

## Essential thrombocythemia masked by vitamin B 12 deficiency megaloblastic anemia: A case report

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### Abstract

The association of megaloblastic vitamin B12 deficiency anemia and essential thrombocythemia is very rarely described in the literature. We reported a case of a 65-year-old patient with an isolated chronic anemic syndrome secondary to megaloblastic vitamin B12 deficiency anemia treated with vitamin B12 therapy by injection. The evolution was marked three months after treatment by the an ischemic cerebrovascular accident and thrombocytosis. Additional investigations confirmed essential thrombocythemia. The patient was put under hydroxyuria and an anticoagulant treatment with a good evolution.

**Keywords:** Megaloblastic anemia; Thrombocytosis; Essential thrombocythemia; Thrombosis

### 1. Introduction

Essential thrombocythemia (ET) is a myeloproliferative disorder characterized by chronic thrombocytosis with megakaryocytic hyperplasia and giant megakaryocytes. It mainly affects adults between 50 and 60 years old with equal frequency in each genders. Due to its chronic clinical evolution, many essential thrombocythemia cases are undetected. Vitamin B12 deficiencies may reveal or could be associated with them especially in developing countries where nutritional deficiencies are frequent. In this paper, we reported a case of a patient with essential thrombocythemia which was undetected due to concomitant vitamin B12 deficiency [1,2].

### 2. Case presentation

This case is about a 65-year-old male patient, strictly vegetarian, with no particular medical history, who has had asthenia for four months with mucocutaneous pallor. Other than that he had a good overall health.

At the initial clinical examination, a conscious patient with a Glasgow score at 15/15 was found. He was afebrile (36.8 C) with a blood pressure at 13/8 cmHg. The oxygen saturation was at 100%, the heart beat was at 75 beats/minute. The patient had a discolored conjunctivae and the absence of hepatomegaly and splenomegaly was noted. The lymph node areas were free and the rest of the somatic examination was normal.

The biological assessment showed on the blood count an aregenerative normochromic macrocytic anemia with the hemoglobin at 6 g/dl, the mean corpuscular volume at 118 femtolitre, the corpuscular hemoglobin content at 29 and reticulocytes at 55 10<sup>9</sup>/L, a platelet count at 160 10<sup>9</sup>/L, with a white blood cells count at 4.9 10<sup>9</sup>/L, the polynuclear neutrophils (PNN) count at 1.9 10<sup>9</sup>/L, and the lymphocytes count at 2.4 10<sup>9</sup>/L.

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The blood smear showed the presence of macrocytes, macroovalocytes with polysegmented PNNs.

The myelogram was demonstrated the presence of a few megakaryocytes (R+++ M++) showing erythroblastic hyperplasia with a megaloblastic aspect in favor of megaloblastic anemia deficient in vitamin B12 or B9.

The vitamin assay showed a vitamin B12 deficiency with a serum level of 80 pg/ml. The vitamin B9 and ferritin assays were normal. The etiological assessment demonstrated chronic gastritis without helicobacter pylori on esogastroduodenal fibroscopy with negative anti- intrinsic factor antibodies. The diagnosis retained was a deficiency megaloblastic anemia due to lack of intake.

The patient was put on vitamin B12 therapy by intramuscularly injection (the oral form was not available). The dosage was as follows: one injection of 5000 IU/day (the only form available) for a week, then an injection/week for one month, then one injection/month continuously.

The clinical case has complicated three months later by the occurrence of an ischemic cerebrovascular accident revealed by aphasia and left hemiparesis. Also, the blood count showed thrombocytosis at 1500 10<sup>9</sup>/L with normal hemoglobin values, normal mean corpuscular volume as well as the leukocyte formula. Bone marrow biopsy showed megakaryocytic hyperplasia with giant megakaryocytes without bone marrow fibrosis and without tumor cells. The JAK 2 mutation was positive and the BCR ABL rearrangement was negative. Finally, the team declared an essential thrombocythemia diagnosis.

The patient was put on hydroxyuria with two capsules/day and on low molecular weight heparin. The patient had good outcomes as he presented a normalization of the blood count and an improvement of neurological signs.

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### 3. Discussion

The exact Essential thrombocythemia is a chronic myeloproliferative syndrome which is often difficult to diagnose since there is no specific marker. it represents a diagnosis of elimination.

The diagnostic criteria for essential thrombocythemia established by the World Health Organization (WHO) in 2016 are:

- A platelet count > 450 10<sup>9</sup>/L
- A BOM showing megakaryocyte proliferation with mature giant megakaryocytes with a hyperlobed nucleus. No significant increase in the granulocyte or erythroblast lineage, and the absence of bone marrow fibrosis > grade 1.
- No WHO criteria evoking BCR-ABL1+ chronic myeloid leukemia, polycythemia vera, primary myelofibrosis, myelodysplastic syndrome or other myeloid neoplasia.
- Positive JAK2, CALR or MPL mutation or the presence of a clonal marker or absence of a sign in favor of reactive thrombocytosis.

The diagnosis of ET requires the presence of the 4 criteria mentioned above [3].

Our patient developed thrombocytosis at 1500G/L after a vitamin B12 treatment. The diagnosis of essential thrombocythemia was confirmed by the presence of thrombocytosis and megaryocyte hyperplasia with some giant megakaryocytes at the BOM, as well as the JAK 2 mutation and the absence of WHO criteria for other myeloid neoplasms.

Megaloblastic vitamin B12 deficiency anemia is prevalent worldwide, particularly in developing countries where nutritional diets are inadequate.

Its diagnosis is based on the plasma dosage (Normal values are between 200 - 800 ng/L) [4]. Our patient had a collapsed plasma level of vitamin B12.

In the literature, it is reported an increased incidence of arterial and venous thrombotic events in patients with associated vitamin B12 or vitamin B9 deficiency with chronic myeloproliferative syndromes since the latter are characterized by thrombocytosis while vitamin B9 and B12 deficiencies are responsible for hyperhomocysteinemia (accumulation of homocysteine) which is a risk factor for thrombosis [8]. Our patient presented an ischemic stroke three months after the vitamin B12 administration.

The coexistence of these two diseases often makes the diagnosis of essential thrombocythemia difficult as it requires a study of the bone marrow as well as molecular markers. Nevertheless, diagnosing nutritional deficiencies is usually straightforward. In addition, patients show significant clinical improvement after treatment of deficiency states.

Subsequent investigations are usually delayed. As a result, many essential thrombocythemia cases remain undetected for a long time. Indeed the lack of regular follow-up and inadequate documentation further delay their diagnosis [7].

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#### 4. Conclusion

Essential thrombocythemia is among the most common chronic myeloproliferative disorders. Due to the indolent evolution of this disease and the frequency of deficiency anemia in developing countries, the association of these two disorders is often neglected.

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#### Compliance with ethical standards

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Pr. TAZI, Dr. BENHALIMA, participated in design and development of the case report, managing and treating the patient, writing of the case report and final approval of the submitted version after critical review.

##### *Disclosure of conflict of interest*

All the authors: Yasmina BENHALIMA, Ilias TAZI, Fatimzahra LAHLIMI and Benmoussa Amine report no conflict of interest in relation to the subject matter.

##### *Statement of informed consent*

Statement of informant consent: Informed consent was obtained. The patient understands that her name and initials will not be published and has given her consent for clinical information to be reported in a case report.

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