Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Cardiology

A Rare Case of Essential Thrombocythemia Revealed by an Acute Coronary Syndrome: Management Difficulties and Therapeutic Challenges

Youssef Fihri[1*], Nada Alloul[2], Jihane Fagouri[1], Driss Britel[1], Hicham Faliouni[1], AatefBenyass[1], Zouhair Lakhal[1]

[1]Cardiology center- Military hospital Mohamed V -Rabat, Morocco
[2]Hematology laboratory - Hospital Ibn Sina -Rabat, Morocco

DOI: 10.36347/sjmcr.2023.v11i09.017 | **Received:** 15.07.2023 | **Accepted:** 27.08.2023 | **Published:** 11.09.2023

***Corresponding author:** Youssef Fihri
Cardiology center- Military hospital Mohamed V -Rabat, Morocco

Abstract **Case Report**

Essential thrombocythemia is a clonal abnormality of the multipotent hematopoietic stem cell and results in an increased number of platelets. Patients are at risk of microvascular thrombosis and hemorrhage. The occurrence of an acute coronary syndrome may be a rare revealing mode of discovery of essential thrombocythemia. We report the case of a 67-year-old patient admitted for management of an acute coronary syndrome with the discovery during his assessment of a thrombocythemia reaching up to 966,000/mm3. in the context of the etiological assessment of the thrombocytosis, the diagnosis of essential thrombocythemia was retained. Acute coronary syndrome occurs in 9.4% of patients with essential thrombocytosis. In patients with ET, there is a vicious cycle in which the marked increase of activated platelets causes vascular endothelial damage, induces the instability of coronary plaque, evokes the rupture or erosion of the plaque, and consequently activates other resting platelet. The diagnosis of ACS in patients with essential thrombocythemia is similar to that of the general population, nevertheless in terms of treatment, Antithrombotic treatment remains a difficult decision to take. It is necessary to balance the risk of thrombosis and hemorrhage. the optimal long-term treatment of acute coronary syndrome is a dual antiplatelet therapy (DAT) with clopidogrel and Aspirin and adding Hydroxyurea to the DAPT makes the treatment optimal.

Keywords: Essential Thrombocythemia; Acute Coronary Syndrome; Treatment.

INTRODUCTION

In terms of cardiology, and particularly in ischemic heart disease, the cardiologist most often reasons in the face of the possibility that the acute coronary syndrome is secondary to the most probable etiology, which is atherosclerosis. Nevertheless, we must always have the idea that ischemic heart disease can be secondary to other etiologies, therefore we must always keep in mind that we must see the bigger picture and evoke certain etiologies in case of ischemic heart disease especially in case of occurrence in a patient without traditional cardiovascular risk factors.

My eloproliferative diseases are a group of diseases characterized by the clonal and malignant proliferation of one or more myeloid cell lines. It is a pathology of the hematopoietic stem cell. The constant fact is the hyperplasia of one or more myeloid lineages, with terminal cell differentiation. These are chronic diseases, but whose terminal evolution can be done in the form of a transformation into acute leukemia.

Through a clinical case, we shed light on the rather rare association of myeloproliferative syndromes and acute coronary syndrome as well as the means of diagnosis and management.

CASE REPORT

We report the case of a 63-year-old patient with active smoking as cardiovascular risk factors, admitted to the cardiovascular emergency unit for management of constrictive retrosternal chest pain radiating to the left upper limb that was prolonged and progressing two hours before admission.

The clinical examination finds a conscious patient, still suffering, BP at 118/72mmh and a heart rate at 91 bpm, the cardiovascular and pleuropulmonary examinations were normal.

The electrocardiogram shows a regular sinus rhythm with an HR of 66 bpm, the heart axis deviated to the left with biphasic T waves in the anteroseptal and

negative T waves in the apical and lateral territory with the presence of a left anterior hemiblock.

Chest x-ray showed no cardiomegaly or lung parenchymal abnormality.

Echocardiography finds an non dilated left ventricle showing a segmental kinetics disorder with akinesia of the apex and adjacent segments, and hypokinesia of the anteroseptal wall with an LVEF at 45%(SBP), a non-dilated atria and low left ventricular filling pressures without significant valvulopathy and a low probability of PH.

The blood work showed a troponin at 82 times normal and a second troponin performed an hour apart at 93 times normal. The rest of the assessment showed hemoglobin at 15.7g/dl, WBC at 11,400 and platelets at 695,000/mm3, K+ 3.7 and creatinine at 8, TP at 76%.

