Complement System Abnormalities in patients with Atypical Hemolytic Uremic Syndrome (aHUS) and Catastrophic Antiphospholipid Syndrome (CAPS)

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Introduction

The role of alternative complement pathway (AP) abnormalities in the pathogenesis of aHUS is well studied. However, studies on the state of AP in patients (pts) with CAPS are virtually absent.

The aim of our study was to assess the state of AP in pts with CAPS and aHUS and compare the clinical manifestations of TMA in both groups.

Patients and Methods

The study enrolled 67pts with a diagnosis of CAPS (28 pts) and aHUS (39 pts). ADAMTS13 activity was investigated in 6 pts with CAPS and 25 with aHUS. Studies of the complement system are made of 10 pts with CAPS and 18 aHUS. Factor H, I, B, D content, functional activity of factor H, and complement components C3, C4 was determined in serum by ELISA kit. Determination of the complement factor H activity was evaluated by the number of factor H bound to C3b (only functionally active molecule of factor H can bind to C3b).

Results

The demographic features, clinical and laboratory data are shown in Table 1. Among the most significant precipitating factors in both groups there have been various infections – 21,5% in CAPS pts and 18% in aHUS pts. In both groups kidney damage was observed in 100% of pts. In CAPS group, compared to aHUS often noted heart disease - 77% vs 32% (p<0,005) and skin lesion - 65% vs 0% (p<0,005). In aHUS group often observed pancreas defeat -31% vs 0 % (p<0,005). For other parameters, we obtained similar data for both groups, but in CAPS pts multiple organ failure was more severe. Index of organ damage in CAPS pts was significantly higher than in those with aHUS - 4.8 and 2.8, respectively (p = 0.002, Figure 1). The average value of ADAMTS13 activity was 48,3% in CAPS and 75,5% in aHUS group. Patients with CAPS and aHUS showed similar changes in complement biomarkers (Table 2) . We found a strong inverse correlation between the activity of factor H and the number of affected organs only in aHUS group (r = -0,569, p = 0,05). Complement biomarkers interactions were similar in both groups (Figure 2).

Table 1. Demographic and Median Clinical Data in CAPS and aHUS

Clinical diagnosis	Age	Sex (M/F)	Hb (120-150g/l)	Platelets (150-400x10*9)	LDH (208-378 u/L)	Creatinine (53-115 umol/L)	ADAMTS-13, % (93-113%)
CAPS n=28	34.89 (±11)	12/16	82.3 (50-110)	120x10*9 (4-300)	760 (360-2000)	344 (50-1000)	n=6 48.33 (24-77)
aHUS n=39	28.82 (±13)	22/17	69.1 (20-110)	87x10*9 (24-190)	1598 (341-12424)	805 (180-2700)	n=25 75.52 (36-123)
p (CAPS vs aHUS)	*0.06*		*0.144*	*0.665*	*0.609*	***0.000***	***0.01***

Figure 1. Number of affected organs in CAPS and aHUS groups.

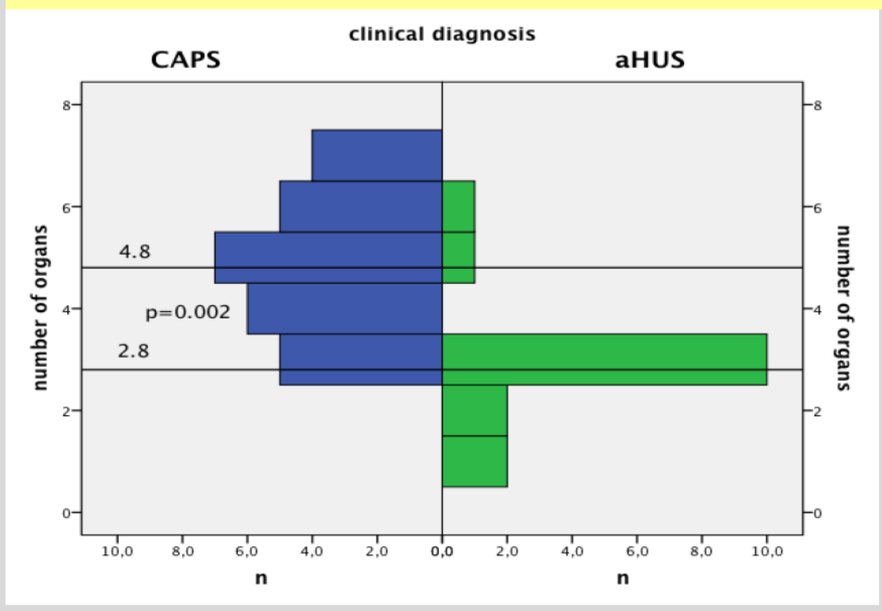


Table 2. Complement analysis (median value) in CAPS and aHUS groups

diagnosis	CFH, ug/ml	Activity CFH, %	CFI, ug/ml	CFB, ug/ml	CFD, ng/ml
control	140-260	70-130	178-331	280-520	78-145
CAPS	797,33 (±156,26)	26 (±13)	260,11 (±122,94)	676 [346;1392]	292,56 (±171,13)
aHUS	726,79 (±221,39)	59 (±32)	407,43 (±187,11)	426,5 [367;496]	388,50 (±190,53)
p (CAPS vs aHUS)	*0,451*	*0,025*	*0,015*	*0,346*	*0,344*

