Atypical haemolytic-uraemic syndrome in a young patient with renal, neurological, ocular and cardiovascular involvement☆

Síndrome hemolítico urémico atípico en un paciente joven con compromiso renal, neurológico, ocular y cardiovascular

To the Editor,

We present the case of a 23-year-old man with a 3-month history of headache, loss of vision, loss of appetite, and foamy urine. In the previous week, he had been bedridden, with sensory disturbances, oliguria, and dyspnoea. Upon initial assessment he appeared generally unwell, drowsy, disorientated, tachycardic, hypertensive, and tachypnoeic. He had asterixis, uraemic breath, jugular venous distension, breath sounds with bibasal rales, and oedema of lower limbs. Lab test on admission showed elevated nitrogen products, metabolic acidosis with a wide anion gap, evidence of non-immune microangiopathic haemolytic anaemia and thrombocytopenia (Table 1). Further tests were requested, including ADAMTS13 activity, and infection and immune profiles, which were negative (Table 1). Treatment was started with haemodialysis, parenteral labetalol, red cell transfusion, and plasma exchange. Once uraemia and hypertensive crisis were controlled, ophthalmological examination revealed a marked loss of visual acuity (RE: 20/400 + 1; LE: 20/150 − 1) and hypertensive retinopathy. On day 7, haemolytic activity was controlled, which allowed discontinuation of plasma exchanges. However, the patient relapsed 48 h later, plasma exchanges were restarted and a definitive diagnosis was made of aHUS (Fig. 1). Treatment with eculizumab was initiated, and plasma exchanges were stopped. The patient made adequate progress, with recovery of vision (20/30 in both eyes), however, dialysis had to be maintained. Genetic studies to detect complement mutations associated with aHUS were negative (Table 1). At 9 month follow-up, the patient remained dialysis-dependent; therefore, a diagnosis was made of end-stage renal disease (ESRD) secondary to aHUS, and the workup for renal transplantation was initiated.

Atypical HUS is an extremely rare chronic genetic disease. It is caused by an abnormality in the regulation of complement and can lead to severe sequelae in multiple organs and even death.[1–4] It is characterised by the triad of microangiopathic haemolytic anaemia, thrombocytopenia, and renal failure, though it can affect any organ.[1,2] Our patient displayed renal, haematological, neurological, cardiovascular, and ocular involvement; ocular damage is not frequently reported in the literature.[1,2]

In more than half of the patients with aHUS, it is possible to identify the complement mutation or the mutation in other molecules leading to abnormal complement regulation. However, genetic study is not necessary for diagnosis and initiation of therapy. However genetic studies should be performed to establish prognosis, as some mutations are more aggressive than others. Moreover, genetic study allows more adequate strategy for renal transplantion.[1,2,5] Up to 30% of patients have no documented genetic mutation,[4,6] as it was the case in our patient.

The treatment of choice for aHUS is eculizumab, a humanised monoclonal antibody that blocks the cleavage of the C5 component of complement, thus preventing the release of the anaphylatoxin C5a and the formation of the membrane attack complex C5b-9. This prevents endothelial damage and the generation of thrombotic microangiopathy.[1,7,8] As a prerequisite for starting eculizumab, the patient must be vaccinated against meningococcus and start antibiotic prophylaxis directed against meningococcus whilst the vaccine becomes effective. The earlier eculizumab is started in patients with aHUS, the higher the likelihood of recovery and the fewer sequelae.[5,9] Nonetheless, whilst the diagnosis of aHUS is being established, plasma exchanges can stabilise the patient's haemolytic activity, therefore these should be started early if the clinical picture is one of a thrombotic microangiopathy. It should be kept in mind that blood samples should be obtained for ADAMTS13 activity and autoantibody profile prior to plasma exchange to avoid missing other diagnoses.[1,5,7] If the definitive diagnosis is aHUS, treatment should be changed to eculizumab, as long-term plasma therapy has not been shown to change the devastating course of aHUS.[1,5,9,10] In our patient, plasma exchanges were performed initially, achieving control of haemolytic activity; once the diagnosis of aHUS was established, treatment was changed to eculizumab, achieving a good response with no further need for plasma exchange and no further relapses (Fig. 1). However, the patient was left with the sequela of ESRD.