The patient was treated as a high-risk NSTEMI with DAPT plus enoxaparin. Since the patient continued to have anginal recurrences despite the initiation of treatment, the patient was sent to the KT room for coronary angiography.

Coronary angiography showed sub occlusive stenosis of the proximal left anterior descending artery right at the start of the first diagonal (medina 1-1-0 bifurcation lesion) with a thrombotic aspect.

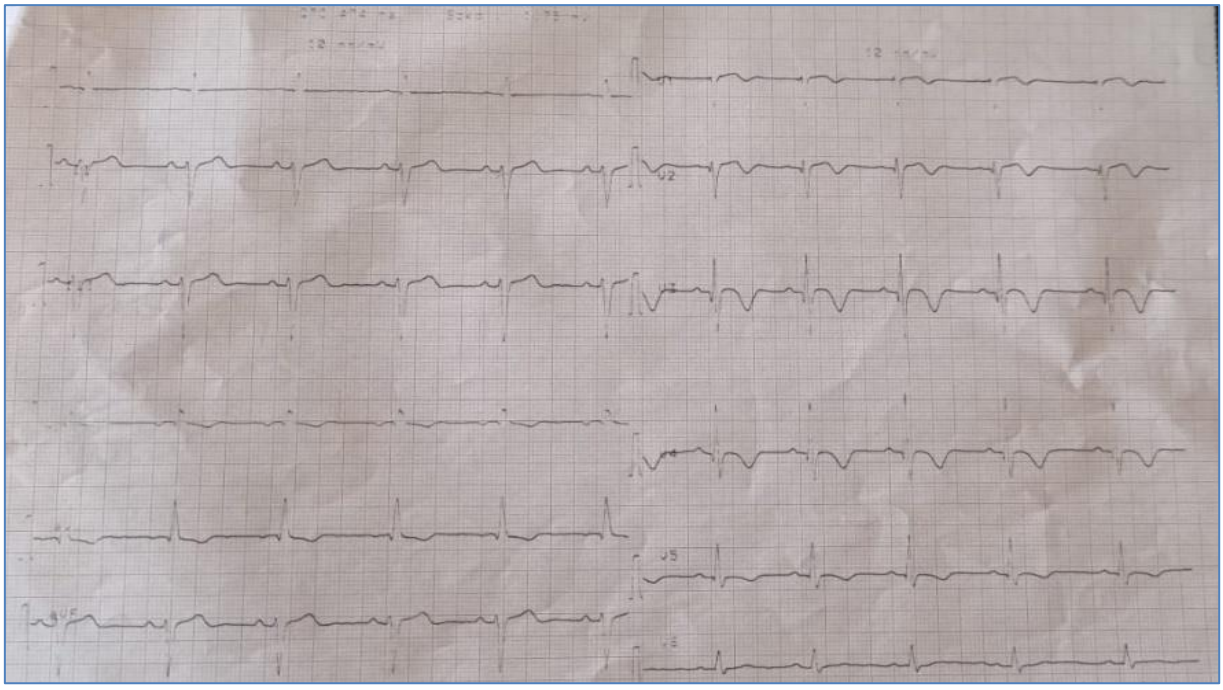

Image: Electrocardiogram at the admission in the intensive care unit

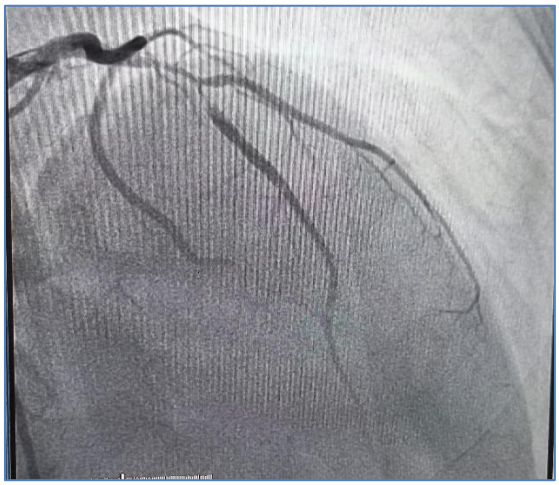

Image: Coronarography showing subocclusive stenosis of the proximal left anterior descending right artery at the start of the first diagonal (medina 1-1-0 bifurcation lesion)

The evolution was marked the evening of his angioplasty by the occurrence of bleeding at the femoral puncture point. Bleeding was managed with manual compression and local hemostats. CBC control in the evening showed an increase in platelet count to 742,000/mm3 then to 966,000/mm3. After discussion with the clinical hematology team, a list of examinations was requested including a blood smear in search of myelemia, ferritin assay with search for JAK2 / CARL / MPL mutation and the Bone marrow biopsy

The search for the mutation JAK2 V617F came back positive. as for the Bone marrow biopsy did not come back in favor of myelofibrosis.

