European School of Internal Medicine, Latvia, Riga

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*Clinical Case presentation

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named after I.I. Mechnikov

Patient

* A 31-year-old woman was admitted to the department of therapy and rheumatology of North-Western State Medical University named after I.I. Mechnikov because suffering from undiagnosed medical condition for 3 years.
* Main complaints:

- fatigue;
- arthralgia and morning stiffness (about 20 minutes)

Joints: metacarpophalangeal, proximal interphalangeal, elbows, shoulders, ankles;

- easy bruising.

* Medication intake: 20 mg/day prednisone

*2011

* At 12 weeks of gestation – first time platelets $42*10^9$/L (150-350).
* At 25 weeks of gestation - fetal malnutrition, at 29 weeks - oligohydramnios, increased blood pressure (130/100 mm Hg).
* Every morning - pain in the umbilical region
* Hospitalization with pre-eclampsia – platelets $42*10^9$/L, Hb 81 g/L, red blood cells $2,2*10^{12}$ / L, 24h-proteinuria 5.7 g/24h, ERS 52 mm/h

→ Cesarean section at 29 weeks.

* Postoperatively - platelets $6*10^9$/L, 24h-proteinuria 7 g/24h, hypoproteinemia, AST 5 times ULN, ALT 5 times ULN, ALP 4 times ULN.

Diagnosis: Severe pre-eclampsia. HELLP-syndrome. Disseminated intravascular coagulation

* Blood transfusions, fresh frozen plasma + prednisone 90 mg for 7 days with positive effect - platelets $42*10^9$/L, 24 h proteinuria 1.71 g/24h.
* After 25 days after birth the child died. Intrauterine infection (pneumonia), disseminated intravascular coagulation, brain hemorrhage.

*2012

* Hospitalization at the department of nephrology - platelets $17*10^9$/L, 24h-proteinuria 3.3 g/24h, ERS 54 mm/h
* Episode of thrombosis - thrombosis of all subcutaneous veins (intermedia basilica, cephalica, cubiti) of the right upper extremity.

Diagnosis: Severe pre-eclampsia. HELLP-syndrome. Chronic kidneys disease? (glomerulonephritis? lupus nephritis?). Postejection thrombosis of subcutaneous veins of the upper extremity.

* Recommendations: Continue prednisone 30 mg/day, was referred to rheumatologist.
* Rheumatologist: immunological tests during prednisone 30 mg/day - antinuclear factor, double-stranded DNA titer were normal.
* Recommendations: dose reduction to complete abolition, observation in dynamic.

*2013

* 2 weeks after complete abolition of prednisone - the appearance of arthralgia and morning stiffness (20 minutes) Joints: metacarpophalangeal, proximal interphalangeal, elbows, shoulders, ankles.
* June 2013 at the seaside - episode of hemorrhagic rash on legs, itching malar rash over the cheeks.
* General practitioner (Local clinic): platelets 104*109/L, ESR 46 mm/h, ANF 1: 160 (norm<1:160), 24h-proteinuria 1.5 g/24h

Diagnosis: Systemic lupus erythematosus

* Recommendation: 20 mg/day prednisone and was referred to the Federal Hospital.

*2013

* Main complaints:
- fatigue;
- arthralgia and morning stiffness (about 20 minutes)

Joints: metacarpophalangeal, proximal interphalangeal, elbows, shoulders, ankles;

- easy bruising.

* Physical examination with no significant alterations

* Laboratory tests:
- Platelets $122*10^9$/L, red blood cells $3,7*10^{12}$/ L,
- ERS 27 mm/h,
- LDH 3 times ULN,
- Rheumatoid Factor 2 times ULN,
- C-Reactive Protein 5 times ULN,
- Positive lupus anticoagulant,
- Rest of the laboratory work-up was within normal limits.

*Ideas???

*Differential Diagnosis

Normocytic anemia+ reticulocytosis + Elevated LDH level = Hemolytic Anemia
Autoimmune hemolytic anemia?
Coomb's test negative

Rheumatoid arthritis?
With systemic symptoms?
Without synovitis? ACPA negative, X-ray no erosion
Systemic lupus erythematosus?
No immune features

Bone failure?
Hypoplastic bone marrow, an erythroid marrow with suboptimal reticulocytosis

Abdominal pain -
Episode of mesenteric artery ischemia during pregnancy?

What else???

Thrombocytopenia+
Episode of thrombosis of subdermal veins
(such atypical place)

* FLAER and multiparameter flow cytometry of peripheral blood

Cells	**GPI-Ap deficiency**	Result
Red blood cells	Type II (partial deficiency CD59)	**31,99%**
	Type III (complete deficiency CD59)	**7,58%**
	Total GPI-Ap deficiency	**39,57%**
Granulocytes	FLAER-/CD24-	**92,37%**
Monocytes	FLAER-/CD14-	**93,28%**

Заключение: Среди эритроцитов и лейкоцитов (гранулоцитов и моноцитов) выявлен ПНГ-клон.

Paroxysmal Nocturnal Hemoglobinuria

313 in Russian Federation

- The national register of orphan diseases
- The government supports patients with free treatment
- Soliris (eculizumab) - World's Most Expensive treatment

Paroxysmal Nocturnal Hemoglobinuria

- Somatic mutation of the X-linked PIG-A gene – leads to deficiency of glycophosphatidylinositol-anchored membrane proteins – the increase of sensitivity of cells to complement-mediated lysis
- «The great impersonator» - variety of symptoms from esophageal spasms in the morning to impotence.
- Triad of pathophysiologic events - Intravenous hemolysis, thrombosis (ep. Atypical veins – hepatic, abdominal, subdermal), bone marrow failure (pancytopenia)
- Manifestation during pregnancy is very common
- High sensitivity – FLAER (flow cytometry assay with the use of fluorescent aerolysin), which binds GPI-Ap
- Stem cell transplantation, anti-complement antibodies (C5)
- The cause of death - thrombosis


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