Link Between Biochemical, Biological and Clinical Assessment
Focused on Polycythemia Vera and Stroke

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This case presentation is of a 58 years old female patient who develops a stroke in 2011 with significant biochemical and biological changes. These manifestations prove to be the result of a hematology disorder, more precise a myeloproliferative neoplasm, Polycythemia Vera. The disease was unidentified and with non-specific symptomology until the occurrence of stroke. The particularity of this case is the presence of severe cardiovascular disease (stage III hypertension. Obstructive hypertrophic cardiomyopathy, chronic ischemic silent disease), with cerebral manifestations (stroke) and associated with mixt hepatitis (alcoholic and deficiency), hypercholesterolemia and hyperuricemia. This biological context represent a real challenge both etiologically and therapeutically (pharmacology and non-pharmacology).

Keywords: Polycythemia Vera, stroke, hyperuricemia

Polycythemia Vera (PV) is a myeloproliferative neoplasm characterized by an absolute erythrocytosis not driven by erythropoietin [1]. Like others myeloproliferative neoplasm, PV has a high risk of evolution to leukemia and thrombosis [2]. It is characterized by an increased in the number of leukocytes and platelets to a critical level that altercate with the blood flow. The onset is with non-specific signs and symptoms. Face erosion may occur, intermittent pruritus, headache, vertigo, tinnitus and peripheral and coronary manifestations. The thrombosis context may easily conduct to a pulmonary and cerebral embolism. In the context where coronary heart disease is important and involves cardiomyopathy, there is a risk of sudden death. In 2005 Kralovics and his colleagues observed a dominant gain in function mutation in Janus- associated kinase 2 (JAK2) gene on chromosome 9 in more than 80% of the patients (mutation of the JAK2 V617F) [3]. In 2008 World Health organization establishes the criteria for diagnosis of PV [4].

To evaluate the complications and the progression of the disease, to biochemical and biological picture, it is associated the abdominal ultrasound investigation (evaluation of the liver, spleen), medullar puncture from the iliac crest. Treatment for Polycythemia Vera is a symptomatic and prevention for the vascular complications. Bleeding is performed (phlebotomy) for vascular decongestion, blood is removed and electrolyte and plasma are introduced. Aspirin is often associated with anti-inflammatory and cytotoxicity in the treatment with hydroxyurea and/or non-interferon therapy. Patient education include basic food hygiene rules (norm caloric, norm protein – if unchanged uric acid value), sufficient hydration (vitamin, mineral and oligo elements) [6, 9,10].

Experimental part
Materials and methods
We evaluate the biochemical and biological samples with ANALIZOR AUTOMAT - A 25 - BIOSYSTEMS analyzer and on ABACUS 3 hematology examiner during six admissions in Rehabilitation Department. The biochemical and biological results were analyzed during 2012-2016, in connections with the biological, clinical and functional evolution in a context of severe cardiovascular, hematological, neurological and digestive plural pathology. Biochemical and biological assessment was required to establish the appropriateness of applying the rehabilitation program (energy, caloric, hydric), mandatory adapted to the level of physical stress and exercise training of the patient in the Rehabilitation Department.

Case report
Our report presents a 58 years old, female patient, coming from rural environment, with no significant co-morbidities known until 2011, the moment she was hospitalized in Neurological Department of Psychiatry and Neurology Hospital. Anamnesis reveals that the patient was

<table>
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<tr>
<th>Major criteria:</th>
<th>2008 WORLD HEALTH ORGANIZATION CRITERIA FOR THE DIAGNOSIS OF POLYCYTHEMIA VERA</th>
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<tbody>
<tr>
<td>A1. Hemoglobin ~18.5 g/dl male/16.5 g/dl female; or other evidence of increased red cell mass</td>
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<tr>
<td>A2. Presence of JAK2 V617F or other functionally similar mutation</td>
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<tr>
<td>Minor criteria:</td>
<td></td>
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<tr>
<td>B1. Marrow morphology</td>
<td></td>
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<tr>
<td>B2. Low serum erythropoietin</td>
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<td>B3. Bone marrow endothelial erythroid colony formation</td>
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<td>Marrow morphology: hyper cellular marrow with three lines hyperplasia; clustering of pleomorphic megakaryocytes; absent stromal iron; no major inflammatory features.</td>
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<tr>
<td>Requirements for diagnosis:</td>
<td></td>
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<tr>
<td>A1=A2=any from B</td>
<td></td>
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<tr>
<td>A1* any two from B</td>
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Table 1

