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Essential Thrombocythemia Complicated with Acute Myocardial Infarction

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Authors' contributions

This work was carried out in collaboration between all authors. Author HL did substantial contributions to conception and design, acquisition of data, drafting the article, revised it critically for important intellectual content, final approval of the version to be published. Authors ALA, NNT, MNNH and HHKS equally managed the analyses of the study, equally contributed the literature searches. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Aims: Essential thrombocythemia or thrombocytosis is an uncommon disease. It involves an overproduction of megakaryocytes in the marrow. These platelets may not function normally and can cause a blockage in blood vessels and other complications. We report one case of essential thrombocytosis with different clinical presentations.

Presentation of Case: A 50 year old gentleman came to Hospital and admitted with the diagnosis of Acute Myocardial Infarction. Further investigation via Full Blood Count revealed Essential Thrombocytosis. Management with PCI (Percutaneous Coronary Intervention) and discharged with hydroxyurea.

Discussion: We treated our patients with aspirin and hydroxyurea. As similarly noted in follow up of blood complete picture shows that it reduced the platelet count and patient showed much improvement.

Conclusion: This case is reported because it is not a common disease and to demonstrate that routine examination of blood complete picture is very important.

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1. INTRODUCTION

Essential thrombocytosis (ET), or primary thrombocythemia, is a rare disorder in which the body produces too many platelets for unknown reasons. This can cause abnormal blood clotting or bleeding. The condition usually affects people in the middle age group, although it can be seen in younger patients, especially in women less than 40 years old. Patients with ET have an excellent chance of living a normal life span if they are properly monitored and treated as necessary. A small number of patients may develop acute leukemia or a bone marrow disorder called myelofibrosis.

The classic myeloproliferative disorder includes polycythemia vera, primary myelofibrosis and essential thrombocythemia [1]. Essential thrombocythemia is neither a cytogenetically nor a morphological defined disease entity, but rather is a diagnosis of exclusion. Therefore, the diagnosis of essential thrombocythemia requires that both reactive thrombocytosis and other chronic myeloid disorders to be omitted [2]. Most of the patients with essential thrombocythemia enjoy a normal life expectancy without associated disease-related complications [3,4]. In morphological and cytogenetically defined essential thrombocythemia the delayed development of either acute myeloid leukemia (AML) or post essential thrombocythemia myelofibrosis is unusual [5].

2. CASE REPORT

A 50 year old gentleman complained of chest pain and admitted to a Hospital located in southern part of Malaysia, in January 2006 with the Diagnosis of Acute Myocardial Infarction. History of Thyrotoxicosis present. Angiography was done. > 90% stenosis present. Two coronary artery disease, Left anterior descending coronary artery (LAD) and Right coronary artery (RCA) were affected. Image of Angiogram showed that there are several calcified plaque, occlusion at proximal and middle segments of LAD which causes moderate to severe (70-90%) luminal narrowing. Right coronary artery (RCA), small calcified plaque at proximal and distal segment causes mild luminal narrowing. Echocardiogram also was done and showed that EF (ejection fraction) 28% with dilated cardiac chamber in hypokinetic segments. Bone marrow aspiration and biopsy showed that hyperplasia of megakaryocytes in the bone marrow.

Table 1. Laboratory results

Lab investigation	Value
Urea	2.9 mmol/L
Sodium	135 mmol/L
Potassium	3.6 mmol/L
Hb	14.5 g/dL
WBC	12.3 x 10 ⁹ /L
Platelets*	1125 x 10 ⁹ /L
TSH	2.06 uU/ml
T4*	15.65 ug/dl
Liver function test (LFT)	Normal
Total Cholesterol	2.2 mmol/L
Triglycerides (TG)	0.7 mmol/L
Fasting blood sugar (FBS)	5.8 mmol/L
Random blood sugar (RBS)	8.0mmol/L
PT, APTT	Normal
Troponin T and I	3 times high (Troponin T normal value less than 0.01 mcg/L) (Troponin I normal value less than 0.12 mcg/L)
JAK2 V617F mutation analysis*	Positive

- Means above the normal range.
- JAK2 gene ; Janus kinase 2

Table 2. Laboratory results. (As in last follow up)