After discussion with the heart team and taking into account the hemorrhagic and ischemic risk, the patient benefited from a mono-bypass of the LAD with good evolution.

The patient was released on Aspirin with Hydroxycarbamide, beta-blocker, statins and ACE inhibitor with good evolution without other bleeding episodes and follow-up with the hematologist.

DISCUSSION

Myeloproliferative syndromes or neoplasms (or MPN) are hematological malignancies characterized by the clonal proliferation of myeloid cells. [1]. Bleeding tendency, thromboembolic complications, and qualitative platelet defects are all recognized in MPNs, which include essential thrombocythemia (ET), polycythemia vera (PV), chronic idiopathic MF, and chronic myelogenous leukemia [2]. MPNs are associated with hypercoagulable states and thrombotic complications are more prevalent than bleeding complications. Thrombotic occlusions occur more frequently in arteries than veins. Stroke is the most frequent presentation, followed by MI and peripheral arterial occlusion [3].

Patients with MPNs have a heightened risk for cardiovascular complications, including arterial thrombosis, heart failure, pulmonary hypertension, and accelerated atherosclerosis, depending on the form of MPN and the driver mutation associated with it. Increased inflammation is associated with MPNs and may contribute to increased cardiovascular disease risk in these patients. Patients with MPNs have altered numbers and functions of blood cells, including red cells, leukocytes, and platelets, which contribute to the risk for cardiovascular events, especially thrombosis and bleeding [4]. The renin-angiotensin system may also participate in a common pathophysiologic pathway in MPN and cardiovascular disease, though further studies are needed to elucidate its role in cardiovascular disease in patients with MPNs [4].

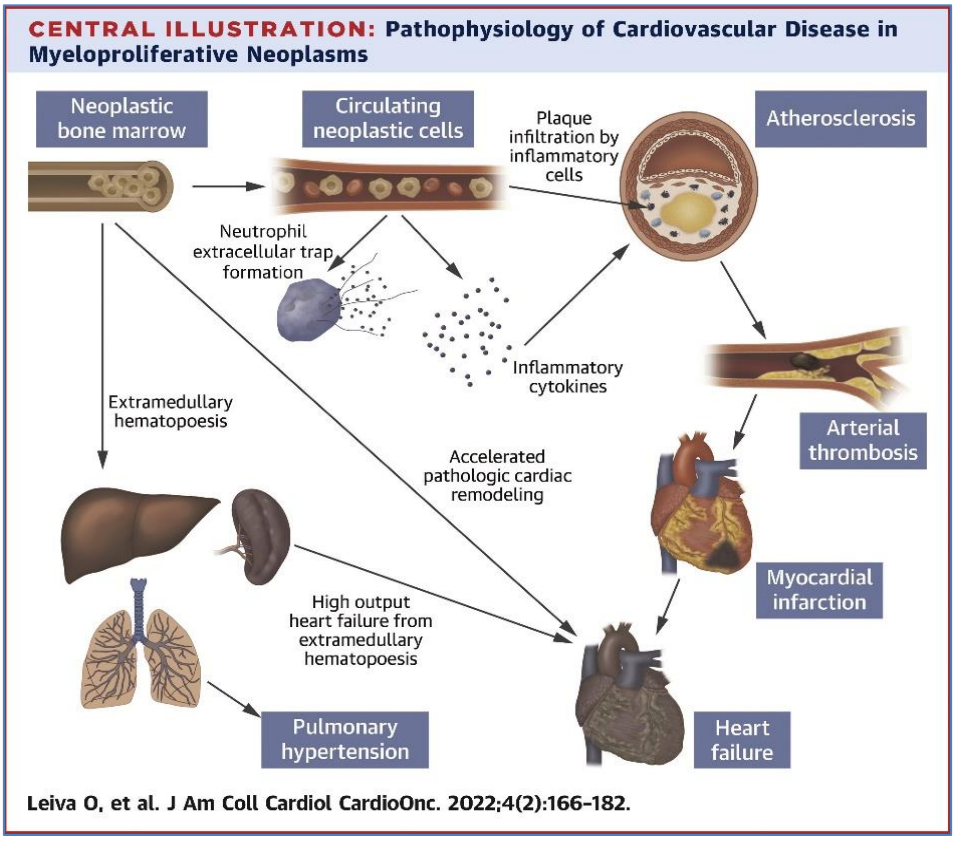

Figure: Pathophysiology of Cardiovascular Disease in Myeloproliferative Neoplasms (4)

In 2005, four independent teams, identified a mutation of the JAK2 protein (JAK2 V617F) present in a majority of patients with PV. This molecular anomaly has also been found in many cases of essential thrombocythemia. The discovery of the JAK2 V617F mutation has completely changed the diagnosis of PV and now not only allows a better understanding of the pathways metabolic pathways leading to pathology, but also the development of a targeted molecular therapy associated with a efficient molecular monitoring. [1].