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Table 1 – Laboratory results.

Urine	Appearance	pH	Density	Proteinuria	Red blood cells	Leucocytes	Proteinuria
cytochemistry	Turbid	8	1.015	>300 mg/dL	>50/HPF	21–50/HPF	850 mg/day
Capillary gases	pH	HCO_3	PCO_2	PO_2	PaO_2/FiO_2	Lactate	Base excess
	7.24	9.6 mmol/L	22 mmHg	121 mmHg	242	1.3 mmol	−15.7 mmol/L
Renal and	Creatinine	BUN	Uric acid	Sodium	Potassium	Chloride	Phosphorus
metabolic profile	19.7 mg/dL	128 mg/dL	8.5 mg/dL	140 mEq/L	4.2 mEq/L	100 mEq/L	8 mg/dL
	Corrected calcium	Ionised calcium	Magnesium	Albumin	Glucose	Total cholesterol	HDL-cholesterol
	6.7 mg/dl	0.65 mmol/L	1.53 mg/dL	2.8 g/dL	92 mg/dL	108 mg/dL	31 mg/dL
	LDL-cholesterol	Triglycerides	Vitamin D	PTH	Vitamin B_{12}	Ferritin	Folic acid
	63.6 mg/dL	61 mg/dL	19.3 ng/mL	751 pg/mL	286 pg/mL	551 ng/mL	7.7 ng/mL
Haematological	Haemoglobin	Haematocrit	Leucocytes	Neutrophils	Lymphocytes	Monocytes	Basophils
profile	5.1 g/dL	14%	6.200 mm^3	80.2%	11.3%	8.1%	0.4%
	Eosinophils	Platelets	Corrected reticulocytes	PBF	LDH	Haptoglobin	ADAMTS13 activity
	0%	82,000 mm^{-3}	5.2%	Schistocytes ++	547 U/L	10.6 mg/dL	74.5%
	PTT	PTT control	PT	INR	Fibrinogen		
	30 s	26.1	11.3 s	1.04	435 mg/dL		
Liver profile	TB	DB	IB	AST	ALT	ALP	
	1.5 mg/dL	0.4 mg/dL	1.1 mg/dL	22 U/L	18 U/L	77 U/L	
Immunological	C3	C4	ANA	ENA	MPOAb	PR3Ab	Direct Coombs
studies	106 mg/dL	28.8 mg/dL	Negative	Negative	Negative	Negative	Negative
Complement genetic study	No pathological mutations were found for: ADAMTS13, C3, CD46, CFB, CFH, CFHR1, CFHR2, CFHR3, CFHR4, CFHR5, CFI, DGKE, PIGA, THBD						
Other	Protein electrophoresis		HIV	Hepatitis B	Hepatitis C	VDRL	Renal biopsy
investigations	Hypoalbuminemia, non-specific elevation of alpha 1 band and B2		Negative	Negative	Negative	Negative	Thrombotic microangiopathy
	Plain CT head		Echocardiography		Renal ultrasound		
	Normal		Pulmonary hypertension and mild pericardial effusion		Small echogenic kidneys with loss of corticomedullary differentiation		

ALP, alkaline phosphatase; ALT, alanine aminotransferase; ANA, antinuclear antibodies; AST, aspartate aminotransferase; BUN, blood urea nitrogen; C3, complement C3; C4, complement C4; CT, computed tomography; DB, direct bilirubin; ENA, antibodies against the extractable nuclear antigens anti-RNP, -Sm, -Ro, and -La; HCO_3, serum bicarbonate; HDL cholesterol, high-density lipoprotein cholesterol; HIV, human immunodeficiency virus antibody; HPF, high-power field; IB, indirect bilirubin; LDH, lactate dehydrogenase; LDL cholesterol, low-density lipoprotein cholesterol; MPOAb, anti-myeloperoxidase antibodies; PBF, peripheral blood film; PCO_2, partial pressure of carbon dioxide; PO_2, partial pressure of oxygen; PR3Ab, anti-proteinase 3 antibodies; PTH, parathyroid hormone; TB, total bilirubin; VDRL, non-treponemal test for syphilis.

