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The endogenous TLR-4 ligands MRP8/14 as biomarkers of inflammation in Familial Mediterranean Fever (FMF)

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Background

The pro-inflammatory Damage Associated Molecular Pattern (DAMP) molecules Myeloid-Related Protein (MRP)-8/14 have been recently identified as ligands and activators of TLR-4. Familial Mediterranean Fever (FMF) is an auto-inflammatory syndrome associated with activation of phagocytic cells and oversecretion of the proinflammatory cytokine IL-1β. Our aim was to evaluate MRP8/14 serum levels in FMF patients during high inflammatory episodes and during successful therapy.

Patients and methods

70 genetically proven FMF patients were followed up longitudinally over a period of 18 months. Serum concentration of MRP-8/14 determined by ELISA and additionally ESR, CRP and SAA as classical inflammation markers were analysed before starting of therapy and during colchicine treatment. As control groups we measured 17 Neonatal-Onset Multisystem Inflammatory Disease (NOMID), and 18 Muckle Wells Syndrome (MWS) patients.

Results

The mean serum levels of MRP8/14 in inflammatory episodes in FMF (343,210 ± 202,210 ng/ml; n = 17) were significantly higher than in NOMID (2,830 ± 580 ng/ml; $p < 0.001$), or in MWS (3,205 ± 585 ng/ml; $p < 0.001$). FMF patients treated with colchicine and not exhibiting any attacks during the study period (5,480 ± 1,900 ng/ml; n = 28) had significantly lower MRP8/14 levels than patients treated with colchicine exhibiting complains typical for FMF (34,700 ± 14,580 ng/ml; $p < 0.001$; n = 20), and also than Homozygous patients never experiencing any clinical signs without colchicine treatment (22,310 ± 10,110 ng/ml; $p < 0.05$ n = 5).

Conclusion

MRP8/14 as a marker of phagocyte activation is highly oversecreted in patients with FMF. Measurement of MRP8/14-levels in FMF might be a valuable tool to reflect disease activity, response to anti-inflammatory therapy, and even subclinical inflammatory activity.