In a study by Pósfai and al, 263 patients diagnosed with either ET or PV were included. In a retrospective analysis, the clinical characteristics of 14 patients who suffered myocardial infarction (MI) during their hematological follow-up were compared to 162 MPD patients who did not exhibit any kind of thrombotic complication. The JAK2 V617F mutation was present in most of the cases (10/14, 71.4%), and cardiovascular risk factors appeared in the majority of patients [5]. PV and ET, which share very similar clinical features and may be indistinguishable in their early phases, are characterized by inappropriately increased production of neutrophils, erythrocytes, and platelets [6].

Essential thrombocythemia is a clonal abnormality of the multipotent hematopoietic stem cell and results in an increase in platelets. Patients are at risk for microvascular thrombosis and hemorrhage. The platelet count must be greater than 600,000 /µl to speak of ET and it is generally greater than 1,000,000 /µl, with characteristic bone marrow findings, exclusion of a reactive thrombocytosis or other myeloproliferative disorders like polycythemia vera (PV), chronic idiopathic myelofibrosis (IMF), and chronic myeloid leukemia (CML) In terms of pathophysiology, there is no correlation between platelet blood level and the risk of thrombosis and many studies suggests a contributory role of higher leukocyte counts and JAK2 mutation status and allele burden for development of thrombosis [7]. It is conceivable that in patients with ET, there is a vicious cycle in which the marked increase of activated platelets causes vascular endothelial damage, induces the instability of coronary plaque, evokes the rupture or erosion of the plaque, and consequently activates other resting platelets [8]. However, the underlying pathophysiological mechanisms still remains unclear.

Acute coronary syndrome occurs in 9.4% of patients with essential thrombocytosis (7). Mitsunori *et al.,* summarized 21 reported cases until 2003, 13 was diagnosed as acute myocardial infarction and 8 were diagnosed as unstable angina pectoris [9]. A vascular event represents the most frequent complication of ET. In a study by Dameshek and al, the incidence of thrombosis was reported to be 25% of 132 ET patients, among which Arterial thrombosis occurs more often than venous (10). Vessel stenosis could be thrombotic, or just minor. The LAD was the most commonly involved vessel. The possible reason is that the LAD artery is burdened with relatively high systolic pressure and high shear stress of blood flow which makes it susceptible to endothelial damage [8].

The mainstay of treatment for an acute coronary syndrome occurring in a patient with essential thrombocythemia is cytoreduction, anti-thrombosis therapy, and revascularization. Advanced age of 60 years or more, a history of serious bleeding or thrombosis, or a platelet level over 1500 × 109/L, are indications for cytoreductive drugs [11]. He myelosuppressive agent of choice in patients who suffer from ET and have risk of vascular thrombosis or bleeding is Hydroxyurea [11]. The revascularization strategy remains a dilemma because of both high surgical risk of patients but also the risk of stent thrombosis which is not to be neglected in case of essential thrombocythemia. A study by Bhatia and al, a total of 677,304 patients admitted for ACS, 2,485 patients among them had a secondary diagnosis of MPN were studied in terms of revascularization. The conclusion is that in patients with ACS and concomitant MPN, CABG was the preferred mode of revascularization over PCI [12].

In the other hand, other work like the paper published by Bošnjak and al, suggests that primary angioplasty remains the best choice for revascularization [11]. When catheterization laboratory is not available, administration of a fibrinolytic therapy is an alternative. Introduction of unfractionated or LMWH and glycoprotein IIb/IIIa receptor inhibitors are also recommended therapies [11]. In case of angioplasty, the major concern is stent thrombus and restenosis. It is commonly believed that PCI and stent implantation may be associated with a higher rate of complications and adverse events in this subset of patient. In the study by Zheng Y and al, although most patients received dual antiplatelet and cytoreduction therapy, 3 of 8 patients developed stent thrombus and restenosis in the follow-up. The proportion is relatively high [8]. Antithrombotic treatment remains the most difficult dilemma to overcome, it is necessary to balance the risk of thrombosis and hemorrhage. The gold standard in long-term treatment of acute coronary syndrome is a dual antiplatelet therapy (DAT) with clopidogrel and Aspirin. Adding Hydroxyurea to the DAPT make the treatment optimal [11].

