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CLINICAL CASE PRESENTATION

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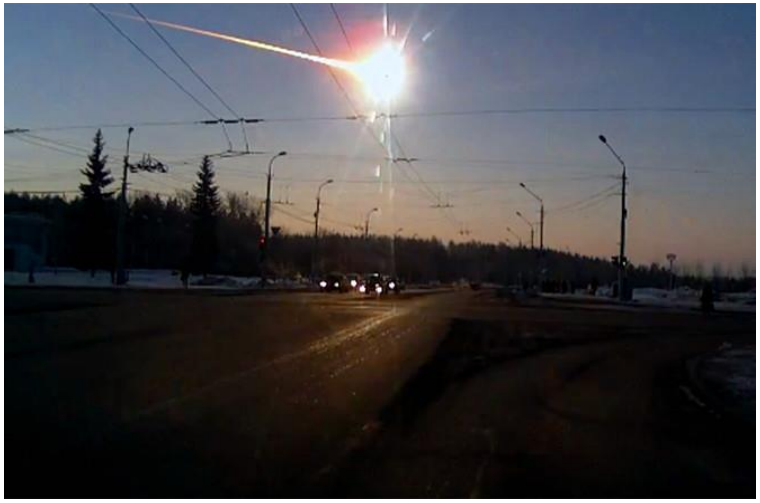
CHELYABINSK



CLINICAL HISTORY

Patient R., male, 37 years old

- Since 2008 – arterial hypertension (episodic, increased blood pressure maximal level -140/100 mm Hg)
- January 2013 - Itching, particularly after exposure to hot water.
- October 2013 – headache, dizziness, increased blood pressure 140/96 mm Hg, transient weakness and paresthesia in the right hand.
- November 2013 - partial logaphasia within 4-5 days with spontaneous recovery.
- December 2013 - dizziness recurrence, transient weakness and paresthesia in the right hand within 7 days
- MRI in the vascular mode - 3 ischemic foci: 2 foci in the cerebellum and 1 focus in the region of the left frontal lobe.

Patient had 2 episodes of ischemic stroke in the area of the left middle cerebral artery

Past medical history

- **Heredity** is not burdened by arterial and venous thrombosis up to 50 years, no cancer

- **Risk factors for cardiovascular disease**

  smoking (30 pack-years), overweight (BMI 26 kg/m^2)

- No abuse alcohol

- No traumatic brain injury

Clinical examination

(December 2013)

- Weight: 82 kg
- Height: 1,74 m
- RR: 16/min
- BP: 120/92 mm Hg
- HR: 80 bpm
- Hyperemia of the face
- Conjunctival injection
- The lever and spleen are not enlarged
- Hemiparesis on the right side (global right side muscle strength score was 3-4).

Differential Diagnosis

- **Hereditary thrombophilia** *(antithrombin deficiency, protein C deficiency, protein S deficiency, elevated plasma levels of factor VIII, antiphospholipid syndrome, hyperhomocysteinemia, factor V Leiden mutation, prothrombin 20210 mutation)*
- **Cardioembolic stroke** *(arrhythmia, patent foramen ovale)*
- **Atherothrombosis**
- **Vascular abnormalities** *(artery dissection, fibromuscular dysplasia and etc.)*
- **Myeloproliferative disorders** *(polycythemia vera, essential thrombocythemia)*
- **Paroxysmal nocturnal hemoglobinuria**

Laboratory tests:

- **Complete blood count (17.12.2013):** Hb **17.4** g / L (13.0-16.0) [2012: Hb 14.7 g / L], Platelets **600** $\times 10^9$/L (150-350), Ht **50**% (<44), leukocytes **9,6** $\times 10^9$/L (4-9)

- **Biochemical analysis of blood:** uric acid **0,6** mmol/l (0.2-0.42); total cholesterol, LDC, HDL, triglycerides, electrolytes, creatinin, bilirubin, ALAT, ASAT, CRP, iron – normal values

- Vitamin B12, folate, complement, anti-nuclear antibody, coagulation testing – normal values

Other investigations

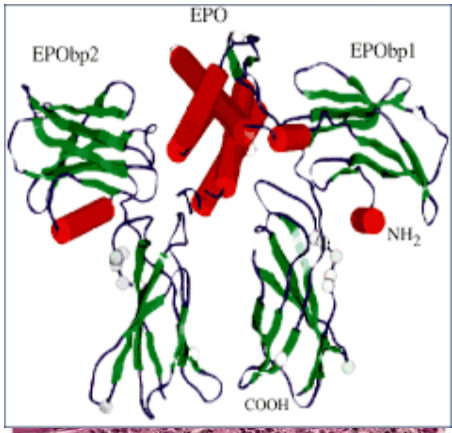
	RESULT	UNITS	REFERENCE INTERVAL
Antithrombin (at III) activity	95	%	80-120
Protein C activity	133	%	> 70
Protein C resistance	2,58		> 2,3
Protein S activity	83	%	> 70
Lupus anticoagulant	1,09	NR	< 1,2
Anticardiolipin antibodies (a-CL) IgM	1,9	GPL	< 10
Anticardiolipin antibodies (a-CL) IgG	2,5	GPL	< 10
Anti-b2-glycoprotein-I antibodies IgM+IgG	3,5	GPL	< 10
Factor V Leiden Mutation	Not found	GPL	< 10
Factor II prothrombin 20210 mutation	Not found		
Homocysteine	8,6	µmol/L	5-15
Factor VIII	126	%	50-150