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chronical alcohol addicted. She was accusing motor impairment in the right half body, installed during the previous day. Clinical and Para clinical assessment and examination (imaging investigation and blood samples) established the diagnosis of Polycythemia Vera, according to World Health Organization criteria for the diagnosis of Polycythemia Vera (2008). After 6 days of hospitalization the patient is transferred to Rehabilitation Department in order to begin the proper rehabilitation treatment program after stroke.

The clinical examination performed during the first hospitalization in September 2012 finds right hemiplegic motor deficit, with generalized hypotonic muscles, especially in right quadriceps and deltoid muscles. The patient accused pain when mobilizing the right upper limb (VAS=8-9), with vicious position (abduction of the right arm, with the forearm flexion on the arm, fingers in pronation and flexion – partially reducible). Passive movements of the scapula-humeral joint was significant reduced (abduction 30°, flexion 30°, extension 0°). ROM of the upper limb was 1/5 in distal part and 2/5 proximal. Lower limb examination with a small reduction of the Achilles tendon, ROM 2/5 with impairment of planar dorsal-flexion and with high level of spasticity (Ashworth 3) for planar and fingers and the vicious position of the foot- in inversion. Babinski reflex was negative, bicipital and tricipital reflex (ROT) on right hemi body and inconstant and no systematized in the left hemi body. Functional evaluation showed that the patient needs help for ADL (activity of daily living) except feeding since she is left-handed (Barthel index =35/100). Control of sphincters is present. Cognitive evaluation (MMSE=29/30) demonstrates that the patient has no deterioration; she can read and write correctly. The Para clinical examination showed leukocytosis, erythrocytosis and doubled level of the hematocrit from normal, which restrains from electrotherapy procedures.

The second admission in March 2013, compared to the first hospitalization in Rehabilitation Department revealed that the patient presented a higher reduction of the global mobility, due to the lack of constant pharmacological-treatment (Hydrea) and no rehabilitation program (bed dependent). During this hospitalization the patient was found with high blood pressure and high levels of the hepatic enzymes. Also, an orthotics is now recommended due to the shortness of the Achilles tendon. The lower limb ROM improved, the patient being able to maintain the orthostatic position, but walking is possible with larger floor base and only for short distance (2-3 steps). She needs help from a person for walking using also a walk frame. The Barthel score improved to 60/100 and the MMSE score regressed to 25/30. Paraclinic assessment revealed a small reduction of hematocrit and hemoglobin levels, but also an increased level of uric acid, urea and hepatic enzymes.

During the third hospitalization (March 2014), the patient is accusing headache, vertigo, pruritus and multiple arthralgia and a decreased level of physical performance. Clinical evaluation shows knee and ankle edema. The passive moments have improved, still with increased spasticity for planar zone and fingers. Due to high intensity of pain (VAS=9) gait is performed with difficulty. Paraclinical results showed high levels of urea and uric acid, hemoglobin (but lower than 2012) and increased transaminases (TGO, TGP). Cognitive evaluation scale decreased (MMSE = 23/30) and Barthel index was 45/100. During this rehabilitation program the supportive hepatic treatment and central muscle relaxant (Lioresal) was initiated.

