Changes in Cerebral Blood Flow in Patients with Familial Mediterranean Fever

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ABSTRACT

Introduction: It is known that there is a relationship between systemic inflammation and atherosclerosis. Atherosclerosis is one of the best-known causes of cerebrovascular diseases. The aim of this study was to assess cerebral blood flow velocity using transcranial Doppler (TCD) ultrasonography in patients with familial Mediterranean fever (FMF).

Methods: A total of 30 patients aged from 20 to 50 years with FMF were enrolled in the FMF group consecutively. The control group (non-FMF group) consisted of 30 age- and sex-matched randomly selected patients without FMF who had other diagnoses such as fibromyalgia and did not have risk factors for atherosclerosis. Bilateral peak-systolic, end-diastolic, and mean blood flow velocities in the middle cerebral artery (MCA), values of Gosling's pulsatility index, and values of Prouclet's resistance index were recorded using TCD ultrasonography by a neurosonologist blinded to the FMF and control groups.

Results: There were 30 participants in the FMF group in remission (male/female: 4/26, mean age: 34.7±5.9 years) and 30 participants in the control group (male/female: 4/26, mean age: 32.3±4.7 years). C-reactive protein levels and bilateral blood flow velocities in the MCA were significantly higher in the FMF group than in the control group.

Conclusions: This study suggests that persistent clinical and subclinical inflammation in patients with FMF causes an increase in cerebral blood flow velocities. Our findings provide an insight into this association between FMF and cerebrovascular diseases.

Keywords: FMF, inflammation, atherosclerosis, TCD, stroke
Recently, there has been considerable attention concerning the possible ischemic cerebrovascular diseases has not been studied thoroughly (5). Reports of neurological manifestations have been reported in FMF patients. The association between FMF and nervous system manifestations is rare in FMF. Neurological symptoms such as transient ischaemic attacks and arterial claudication have been reported in peripheral vasculitis patients with FMF (6). The occurrence of nervous system manifestations is rare in FMF. Neurological symptoms such as transient ischaemic attacks and arterial claudication have been reported in peripheral vasculitis patients with FMF (6).

**DISCUSSION**

This study suggests that persistent clinical and subclinical inflammation associated with atherosclerosis in patients with FMF causes increases in cerebral blood flow velocities. Our findings provide an insight into this association between FMF and cerebrovascular diseases.

**RESULTS**

The mean ages were 34.7±5.9 years in the FMF group (male/female: 4:26) and 32.3±4.7 years in the non-FMF group (male/female: 4:26). Clinical features of the FMF patients are given in Table 1. The median colchicine dose used by the FMF patients was 1.50 mg/day. None of the patients with FMF had amyloidosis. The mean values of CRP levels and ESR were 5.8±3.5 mg/L (normal range: 0-5 mg/L) and 17.4±8.5 mm/h, respectively, in the FMF group. CRP levels were significantly higher in the FMF group than in the non-FMF group (5.8±3.5 mg/L versus 3.2±1.05 mg/L). Bilateral peak-systolic, end-diastolic, and mean blood flow velocities in the MCA were significantly higher in the FMF group than in the non-FMF group (Table 2). The values of the pulsatility index and resistance index were not significantly different between the two groups.

**DISCUSSION**

The occurrence of nervous system manifestations is rare in FMF. Neurologic disorders such as PRES, demyelinating disorders, and ischemic stroke have been reported in FMF patients. The association between FMF and ischemic cerebrovascular diseases has not been studied thoroughly (5). Recently, there has been considerable attention concerning the possible causal role of systemic inflammation in the development of atherosclerosis in patients with FMF (9). We attempted to determine cerebral blood flow velocities using TCD ultrasonography in patients with FMF, because increased cerebral blood flow velocities are significantly associated with ischemic cerebrovascular diseases (10).

We found that the peak-systolic, end-diastolic, and mean blood flow velocities were significantly higher in the FMF group than in the non-FMF group. However, the values of the pulsatility index and resistance index were not significantly different between the two groups. Correct interpretation of the pulsatility index is complex, because it depends not only on cerebrovascular resistance but also on several systemic and cerebral variables (11,12). The Rotterdam Study reported that increased mild-to-moderate cerebral blood flow velocity was due to diffuse atherosclerosis or vasoconstriction. Therefore, the mechanisms that underlie this condition (increased velocities but normal pulsatility index values) are most likely to be due to mild diffuse subclinical atherosclerosis (10,12).

It has been reported that inflammation (assessed by a high-sensitivity CRP assay) was frequently present in FMF, even in patients receiving colchicine therapy and in remission, which was the case for the present FMF patients (13). Studies investigating markers of early arterial wall alterations in FMF are also scarce and controversial. The intima media thickness (IMT) of the carotid arteries and endothelial dysfunction are used to define preclinical atherosclerosis. Significant increases in both IMT in the carotid and femoral arteries and blood flow velocities have been reported in patients with FMF in comparison with healthy controls (14,15).

This study suggests that persistent clinical and subclinical inflammation associated with atherosclerosis in patients with FMF causes increases in cerebral blood flow velocities. Our findings provide an insight into this association between FMF and cerebrovascular diseases.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Kahramanmaraş Sütçü İmam University School of Medicine.

**Informed Consent:** Written informed consent was obtained from all participants who participated in this study.

**Peer-review:** Externally peer-reviewed.


**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**REFERENCES**