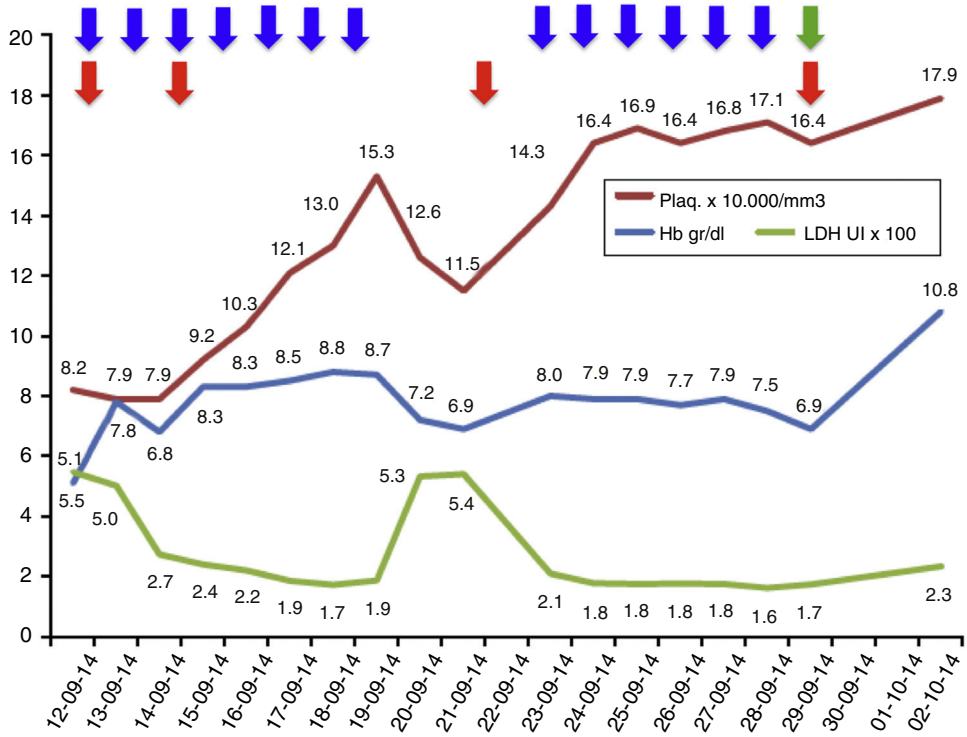

Fig. 1 – Results of laboratory investigations during treatment.
Laboratory parameters during treatment: 13 sessions of plasma exchange (blue arrows); total 4 red cell transfusions (red arrow); eculizumab, started on 29 September 2014 (green arrow). The LDH values are at a scale of 1 x 10^2 and the platelet values are at a scale of 1 x 10^4.

Conclusion

Atypical HUS is a rare genetic disease that affects children and adults, characterised by the presence of non-immune microangiopathic haemolytic anaemia, thrombocytopenia and multi-organ damage. The clinical course can be devastating and endanger patients' life and quality of life, leaving them with severe sequelae such as ESRD. Treatment with eculizumab must be started early to halt multi-organ damage and avoid death.

Conflicts of interest

Dr Nieto-Ríos and Dr Serna-Higuita have delivered conferences sponsored by Alexion Pharma. The other authors declare no conflicts of interest with the content of this article.

