**To whom correspondence should be addressed.*

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Epithelial cell-derived neutrophil activator-78 levels in children with familial Mediterranean fever

Sir,

Familial Mediterranean Fever (FMF) is an autosomal recessive disease characterized by recurrent attacks of fever, peritonitis, pleuritis or arthritis. The exact mechanism triggering the acute attacks in FMF is unclear; neutrophil is the effector cell of the inflammatory response at the serosal surface. Increased chemotaxis of polymorphonuclear leucocytes during attacks has been reported (1, 2).

Chemokines are low molecular weight chemoattractant cytokines secreted by a variety of cells, including leucocytes, epithelial cells, endothelial cells, fibroblasts and numerous other cell types. They are produced in response to exogenous stimuli such as viruses and bacterial toxins, and endogenous stimuli such as interleukin-1, tumor necrosis factor and interferon. These factors mediate chemotaxis and leukocyte activation. They also regulate leukocyte extravasation from blood to the tissue space, the site of inflammation. More than 40 members of the super family and 15 members of chemokine receptors have been identified (3, 4).

Epithelial Cell-Derived Neutrophil Activator (ENA)-78, a recently found chemokine, is a potent stimulator of neutrophils that induces a variety of biological responses such as chemotaxis,enzyme release, the upregulation of surface receptors and intracellular Ca mobilization (3, 5). The production of ENA-78 and other chemokines could establish a chemotactic gradient capable of influencing the increased migration of granulocytes and monocytes/macrophage from the bloodstream through the endothelium and markedly increase chronic inflammation (5, 6). In rheumatoid arthritis the local production of ENA-78 in the joints has been reported (7, 8). The predominance of several chemokines in other collagen diseases such as systemic lupus erytematosus and systemic sclerosis is also described (6, 9).

We analyzed the peripheral blood ENA-78 level in 49 FMF patients in this study. The diagnosis of FMF was established according to the Tel Hashomer criteria. Seventeen patients were evaluated during an acute FMF attack and 32 patients during an attack-free period. All of the patients were receiving colchicine treatment at the time. Peripheral blood ENA-78 levels were measured by ELISA (Quantikine ENA-78, R&D systems, UK, mean normal level: 1449 pg/ml (range: 589-2627pg/ml)).

Mean ENA-78 levels were significantly increased in patients with acute attacks compared with attack-free patients, as were fibrinogen levels and the erythrocyte sedimentation rate (Table I). Our results suggest that ENA-78 may be considered an activity marker and that it could also play a role in the pathogenesis of FMF.

Table I. Main characteristics of the patients.

	With attack (n=17)	Without attack (n=32)	P value
Mean age (years)	10.6 ± 4.5	9.6 ±6.2 years	0.07
Sex (F/M)	9/8	17/15	0.2
ESR (mm/h)	64.07 ± 27.56	31.77 ± 21.85	0.000
Fibrinogen	394.17 ± 101.41	271.89 ± 60.79	0.000
WBC (mm^3)	11.600 ± 2100	9420 ± 2484	0.06
CRP (mg/L)	21.9 ± 14.6	14.2 ± 6.4	0.09
Mean ENA-78 (pg/mL)	2405.88 ± 1041	1646 ± 774.93	0.002

E. BASKIN, *MD, Associate Professor*
U. SAATCI, *MD, Professor*
S. OZEN[1], *MD, Professor*

Department of Pediatric Nephrology, Baskent University, Ankara; [1]Department of Pediatric Nephrology, Hacettepe University, Ankara, Turkey.

Address correspondence to: Associate Prof. Esra Baskin, MD, Baskent University Hospital, Department of Pediatric Nephrology, 6. Cadde No: 72/3, Bahçelievler, 06490 Ankara, Turkey. E-mail: esrabaskin@hotmail.com

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