Lab investigation	Value
WBC	12.4 x 10 ⁹ /L
Hb (Haemoglobin)	8.3 g/dL
Platelets*	574 x 10 ⁹ /L
Liver function test	normal
Fasting Blood Sugar	5.5 mmol/L
Renal Profile	Normal

- Means above the normal range

Diagnosis were Acute Myocardial Infarction, Congestive Cardiac Failure with Myeloproliferative Disorder (Essential Thrombocythemia). Management as planned with Percutaneous Coronary Intervention (PCI) and discharged with tablet Aspirin 100 mg OD, tablet Ticlopidine 250 mg BD, tablet Co-Diovan (80/12.5) (Valsartan 80 mg/Hydrochlorothiazide 12.5 mg) 1/1 OD, tablet Simvastatin 20 mg ON, Tablet Hydroxyurea 500 mg BD. Patient is still under follow-up in medical OPD (outpatient department) and Haematology clinic in the

Hospital. Follow up in April 2006, On examination, patient was stable, BP 120/80, HR 80/min, no oedema, Lungs clear, Cardiovascular system, dual rhythm, no murmur, abdomen soft, not tender, liver 3 cm and Spleen 2 cm palpable. As last follow up in December 2016, patient was stable. No complaint was reported and patient was prescribed with tablet Hydroxyurea 1 G OM, 500 mg ON.

3. DISCUSSION

Essential thrombocythemia is a myeloproliferative disease with a high incidence of thrombotic complications, especially cerebral, myocardial, and peripheral arterial thromboses; pulmonary embolism and deep-vein thrombosis are less frequent [6]. Thrombocytosis is the presence of high platelet counts in the blood more than six hundred thousand per ml [7]. Abnormalities in the number and function of platelets may contribute to thromboembolic complications in patients with essential thrombocythemia [8]. Thrombocytosis can be a reactive (secondary thrombocytosis) or a clonal bone marrow (myeloproliferative) process. Reactive thrombocytosis, which is more common, is caused by increased levels of thrombopoietin (TPO), other cytokines, or catecholamine that may be produced in inflammatory, infectious, stressful or neoplastic conditions. Clonal thrombocytosis is commonly seen in chronic myeloproliferative [9], and myelodysplastic syndrome with 5q-syndrome [10]. According to WHO diagnostic criteria for essential thrombocythemia 2016, four major criteria such as 1. Platelet count $\geq 450 \times 10^9/L$, 2. Bone marrow biopsy showing proliferation mainly of the megakaryocyte lineage with increased numbers of enlarged, mature megakaryocytes with hyper lobulated nuclei; No significant increase or left-shift in neutrophil granulopoiesis or erythropoiesis and very rarely minor (grade 1) increase in reticulin fibers, 3. Not meeting WHO criteria for *BCR-ABL1+* CML, PV, PMF, myelodysplastic syndromes, or other myeloid neoplasms. 4. Presence of *JAK2*, *CALR*, or *MPL* mutation and one minor criteria is presence of a clonal marker or absence of evidence for reactive thrombocytosis. *JAK2* mutation is common to PMF (primary myelofibrosis), PV (Polycythaemia vera), and ET (Essential thrombocythemia). [11] (BM, bone marrow; *CALR*, calreticulin; CML, chronic myelogenous leukemia; Hb, hemoglobin; Hct, hematocrit; JAK, Janus-associated kinase; *MPL*, myeloproliferative leukemia virus oncogene). In Francisco J Camacho, et al. study