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An unusual case of peritonitis after vaginal leak in a patient on peritoneal dialysis☆

Un caso infrecuente de peritonitis tras fuga vaginal en un paciente en diálisis peritoneal

Dear Editor,

Continuous ambulatory peritoneal dialysis (CAPD) is used as an alternative to hemodialysis and has very few complications which include abdominal hernia, peritonitis, processus vaginalis, pleural leakage, and those related to the catheter exit site.[1] It may occasionally be complicated by leakage of dialysate fluid into the abnormal sites.[2,3] We report a case of a woman who experienced vaginal leakage during CAPD and after peritonitis.

A 24 year old female patient was diagnosed with end stage renal disease during pregnancy. There was no other etiological factor, but hypertension. Patient was recommended 20 hours of hemodialysis, but she refused and gave birth to a living child on the 38th gestational week. She has been on CAPD for the last 3 months. Since last week she has started to have abdominal pain accompanied with nausea and fever (>38 °C). With these complaints she was referred to our policlinic and her peritoneal fluid cell count was found 4860/mm^3 (95% polymorphonuclear leukocytes). Cultures were obtained and she was admitted to our hospital with the diagnosis of peritonitis. Blood analysis showed leucocytes 9000/mm^3, hemoglobin: 8.8 g/dl (11.5–16), C-reactive protein: 14.2 mg/dl (0–0.5), sedimentation: 135 mm/hour. *Pseudomonas aeruginosa* was detected in blood cultures. She was on empiric ceftazidime and cefazolin treatment and treatment was continued because *P. aeruginosa* was found sensitive to this treatment. Urine culture remained sterile. Patient stated that there is dialysate in her vagina. She was consulted with obstetrics and gynecology regarding any fistulas. A urine catheter was placed and it is understood that origin of dialysate was vagina. Contrast enhanced computerized tomography was done showing a vaginal fistula (Figs. 1 and 2). CAPD catheter was removed. Surgical operation was found unnecessary and hemodialysis was started. Patient was discharged after 3 weeks of ant biotherapy.

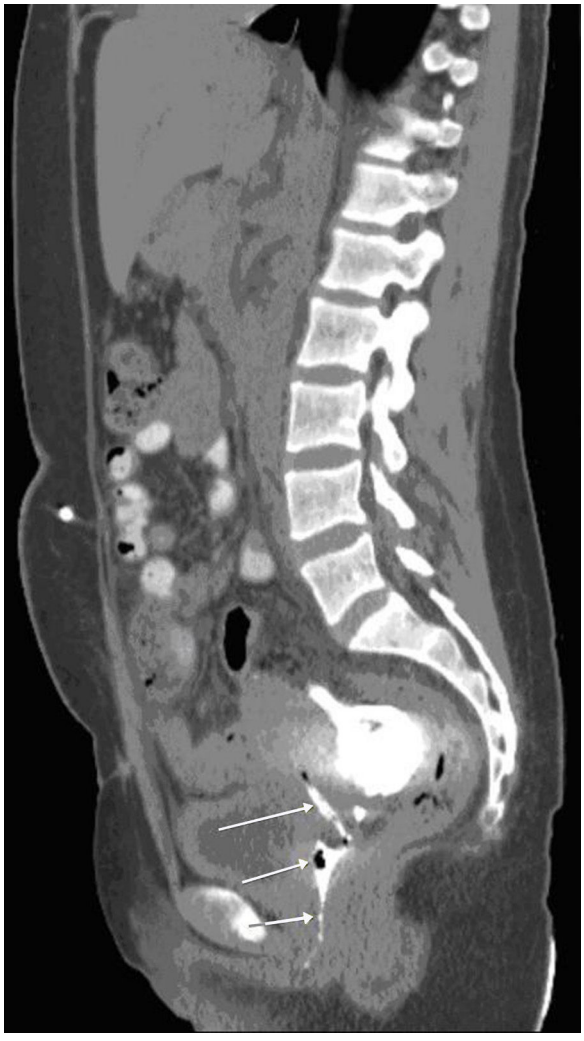

Fig. 1 – Arrows shows vaginal leak.

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