ROLE OF COMPLEMENT IN SCLERODERMA RENAL CRISIS

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INTRODUCTION

Systemic sclerosis is a systemic autoimmune disease characterized by fibrosis and vascular obliteration. Scleroderma renal crisis (SRC) is a rare but severe renal complication, in which there is hypertension, acute renal failure and haemolysis, indicating thrombotic microangiopathy (TMA).

OBJECTIVE

To investigate whether the occurrence of SRC could be associated with anomaly in the alternative complement pathway.

METHODS

We conducted a multicenter retrospective study of 21 patients with SRC in whom an analysis of complement was available in the HEGP Immunology department between 2009 and 2015.

RESULTS

Patients characteristics

Median age (year)	60 (22-83)
Female	16/21 (76,2%)
Systemic scleroderma classification	
Limited	3/19 (15,8%)
Diffuse	11/19 (57,9%)
« Sine scleroderma »	5/19 (26,3%)
anti RNApolIII antibody	6/20 (30%)
Previous medication	
None	5/21 (23,8%)
Steroids	13/21 (61,9%)

Crisis characteristics

Median maximal SBP (mmHg)	183 (98-260)
Median maximal DBP (mmHg)	100 (76,2%)
Need for dialysis	14/21 (66,7%)
Dialysis withdrawal	4/13 (30,8%)
Median Hemoglobin (g/dl)	7,9 (5,6-12,5)
Median Platelets (/mm3)	85000 (28000-364000)
Median Creatinine (µmol/l)	500 (205-890)
M6 Creatinine (µmol/l)	149 (101-500)

Median values of quantitative complement assays

	Median values	Extreme values	Normal values
C3 (mg/l)	930	553-1570	660-1250
C4 (mg/l)	201	98-461	93-380
CH50 (%)	94	52-159	70-130
sC5b9 (ng/dl)	396	306-701	<420
C Factor H (%)	110	58-163	65-140
C Factor I (%)	120	80-157	70-130
C Factor B (mg/l)	141	101-340	90-320
MCP (MFI)	13,7	11-18,9	13-19
anti-H antibody	1patient/19 (titer 320 UI)		

Rare variants detected in the cohort, and comparison of their allelic frequency with that of the general population and the patient's ethnic subgroup

Gène	Detected Variant	Cohort Frequency	General population frequency	Ethnic subgroup frequency
CFI	Ile416Leu	3,3%	0,1% **P=0,03**	1,2% P=0,31
CFH	Ile551Thr	3,6%	0,5% P=0,13	5,5% P=1
	Val1007Leu	3,6%	2,6% P=0,53	27,3% P=0,02
	Ile1059Thr	3,6%	0,7% P=0,17	7,4% P=0,72
	Gln1143Glu	3,6%	1% P=0,24	10,8% P=0,36

There was no quantitative abnormality in complement assays . Anti factor H antibody was found in only one patient. Elevated sC5b9 was found in 1/13 cases studied.
Analysis of the genes encoding factor H, factor I and MCP was performed in 15 patients. We only found one pathogenic variant of *CFI* already described in the atypical Hemolytic Uremic Syndrome (aHUS).

CONCLUSION

In this cohort of patients we have not demonstrated a major role of the alternative complement pathway in the pathophysiology of scleroderma renal crisis, unlike aHUS. But there are cases of overlap between diseases, which may involve the activation of the alternative complement pathway. In those cases, anti-C5 therapy should be discussed.

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