 J to unsuccessfully terminate a detected episode of ventricular fibrillation (VF). The patient required external defibrillation with a 200-J biphasic shock to terminate the VF episode and restore the programmed pacing rate of 70 bpm. No further malignant ventricular arrhythmias were observed. It is important to note that the patient was previously implanted with a dual coil implantable cardioverter-defibrillator (ICD) and a continuous-flow left ventricular assist device (LVAD).

²Department of Internal Medicine, Mustafa Kemal University, Faculty of Medicine, Hatay, Turkey.

e-mail: cakirca.gokhan@gmail.com

Conflict of interest: None declared.

References

- Onen F. Familial Mediterranean fever. *Rheumatol Int* 2006;26:489–96. [CrossRef]
- Candan Z, Akdogan A, Karadağ Ö, Kalyoncu U, Sahin A, Bilgen S, et al. Serum lipid changes and insulin resistance in familial Mediterranean fever. *Eur J Rheumatol* 2014;1:140–3.
- Acay A, Ulu MS, Ahsen A, Ozkececi G, Demir K, Ozuguz U, et al. Atherogenic index as a predictor of atherosclerosis in subjects with familial Mediterranean fever. *Medicina (Kaunas)* 2014;50:329–33. [CrossRef]
- Makay B, Turkyilmaz Z, Unsal E. Mean platelet volume in children with familial mediterranean fever. *Clin Rheumatol* 2009;28:975–8. [CrossRef]
- Arica S, Ozer C, Arica V, Karakuş A, Celik T, Güneşçar R. Evaluation of the mean platelet volume in children with familial Mediterranean fever. *Rheumatol Int* 2011;32:3559–63.
- Korkmaz C, Ozdogan H, Kasapcopur O, Yazici H. Acute phase response in familial Mediterranean fever. *Ann Rheum Dis* 2002;6:79–81. [CrossRef]
- Ahsen A, Ulu MS, Yuksel S, Demir K, Uysal M, Erdogan M, et al. As a new inflammatory marker for familial Mediterranean fever: Neutrophil-to-lymphocyte ratio. *Inflammation* 2013;36:1357–62. [CrossRef]
- Sakalli H, Kal O. Mean platelet volume as a potential predictor of proteinuria and amyloidosis in familial Mediterranean fever. *Clin Rheumatol* 2013;32:1185–90. [CrossRef]

We would like to congratulate the authors on the management of this interesting case and for their important addition to the recently growing literature of prolonged VF in patients with LVADs. Our group recently published a very similar case (Table 1) concerning a 38-year-old male with a previously implanted biventricular ICD and a continuous-flow LVAD; the patient was admitted to the ED due to syncope and recurrent ICD discharges.^[2] Device interrogation revealed appropriately delivered recurrent ICD shocks that failed to terminate the sustained VF episode. An external

Table 1. Observed characteristics between the two cases

Characteristic	Çay et al.	Gul et al.
Age	50 years	38 years
Gender	Male	Male
Significant medical history	Non-ischemic cardiomyopathy, heart failure	Dilated cardiomyopathy, heart failure
Implanted devices		
ICD	Dual-coil	Biventricular
LVAD	Continuous-flow, HeartMate 2	Continuous-flow, HeartMate 3
Reason for presentation	ED admission due to 6 recurrent ICD discharges for VF	ED admission due to recurrent ICD discharges for VF
External defibrillation required	Yes; 200-J biphasic shock	Yes; 200-J biphasic shock
Follow-up	No further malignant arrhythmias	No further malignant arrhythmias; failed DFT

ED: Emergency department; DFT: Defibrillator threshold test; ICD: Implantable cardioverter-defibrillator; LVAD: Left ventricular assist device; VF: Ventricular fibrillation.