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"Transformation of Polycythemia Vera into Acute Myeloid Leukemia": A Case Report with Review of the Literature

Karrati Ilham, Jahdaoui Adil, Ghita El Ghouat, Yahyaoui Hicham, Ait ameur Mustapha, Chakour Mohamed

Hematology Laboratory, Avicenna Military Hospital, Marrakesh, Morocco

Email address:
ilhamkarrati@gmail.com (K. Ilham)

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Abstract: Polycythemia vera (PV), with essential thrombocythemia (ET) and primary myelofibrosis (PMF), belongs to the group of Philadelphia negative myeloproliferative neoplasms (MPN). PV is characterized in virtually all cases by the somatic JAK2 V617F mutation or another functionally similar JAK2 mutation that results in panmyelosis. Two phases of PV are recognized which include an initial polycythemic phase associated with elevated haemoglobin level, elevated haematocrit and increased red blood cells mass, and a later spent phase or post- polycythemic myelofibrosis phase, characterised by cytopenias including anaemia, ineffective haematopoiesis, bone marrow fibrosis, extramedullary haematopoiesis, and hypersplenism. The natural progression of PV includes a low incidence of evolution to a myelodysplastic or blast phase. Leukemic transformation in PV is described as a rare and late event, less common than primary myelofibrosis. The interval between diagnosis and leukemic evolution is highly variable, from a few years to >20 years; which implies a long-lasting exposure to myelosuppressive agents. Among the hematological transformations; evolution to secondary acute myeloid leukemia (AML) is associated with a poor prognosis; here we report a case of an 80 year old woman who progressed unusually to blast phase within two years of diagnosis of PV. The interest of this work lies in the fact that this transformation into AML occurred after a short period of evolution, which is not frequent enough in the literature.

Keywords: Polycythemia Vera, Acute Leukemia, Prognosis

1. Introduction

Myeloproliferative neoplasms (MPNs) are acquired clonal disorders characterized by the proliferation and accumulation of mature blood cells. Classic Philadelphia-negative MPNs include polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF). PV and ET are the most indolent diseases, with a median overall survival (OS) of 12 and 15 years, respectively. The prognosis of these diseases is related to two major complications: thrombosis in the short and midterm and hematological transformations in the long term [1]. The prognosis of leukemic transformation in MPNs remains dismal and appears to be worse than that of primary acute myeloid leukemia (AML) with a median OS below six months [2].

Through this work, we report a typical case of a 80 years old woman followed for Polycythemia vera who progressed unusually to acute myeloid leukemia in a short period from initial diagnosis; in order to describe the observation of this particular entity diagnosed in our formation, rare in our Moroccan context and even in the literature, and to focus on risk factors and prognostic factors related to this pathology.

2. Case Report

Our patient is 80 years old, followed for the past two years for Polycythemia vera (JAK2 positive) treated with aspirin and regular bleeding. She presented to the emergency room with marked mucocutaneous pallor and asthenia and in whom the clinical examination found an anemic syndrome, fever associated with a tumor syndrome (splenomegaly, hepatomegaly and bilateral cervical adenopathies) without hemorrhagic syndrome. The hemogram showed bictytopenia (anemia at 6g/dl, thrombocytopenia at 37,000/mm^3) and hyperleukocytosis at 271,000/mm^3 including a 41%

neutrophilic myelemia of which 7% were blasts (Figure 1).

The myelogram showed a 90% invasion of the granular lineage with a 30% myeloblast rate defining acute myeloid leukemia (Figure 2). The evolution was burdened by the death of the patient one week after her admission.