In 2015, patient returns to Rehabilitation Department twice (March and August) for a new reevaluation of the right hemiparesis and rehabilitation program (the fourth and fifth admission). At this point patient accuses the persistence of pruritus in the left half side of the body, dyspnea at low efforts and sometimes even in resting, fatigue, vertigo, urinary incontinence and dysuria. The locomotor evaluation of the upper right arm identifies more reduced mobility (Abduction 20°; Flexion 45°, Extension 0°) with important pain limitation even in passive movements (Abduction 60°; Flexion 90°, Extension 0°). Paraclinical evaluation showed elevated levels of triglycerides, hemoglobin, hematocrit, uric acid, urea and creatinine but also urinary infection. For the first time during the hospitalization history cardiac ultrasound and a cardiology evaluation were performed with the following conclusions: 1. Obstructive hypertrophic cardiomyopathy (with severe Aortic obstruction, mild middle ventricular

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<th>Table 2</th>
<th>THE EVOLUTION OF BIOLOGICAL AND BIOCHEMICAL PARAMETERS</th>
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<tr>
<td>Lab</td>
<td>Normal values</td>
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<tr>
<td><strong>HEMATOLOGY</strong></td>
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<tr>
<td>WBC</td>
<td>4-9/10^9/L</td>
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<tr>
<td>RBC</td>
<td>4-5.5/10^12/L</td>
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<tr>
<td>HGB</td>
<td>11-16 g/dL</td>
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<td>HCT</td>
<td>35-46 %</td>
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<tr>
<td>MCV</td>
<td>80-100 fL</td>
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<tr>
<td>MCH</td>
<td>26 – 34 pg</td>
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<td>MCHC</td>
<td>31-35 g/dL</td>
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<tr>
<td>PLT</td>
<td>150-350/10^11</td>
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<tr>
<td>LYM</td>
<td>1-5/10^9/L</td>
</tr>
<tr>
<td>GRA</td>
<td>2.8-16/10^9/L</td>
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obstruction). 2. Moderate Mitral and Aortic regurgitation. 3. Mitral stenosis with significant calcification of the posterior valve. The EKG examination revealed a discrete ST segment depression in DI, aVL, V5-V6. Cognitive evaluation scale is decreasing to 20/30 and Barthel index is now 40/100.

In the next year 2016 the patient returned to the Rehabilitation clinic for an even more functional regression, installed progressively in one year. Locomotor evaluation showed an increased level of spasticity associated with a deceased ROM=2/5 for both upper and lower limb. Patient accuses dyspnea at low intensity physical efforts, even in transfers. Paraclinic evaluation showed an increased level of hemoglobin and hematocrit (due to cardiovascular pathology), uric acid, creatinine and urea. Functional index was stationary (Barthel 40/100) and cognitive index decreased (MMSE 18/30). Maintaining orthostatic position was impossible at this point followed by recommendation of wheel chair.

Results and discussions

The particularity of this case is due to the first clinical manifestation of Polycythemia Vera identified with the debut of a stroke. Also is due to the complications of hepatic, cardiovascular and metabolic systems which required periodical evaluation for hematologic and biochemical parametric in order to adjust the rehabilitation program. This evaluation represents the key in the therapeutically management of the rehabilitation program [7, 8].

Another particularity is the lack of patient compliance to the pharmacological and non-pharmacological treatment which caused the rapid decline of cardiovascular system. The high level of uric acid must be noticed in the progression of the disease as a biochemical reaction to treatment and compliance. Interferon therapy may be considered as an alternative treatment for the hepatic and hematological pathology.

Also another special issue about this case is represented by the gender and age of the patient. Generally Polycythemia Vera is diagnosed around the age of 60, especially in men. Our patient is a female which was diagnosed at 50 years old, when the complications of this pathology were already present and imitated the therapy, rehabilitation management and prognosis.

The literature of the last decade shows that discovery of the molecular-target therapies improved treatment for myeloproliferative neoplasms.

The case management requires an interdisciplinary team in order to understand the particularity of the case and to coordinate an individualized rehabilitation program based on functional level, cardio-vascular, hematologic and neurological level repetitively assessed.

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