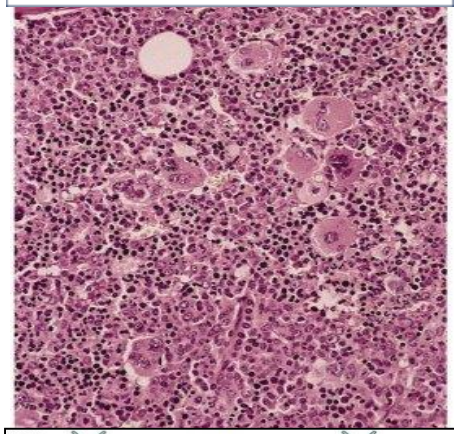
Instrumental investigations

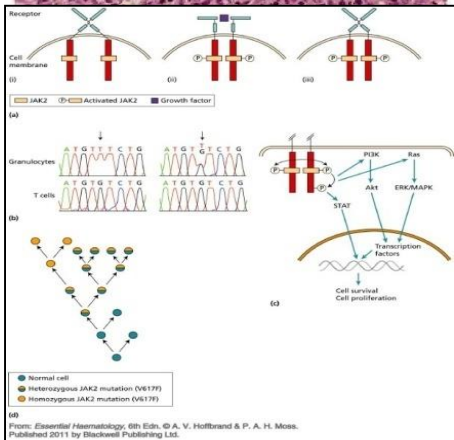
- **Ultrasonography of the carotid arteries, echocardiography, Holter ECG monitoring** - normal.
- **Abdominal ultrasound:** steatosis without hepatosplenomegaly.
- **MRI of the cerebrovascular system:** hemodynamically significant stenosis and malformations were not found.
- **Respiratory function** - normal.

Other investigations

- **Erythropoietin** –2.4 mIU/mL (2,6-18,5)
- **Bone marrow biopsy:** erythroid, granulocytic and megakaryocyte proliferation
- **Mutation in the JAK2 kinase (V617F) – positive**
- Mutation BCR-ABL1 – negative







Revised WHO Criteria for Diagnosis of Polycythemia Vera*

Level	Specifics
Major criteria	**1. Evidence of increased RBC volume, including ≥ 1 of the following:** • Hb >18.5 g/dL in men or > 16.5 g/dL in women • Hb or Hct > 99th percentile of method-specific reference range for age, sex, and altitude of residence • Hb >17 g/dL in men or 15 g/dL in women if associated with a documented and sustained increase of at least 2 g/dL from the patient's baseline value not accounted for by correction of iron deficiency • Elevated RBC mass > 25% above mean normal predicted value **2. Presence of *JAK2 617VF* or other functionally similar mutation (eg,*JAK2* exon 12 mutation)**
Minor criteria	**1. Bone marrow biopsy showing hypercellularity for age with trilineage growth (panmyelosis) and prominent erythroid, granulocytic, and megakaryocytic proliferation** **2. Serum erythropoietin level below the reference range for normal** **3. Endogenous erythroid colony formation in vitro**
Diagnosis requires presence of the 2 major criteria and one minor criterion or the presence of the first major criterion plus 2 minor criteria.	

***** This research was originally published in *Blood*. Adapted from Tefferi A, Thiele J, Orazi A, et al: Proposals and rationale for revision of the World Health Organization diagnostic criteria for polycythemia vera, essential thrombocythemia, and primary myelofibrosis: Recommendations from an ad hoc international expert panel. *Blood* 110:1092, 2007

Diagnosis

Polycythemia vera

Treatment

- **Phlebotomy** (with increasing hematocrit above 45%)
  300 ml per day
- **Interferon alfa-2b** (Lifferon) 3 million IU per day / **(Hydroxyurea)**
- **Low dose aspirin** (Cardiomagnil) 75 mg
- **Antihypertensive drugs** (amlodipin (Norvask) 5 mg, Lisinopril (Diroton) 10 mg)
- **Allopurinol** 300 mg

Treatment

- Research has found that the 1.5-3 years of median survival in the absence of therapy has been extended to at least 10-20 years because of new therapeutic tools
- Phlebotomy is typically performed in people with polycythemia vera to bring their hematocrit down below 45% for men or 42 % for women
- Low dose aspirin (75–81 mg daily) reduces the risk for various thrombotic complications, particularly after ischemic events
- Interferon was administrated taking into consideration the secondary thrombocytosis (600 - 700 $\times 10^9$/L) with the ischemic neuropathy on the treatment of aspirin plus phlebotomy and young age
- Selective JAK-inhibitors are being investigated in clinical trials

Follow up

- **Complete blood count (22.08.2014):** Hb **15.0** g / L (13.0-16.0, Platelets **355** × 10^9/L (150-350), Ht **43,5**% (<44), leukocytes **7,2** × 10^9/L (4-9)
- **Biochemical analysis of blood:** uric acid **0,3** mmol/l (0.2-0.42)
- **No thrombotic events**
- **No plethora**
- **No hemorrhagic complications**

Literary reference

- **The average age at which PV is diagnosed is about 60 to 65 years - in our case – 37 yrs!**

Polycythaemia vera in young people: an analysis of 58 cases diagnosed before 40 years: *

- **approximately 5% of all cases of PV**

They differ from older patients:

- **in the initial clinical severity**
- **the short interval between the first symptoms and the diagnosis**
- **frequent presentation with a life-threatening complication**
- **However, after the initial complications, the overall survival is long (even when including the initial complications)**

*** Najean Y. et al. Br. J. Haematol 1987 Nov;67(3):285-91.**

THANKS FOR YOUR ATTENTION !