CONCLUSION

The management of patients with an acute coronary syndrome associated with ET remains very difficult. The current gold standard is a medical treatment based on aspirin and Hydroxyurea with the addition of clopidogrel in case of angioplasty. The choice of the revascularization technique is made in case-by-case scenario, taking into account the ischemic and hemorrhagic and surgical risk and the complexity of the coronary lesions. However, there is no simple

answer to the question of how to treat patients with ET and myocardial infarction. There are insufficient data on the most appropriate way of treating these patients, which requires further studies with a larger number of patients to allow all the therapeutic progresses to be implemented.

REFERANCES

1. J.- C. Chomel, N. S. C., Mayeur-Rousse, A. G. T. (2009). Les syndromes myéloprolifératifs. 24(2), 0–85. doi:10.1016/j.immbio.2008.10.007
2. McPherson, R. A., & Pincus, M. R. (2021). *Henry's clinical diagnosis and management by laboratory methods E-book*. Elsevier Health Sciences.
3. Toste, J. (2019). When specialties intersect: Acute coronary syndrome as the first clinical manifestation of myeloproliferative neoplasms. *Revista Portuguesa de Cardiologia*, *38*(9), 619-620. doi: 10.1016/j.repce.2019.12.003
4. Leiva, O., Hobbs, G., Ravid, K., & Libby, P. (2022). Cardiovascular disease in myeloproliferative neoplasms: JACC: CardioOncology state-of-the-Art review. *Cardio Oncology*, *4*(2), 166-182. doi: 10.1016/j.jaccao.2022.04.002. PMID: 35818539; PMCID: PMC9270630.
5. Pósfai, É., Marton, I., Borbényi, Z., & Nemes, A. (2016). Myocardial infarction as a thrombotic complication of essential thrombocythemia and polycythemia vera. *Anatolian journal of cardiology*, *16*(6), 397-402. doi: 10.14744/AnatolJCardiol.2015.6125. Epub 2016 Feb 4. PMID: 27182615; PMCID: PMC5331370.
6. Cantoni, S., Colombo, C., Soriano, F., Oreglia, J. A., Sacco, A., Veronese, S., ... & Morici, N. (2022). Rare Causes of Acute Coronary Syndrome: The JAK2 V617F Mutation-Positive Myeloproliferative Neoplasms: A Cardio-Hematological Perspective. *Thrombosis and Haemostasis*, *122*(08), 1429-1431. doi: 10.1055/a-1742-0361. Epub 2022 Jan 17. PMID: 35038762.
7. Rossi, C., Randi, M. L., Zerbinati, P., Rinaldi, V., Girolami, A. (1998). Acute coronary disease in essential thrombocytemia and polycytemia vera. *J Intern Med. 244*, 49–53
8. Zheng, Y., Xu, T., Chen, L., Lin, S., & Chen, S. (2020). Percutaneous coronary intervention in patients with essential thrombocythemia: case reports and literature review. *Platelets*, *31*(6), 815-819. doi: 10.1080/09537104.2019.1665640. Epub 2019 Sep 10. PMID: 31502506.
9. Fujimura, M., Akaike, M., Kato, M., Takamori, N., Abe, M., Nishiuchi, T., ... & Matsumoto, T. (2003). Aggressive antiplatelet therapy before coronary stent implantation in acute coronary syndrome with essential thrombocythemia: a case report. *Angiology*, *54*(4), 485-490. Doi: 10.1177/000331970305400414.
10. Dameshek, W. (1951). Some speculations on the myeloproliferative syndromes. *Blood*, *6*(4), 372-375.
11. Bošnjak, I., Selthofer-Relatić, K., Periša, V., & Steiner, R. (2013). Therapeutic dilemmas in the treatment of acute coronary syndrome as manifestation of essential thrombocythaemia. *Journal of cardiology cases*, *8*(5), 168-171. doi: 10.1016/j.jccase.2013.08.001. PMID: 30546769; PMCID: PMC6277774.
12. Bhatia, K., Handa, S., Das, S., Modi, V., & Joshi, A. (2020). Acute coronary events in patients with myeloproliferative neoplasms-a nationwide analysis of patient characteristics and in-hospital outcomes. *European Heart Journal*, *41*(Supplement_2), ehaa946-1630. doi:10.1093/ehjci/ehaa946.1630