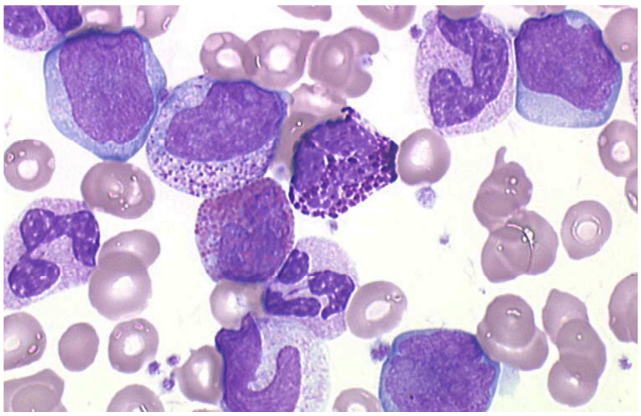

Figure 1. *Blood smear showing myelemia with a blast rate of 7%.*

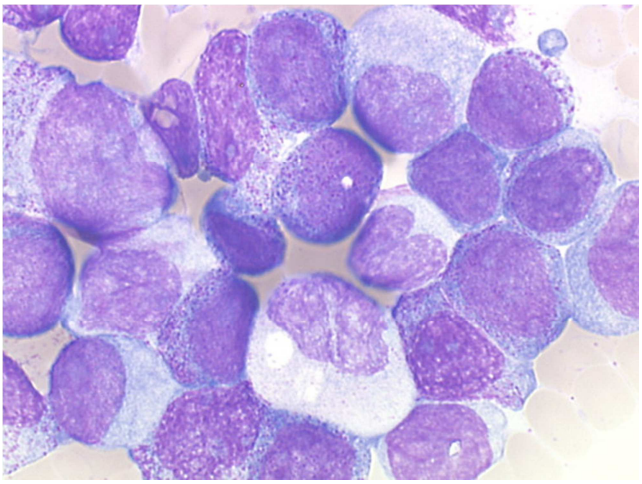

Figure 2. *Bone marrow 90% invaded by the granular lineage with 30% blast rate.*

3. Discussion

Polycythaemia vera is a clonal malignant hemopathy, which belongs to the category of myeloproliferative neoplasms characterized by involvement of the multipotent hematopoietic stem cell which becomes hypersensitive to erythropoietin, itself secondary to the mutation of the erythropoietin gene of a signal transduction protein: Janus Kinase 2 (*JAK2*). The JAK2 gene provides instructions for making a protein that promotes the proliferation of hematopoietic cells. The result is a hyperplasia of the three myeloid lines predominating over the erythroblastic lineage

with an increase in the absolute number of red blood cells or polycythemia, of hematocrit and total blood volume [3].

The Studies have proposed that the JAK2 V617F mutation is the primary molecular event and sufficient to cause the development of a primitive polyglobulia in approximately 96% and *JAK2* exon 12 mutation in approximately 3% of patients [4].

The clinical symptomatology begins in an insidious way. neurological manifestations come to the forefront, they are represented by tinnitus, vertigo, headaches and visual disorders. this symptomatology can manifest itself in a severe way and is expressed by monoplegia, hemiplegia, aphasia... probably related to cerebral ischemia. Hypertension is common. A generalized pruritus called aquagenic, typically occurring after exposure to hot water, can also be observed; clinical examination often reveals mucocutaneous erythrosis, predominant on the face and extremities of the limbs, moderate splenomegaly, sometimes associated with regular hepatomegaly [5].

Thrombotic complications are the most frequent and can occur in different locations (thrombosis deep veins of the lower limbs, cerebral thrombophlebitis, myocardial ischemia, Budd's syndrome-Chiari, a mesenteric ischemia etc.) being responsible for a high morbi-mortality, the prevention of these complications is the cornerstone of therapeutic care.

Transformation to acute leukemia is a rare event in polycythemia vera, with an estimated incidence of about 5 * 1000 person years [6]. The frequency of leukemic evolution in MPN varies according to the disease subtype. In PV, it is 2.3% at 10 years and 7.9% at 20 years. Different factors are associated with leukemic transformation in MPNs which includes advanced age, hyperleucocytosis, the use of cytotoxic myelosuppressive agents, cytogenetic abnormalities, and increased number of mutations in genes associated with myeloid neoplasms [2].

The vast majority of published studies, whether retrospective or prospective, but with a median follow-up of less than 10 years, show a relatively low risk of progression under treatment to myelofibrosis, myelodysplastic syndrome or acute leukemia, of the order of 5% in PV and 2% in essential thrombocythemia. Nevertheless, the results of three french prospective studies with a median follow-up of more than 11 years indicate that this risk is probably higher in the long term [7]. Phlebotomies, are crucial in the beginning as an emergency method to reduce high red blood cells count and viscosity. However, it has been shown by the different reports to increase the risk of metaplasia and must not be considered as a treatment of PV per se [8]. Some studies with long-term follow-up indicate that leukemic transformation is part of the natural evolution of PV. Myelosuppressive agents such as hydroxyurea or pipobroman, when used as the sole treatment, does not seem to increase the natural risk of acute leukemia but the risk increases with sequential use of different cytotoxic agents. It is also established that treatment of patients with pipobroman, chlorambucil, or P32 results in a higher risk of leukemic transformation [9].

Median survival is around 18 months without treatment, mainly related to thrombotic complications, but it is more than 15 years with current treatment and leukemic transformation rate at 10 years is estimated at 3% [10].

Various haematological changes often appear after the tenth year of evolution. polyglobulia is followed up.

anaemia with erythrocyte deformation (red blood cells,

anisopoikilocytosis), hyperleukocytosis of variable importance and moderate erythromyelemia. Extramedullary haematopoiesis, thrombocytopenia and circulating blasts may occur. The osteo-medullary biopsy will show the progressive installation of an collagen myelofibrosis and then a real osteomyelosclerosis with an insufficiency syndrome medullary. Myeloid metaplasia with myelofibrosis or myeloid splenomegaly chronic is thus a late complication of Vaquez's disease. Death occurs on average 2 to 3 years after the appearance of myelofibrosis. The evolution in acute leukaemia is a major cause of mortality, accounting for between 15 and 30 percent of all deaths. The osteo-medullary biopsy will show the progressive installation of a collagen myelofibrosis and then a real osteomyelosclerosis with an insufficiency syndrome medullary. Myeloid metaplasia with myelofibrosis or myeloid splenomegaly chronic is thus a late complication of Vaquez's disease. Death occurs on average 2 to 3 years after the appearance of myelofibrosis. The evolution in acute leukaemia is a major cause of mortality, accounting for between 15 and 30 percent of all deaths and 20% of causes of death according to studies [11].

