РАЗДЕЛ III. МЕДИЦИНА

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Prognostic value of sICAM-1 and sVCAM-1 in hemolytic uremic syndrome

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Introduction. Hemolytic uremic syndrome (HUS) is a rare, but severe condition characterized by triad of symptoms: acute renal failure, thrombocytopenia and non-immune hemolytic anemia. There are 2 main forms of this disorder: typical HUS (tHUS), caused by Shiga-toxin produced by enterohemorrhagic *Escherichia coli* and atypical HUS (aHUS), associated with mutations of genes encoding complement factors or autoantibodies and, as a result, uncontrolled complement activation [1,2]. Endothelial dysfunction induced by effects of Shiga toxin has been recognized as the trigger event in the development of tHUS [3]. Moreover, endothelial activation followed by dysfunction might indicate subclinical complement activation in remission of aHUS. Hence, adhesion molecules as biomarkers of endothelial activation/dysfunction may be useful for assessment of risk of complications and the benefit of therapy. The purpose of this study was to evaluate the levels of cell adhesion molecules as markers of endothelial activation in these patients.

Patients and methods. 27 children with tHUS and 58 children with aHUS in remission were examined. 17 children on 2nd-4th day after onset of tHUS were included in the group 1, 10 children who recovered from tHUS 6 months up to 5 years before study were included in the group 2, 22 children with aHUS treated with eculizumab were included in the group 3, and the group 4 included 16 children with aHUS who did not receive this drug. The duration of remission in groups 3 and 4 was 22±20 months and 22±21 months respectively.

Leucocyte and thrombocyte counts, hemoglobin, creatinine, urea, LDG levels serum concentrations of C3 complement component, soluble intracellular adhesion molecule-1 (sICAM-1) and vascular cell adhesion molecule (sVCAM-1) were determined.

Results. The levels of sICAM-1 were significantly lower and the levels of sVCAM-1 were significantly higher in group 1 than in group 2 (285 (227-297) vs 335 (308-408) ng/ml, $p=0,003$ and 705 (505-1230) vs 355 (325-450) ng/ml, $p=0,003$, respectively). But we didn't find significant differences in initial hemoglobin, LDG, levels, leucocyte and platelet counts as well as in the duration of anuria and dialysis, in serum urea and creatinine levels at the day of discharge when 8 patients with normal sVCAM-1 levels (median 482, 372-565 ng/ml) were compared with 9 patients with high sVCAM-1 levels (median 1230, 1085-1825 ng/ml). Serum levels of C3, sICAM-1 and sVCAM-1 were within normal age ranges in groups 3 and 4, but children from group 3 showed increased sICAM-1 levels (478±102 pg/ml vs 343±50 pg/ml) compared to group 4 ($p<0,05$). No differences in leucocyte and thrombocyte counts, hemoglobin, creatinin, creatinine, urea, LDG and C3 levels were found.

Conclusion. Children with acute tHUS had lower levels of sICAM-1 and higher levels of sVCAM-1 than children with a history of tHUS. This pattern of altered adhesion molecules suggests that different endothelial regulation factors are at play. Eculizumab has proved to be a most efficient therapy for patients with aHUS, blocking C5 and thus the formation of terminal complement cascade [2]. However, optimal duration of eculizumab therapy and whether it can be discontinued in remission still remains unclear [1,5]. In children free of eculizumab therapy no signs of subclinical complement activation or endothelial dysfunction were found. Normal serum levels of C3, sICAM-1 and sVCAM-1

prove that normal endothelial state could be restored in aHUS and this condition is maintained after discontinuation of the targeted therapy. These results suggest that C3, sICAM-1 and sVCAM-1 monitoring may be useful for further management of these patients and for prediction of relapses.

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