Figure 3. ADAMTS-13 activity in CAPS and aHUS

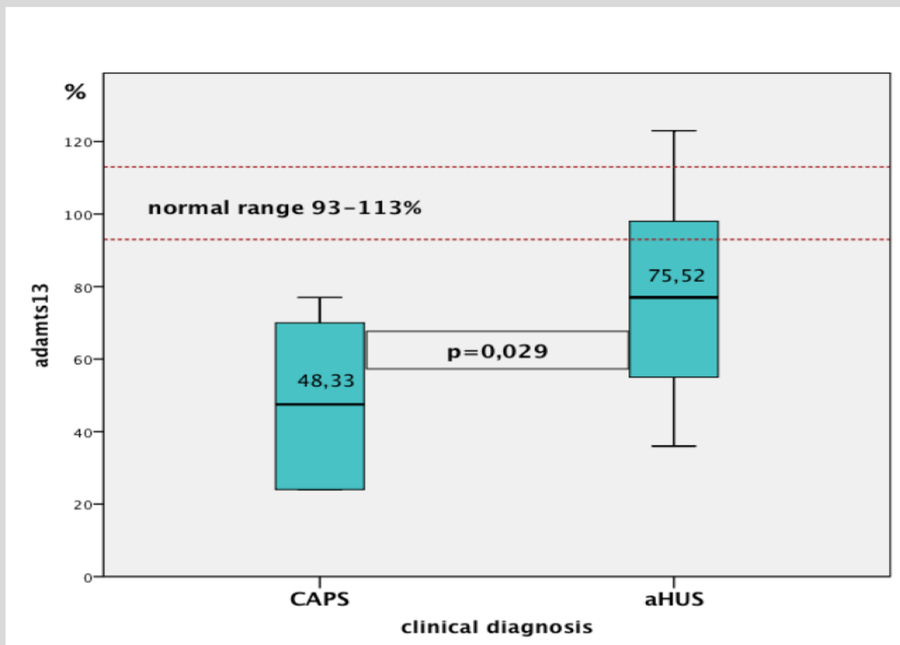
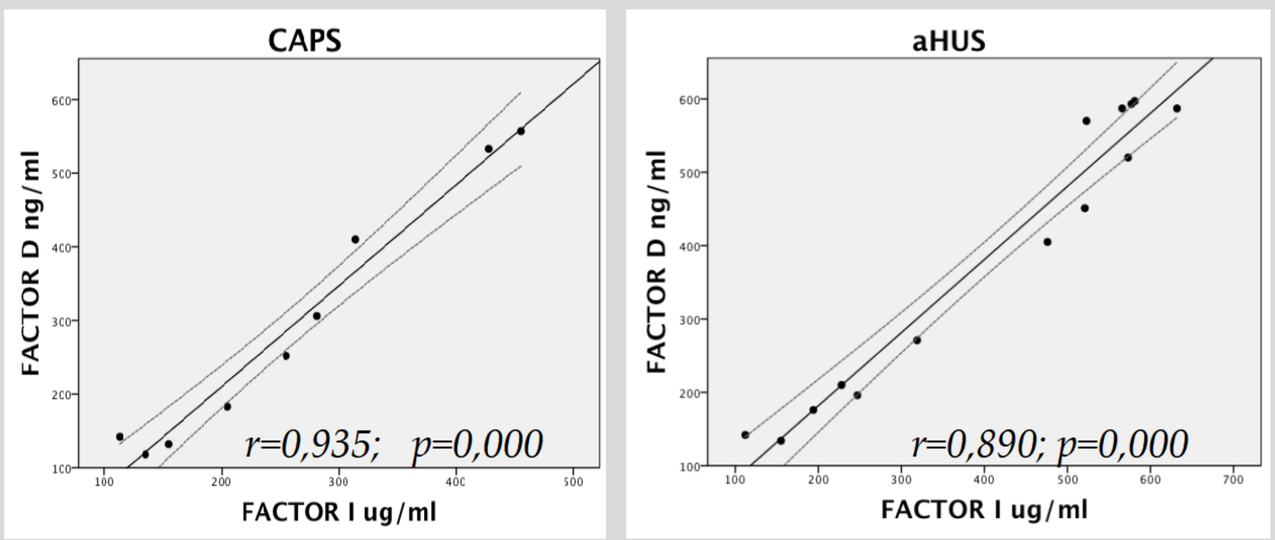


Figure 2. Complement factors interactions



Conclusions

1. APC changes at CAPS are similar to those of aHUS.
2. We suggest that endothelial damage, mediated by complement, may contribute to the pathogenesis of microcirculatory injury in patients with aPL.
3. Lower ADAMTS-13 activity in CAPS reflects more extensive damage to microvasculature with a large number of involved organs.

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