Vascular risk in familial Mediterranean fever

Familial Mediterranean fever (FMF) is an autosomal recessive disorder resulting in improper leukocyte clearance during inflammation. The disease often presents in early childhood and is characterized by recurrent attacks. Current treatment includes suppression of inflammation by colchicine. Typical to other rheumatological diseases, FMF is characterized by elevated white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and serum pro-inflammation markers, such as C-reactive protein and fibrinogen (1). These factors are responsible for increased leukocyte trafficking, vascular permeability, and endothelial dysfunction. These cellular consequences can fundamentally alter the elastic properties of blood vessels. Indeed, rheumatological diseases with recurrent inflammatory attacks, such as FMF, are associated with increased arterial stiffness (2).

In this edition of the Anatolian Journal of Cardiology, data of a cohort of young FMF patients is reported in a study titled "Investigation of the arterial stiffness and associated factors in patients with familial Mediterranean fever" by Çakar et al. (3). In this case-controlled study design, 69 FMF patients and 35 controls were retrospectively studied. The former had significantly higher pulse wave velocity (PWV) amongst other arterial stiffness indices., probably because there were 31 smokers (44%) in the FMF group and only 9 smokers (25%) in the control group, though this was not assessed. Interestingly, augmentation index (both brachial and aortic) was significantly lower in the former compared to controls. It is uncertain if this apparent disparate finding is due to the technique used or if it reflects some residual confounding.

Consistent with their hypotheses, leukocytes, WBC, and pro-inflammatory markers were significantly increased in the FMF group, offering an inflammatory mechanism for the findings. Compared to patients with quiescent disease, arterial stiffness indices were increased in those with an active attack. Further, as there was no significant association between genetic variants of FMF and arterial stiffness indices, it was concluded that arterial stiffness reflects the severity of the condition rather than its origin or type. The most significant results were the findings of a strong correlation of PWV with CRP, WBC, ESR, fibrinogen, and neutrophil–leukocyte ratio in individuals with an active attack. There was a significant relationship between PWV and the disease duration, reflecting disease chronicity. Unfortunately, these results remained unadjusted, and it is therefore not possible to determine which inflammatory measure is the most strongly related to stiffness.

Why are these results significant? As FMF predominantly affects younger people and the disease is persistent and recurrent, adverse changes in the vasculature attributable to the disease may impose a significant increase in lifetime cardiovascular risk (4). Strategies that reduce inflammation in other rheumatological conditions, such as psoriasis, have shown that this can be effective in reducing arterial stiffness (5). No study exists demonstrating this effect in FMF. Overall, this study highlights the paucity of evidence with regards to macrovascular function in this group of patients who may be at increased risk. Given the ease with which the non-invasive technique is employed to measure arterial stiffness, it may be beneficial to consider vascular risk screening as part of a broad primary prevention strategy targeting significant risk factors, including smoking cessation.

Alexander J. Rodríguez
Department of Medicine, Monash University, Monash Medical Centre; Clayton-*Australia*

References

1. Territo MC, Peters RS, Cline MJ. Leukocyte function in familial Mediterranean fever. Am J Hematol 1976; 1: 307-11.
2. Roman MJ, Devereux RB, Schwartz JE, Lockshin MD, Paget SA, Davis A, et al. Arterial stiffness in chronic inflammatory diseases. Hypertension 2005; 46: 194-9.
3. Çakar M, Akhan M, Doğan T, Taşkın G, Öztürk K, Çınar M, et al. Investigation of the arterial stiffness and associated factors in patients with familial mediterranean fever. Anatol J Cardiol 2017; 17: 132-38.
4. Anderson TJ. Arterial stiffness or endothelial dysfunction as a surrogate marker of vascular risk. Can J Cardiol 2006; 22 (Suppl B): 72B-80B.
5. Pina T, Corrales A, Lopez-Mejias R, Armesto S, Gonzalez-Lopez MA, Gomez-Acebo I, et al. Anti-tumor necrosis factor-alpha therapy improves endothelial function and arterial stiffness in patients with moderate to severe psoriasis: A 6-month prospective study. J Dermatol 2016; 43: 1267-72.

Address for correspondence: Alexander J. Rodríguez, B. MedSc (Hons), M. TransMed
Bone and Muscle Health Research Group, Department of Medicine, Monash University
Monash Medical Centre, Level 5, Block E, 246 Clayton Road, Clayton-*Australia*
Phone: +61 (03) 8572 2574 Fax: +61 (04) 432 155 802 E-mail: alexander.rodriguez@monash.edu
Accepted Date: 30.05.2016 **Available Online Date:** 21.07.2016

DOI:10.14744/AnatolJCardiol.2016.22571