ATYPICAL HEMOLYTIC UREMIC SYNDROME - VERY EARLY TREATMENT IS A WAY TO SUCCESS?

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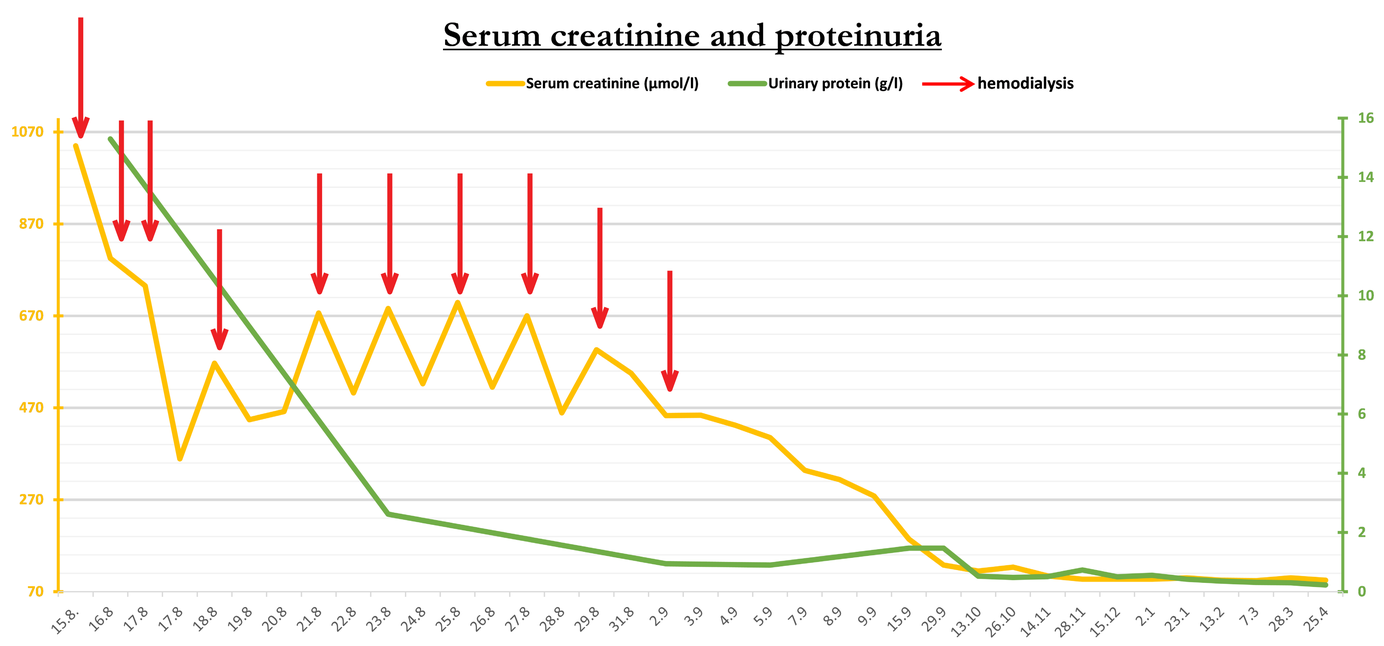
INTRODUCTION: Atypical hemolytic uremic syndrome (aHUS) is a life-threatening thrombotic microangiopathy (TMA) with predominant kidney involvement. It is caused by complement dysregulation. Specific treatment with eculizumab is currently available and it should be initiated as soon as possible[1]. We describe a case of 21-year-old woman treated early with excellent outcomes.

CASE DESCRIPTION: 21-year-old woman was admitted to intensive care unit with signs of acute kidney injury with oligoanuria, moderate thrombocytopenia and microangiopathic hemolytic anemia. Slight diarrhea with subfebrility lasting previous 3 days were noted in her medical history, and further, start of oral contraception a month ago, too. Initial immunology tests were unremarkable, anti-FH and anti-C1q autoantibodies were negative, apart from slightly decreased C3. Serum creatinine was 1040μmol/l, proteinuria 5,72g/l, hemoglobin 67g/l, schistocytes were present and haptoglobin was immeasurably low, platelets (PLT) 107 000/μl, normal were fibrinogen, dimer D, antithrombin, and coagulation times. Thus renal biopsy was performed showing severe TMA. Normal activity of ADAMTS13, negative STEC O157:H7, were found. These findings together lead to diagnosis of aHUS. Initially, pulses of corticosteroids (3x500mg iv) and plasmapheresis commenced, without any appreciable effect. Hemodialysis was necessary for first 7 days. Fourth day after admission eculizumab was administered (900mg iv weekly). Then, during 2 weeks, diuresis was restored fully, proteinuria decreased to mild range, creatinine started to fall reaching 130 μmol/l in four weeks time, at that time PLT were 206 000/μl and hemoglobin 95g/l. Of note, hematologic parameters started to normalize only after second dose of eculizumab, which is quite untypical. Patient was discharged after 3 weeks and now is treated as an outpatient, with nearly normal GFR (1,23 ml/s), residual proteinuria (0,7g/24hrs) and otherwise normal hematological and biochemical lab findings.

DISCUSSION: Atypical hemolytic uremic syndrome is caused by complement dysregulation that is associated with one or more identifiable mutations. In this case genetic analysis was performed*. The results are summarized in the Table 1. Until this time there is no consensus on discontinuation of treatment or at least dosage adjustement. Another problem that is going to be dealt with is future pregnancy of our patient, the prognosis of pregnancy even in treated patients is poor[2]. However main risk factors are serum creatinine, arterial hypertension and proteinuria[3] prior to conception.

* *kindly performed by prof. Zoltán Prohászka, MD, DSc., Semmelw.univ., Budapest*

Protein	Mutation	Comments
C3, exon 5	c. 567G>T, heterozygous	Protein C3 has pivotal role in complement activation. Atypical hemolytic uremic syndrome is caused by gain-of-function mutations in C3 gene. This mutation has not been yet described, *in silico* studies are not suited for gain-of-function predictions. However in close vincinity are described pathogenic mutants, we therefore conclude, that this mutation has crucial role in this aHUS case though functional studies have not yet been performed.
Complement factor H	c.-331C>T, heterozygous	Complement factor H is a major complement regulator. It has both decay acceleration activity and cofactor activity for alternative pathway. This mutation is described as risk factor polymorphism.
MCPggaac	-547 A>G, -231 A>G, IVS9-78G>A, IVS12+638 G>A, c. 2232 T>C, homozygous	Membrane cofactor protein is a membrane bound complement inhibitor, that is found on most cells in human body, its expression is most abundant on renal endothelium. It has cofactor acitivity for both alternative and classical pathway. In this case was found homozygous polymorphism ggaac, that is described as a risk factor, it increases risk of aHUS twofold[4].



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Vojtěch Petr is supported by travel grant by the Czech Society of Nephrology

Presented in ERA-EDTA Congress, June 3-6, 2017, Madrid