In the European Collaboration on Low-dose Aspirin in Polycythemia vera study, malignant transformation was responsible for 13% of deaths [12]. In PV, Thrombotic risk stratification is very important so as to evaluate patients' prognosis at diagnosis. At present, patients are classified into 2 categories: a low-risk group with younger age (<60 years) and no previous thromboses, and a high-risk group with patients older than 60 years and/or with patient with a previous history of thrombotic episode [13]. Furthermore, signs of generalization are generally associated with a worsening of prognosis. It has been shown that study of bone marrow (myelogram, bone marrow biopsy) improves strongly the diagnostic reliability and also enables the recognition of evolving myelofibrotic/leukemic transformation in chronic myeloproliferative disorders [14]. The treatment of these secondary acute leukemias is most often disappointing and has a poor prognosis as it was showen in an italian cohort study in whitch the outcome of patients was gloomy, with a median survival of 2.9 months and no significant differences between palliation and intensive treatments [15].

4. Conclusion

Blast transformation occurs in natural course of PV typically as a rare and late event; but progression of the disease can vary depending on the risk factors. In fact, the effects of long-term use of myelosuppressive agents deserve to be re-evaluated, analyzed and monitored. The Events that appear during the evolution of a treated myeloproliferative syndrome, whether or not they are related to the intrinsic abnormality that presides over the clonal expansion of hematopoiesis, may play a role in leukemic transformation. Alternative therapeutics, therefore need to be assessed prospectively and the notion of individual predisposing factors also deserves to be taken into account.

References

[1] Leukemic evolution of polycythemia vera and essential thrombocythemia: genomic profiles predict time to transformation LUQUE PAZ et al blood advances; 13 OCTOBER 2020 x VOLUME 4, NUMBER 19.

[2] An unusual presentation of blast phase in JAK 2 mutated polycythemia vera L. Abraham and M. Paul Human Pathology: Case Reports 23 (2021) 200460.

[3] Polycythemia vera and essential thrombocythemia: 2013 update on diagnosis, risk-stratification and management; Ayalew Tefferi, Tiziano Barbui American journal of Hematology. 2013 Jun; 88 (6): 507-16.

[4] Critical review on polycythaemia vera; Ozokono P. C1; International Journal of Basic, Applied and Innovative Research, IJBAIR, 2019, 8 (2): 38–46.

[5] Godon A, Dib M, Geneviève F, Ifrah N, Zandecki M. Découverte de blastes sanguins au décours de la polyglobulie de Vaquez. Ann Biol Clin. 2002; 60: 701-706.

[6] Leukemic Transformation of Polycythemia Vera: A Single Center Study of 23 Patients Francesco Passamonti et al. 2005 American Cancer Society.

[7] Management of polycythemia vera and essential thrombo¬cythemia J. J. Kiladjian; Correspondances en Onco-hématologie - Vol. III - n° 3 - juillet-août-septembre 2008.

[8] New Perspectives on Polycythemia Vera: From Diagnosis to Therapy Alessandra Iurlo; International journal of molecular sciences. 2020 Aug 13; 21 (16): 5805.

[9] G. Finazzi, V. Caruso, R. Marchioli, et al., Acute leukemia in polycythemia vera: an analysis of 1638 patients enrolled in a prospective observational study, Blood 105 (2005) 2664–2670.

[10] Tefferi A, Solberg LA, Silverstein MN. A clinical update in polycythemia vera and essential thrombocythemia. Am J Med 2000, 109: 141-149.

[11] Means RT. Polycythemia Vera. In: Lee GR, Foerster J, Lukens J, Paraskevas F, Greer JP, Rodgers GM, eds. Wintrobe's Clinical Hematology, 10th edition.Volume 2. Baltimore: Williams et Wilkins, 1999: 2374-2389.

[12] Life expectancy and prognostic factors for survival in patients with polycythemia vera and essential thrombocythemia; Fransesco Passamonti et al, The American Journal of Medicine November 2004, 17 (10): 755-61.

[13] The Impact of Clinicopathological Studies on Staging and Survival in Essential Thrombocythemia, Chronic Idiopathic Myelofibrosis, and Polycythemia Rubra Vera Hans Michael Kvasnicka1 et al Thieme E-Journals, seminars of thrombosis and hemostasis 2006.

[14] Austrian recommendations for the management of polycythemia vera Sonja Burgstaller et al; Wien Klin Wochenschr. 2018 Sep; 130 (17-18): 535-542.

[15] Risk of leukemic transformation in PV and ET patients Christine Chomienne et al; Pathologie Biologie 52 (2004) 289–293.