[12], the relationship of the ET with the *JAK2* V617F mutation is prominent. This mutation is present in 50%-60% of ET cases and as in young patients with no known CVRF (cardiovascular risk factor) who present an acute coronary syndrome, as well as the hypercoagulability study, the ET must be taken into account as a possible etiology of the process. Antonio Esteves F^o, et al. study [13], showed that the apparently healthy condition of the remaining coronary arteries leads one to the assumption that the infarction could have occurred as a primary result of the coagulopathy. In many published series, the rate of cardiovascular complications related to the presence of ET ranged from 4% to 21% [14]. This disorder may lead to the formation of thrombi and acute arterial occlusion, as well as hemorrhagic complications, probably as a result of platelet dysfunction. Although rare, sudden death and AMI are complications described in hematologic diseases, such as myeloproliferative disorders characterized by significant changes in the platelet count [15]. When the platelet count exceeds 600,000/mm³, ET may cause coronary thrombosis in different arteries [16]. Possible explanations for this phenomenon include: 1) platelet activation as a result of endothelial injury; 2) prolonged arterial spasm with subsequent thrombosis; 3) increased activity of the platelets; 4) changes in the glycoprotein of the platelet granules in patients with ET; and 5) possible selective deficiency of lipoxygenase in individuals with myeloproliferative disorders [18]. Approximately 25-33% of patients with essential thrombocytosis (primary thrombocythemia) are asymptomatic at diagnosis. The remainder report vasomotor symptoms or complications from thrombosis or bleeding. Most symptomatic patients present with symptoms that relate to small- or large-vessel thrombosis.

- Microvascular occlusion of the toes and fingers causes digital pain; gangrene which is characterized by burning pain and dusky extremity congestion
- The pain increases with exposure to heat and improves with cold; a single dose of aspirin may provide relief for several days.

Headache is the most common neurologic symptom. Patients may also report paraesthesia and episodic transient ischemic attacks; transient neurologic symptoms include the following: unsteadiness, dysarthria, dysphoria, vertigo, dizziness, migraine, syncope, scotoma, seizures.

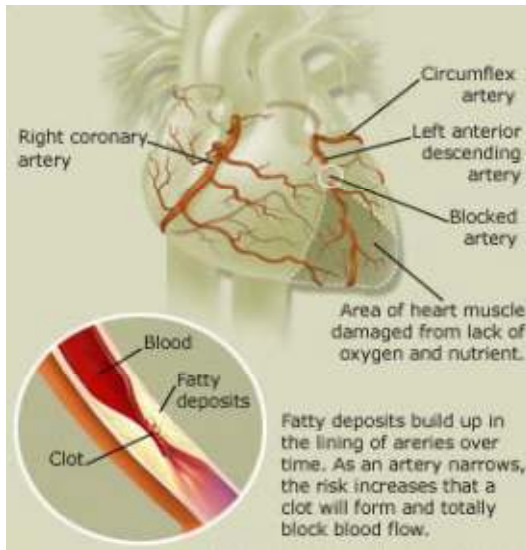


Fig. 1. Diagram showing the Heart attack

Heart attack (coronary thrombosis, myocardial infarction) is a common clinical condition that is associated with the acute formation of a blood clot usually superimposed on a coronary artery which has some pre-existing degree of arterial wall obstruction (see above). This process results in no blood flow to a part of the heart muscle leading to death of some heart muscle downstream from the coronary artery occlusion. Normally there are two main coronary arteries in people; their function is to deliver oxygenated blood to the heart muscle. When gradual blockages develop in these vessels, the chance of heart attack increases. Coronary thrombosis is the formation of a blood clot inside a blood vessel of the heart. This blood clot restricts blood flow within the heart. It is associated with narrowing of blood vessels subsequent to clotting. The condition is considered as a type of ischaemic heart disease, also known as a heart attack or myocardial infarction. Thrombosis in the heart can lead to a myocardial infarction [17]. Coronary thrombosis and myocardial infarction are sometimes used as synonyms. Thrombosis of large veins and arteries is common and may result in occlusion of the leg, coronary, and renal arteries. Other arteries may be involved, including retinal arteries. Venous thrombosis of the splenic, hepatic, or leg and pelvic veins may develop. Priapism is a rare complication. Pulmonary Hypertension may result from pulmonary vasculature occlusion. Hydroxyurea was effective not only in reducing the platelet count in patients with essential thrombocythemia but also in preventing thrombosis. However,

particular care should be exercised in prescribing this drug to young patients because the risk of secondary leukemia is not known [18].

We treated our patients with aspirin and hydroxyurea. As similarly noted in follow up of blood complete picture shows that it reduced the platelet count and patient showed much improvement. Hydroxyurea is effective in preventing thrombosis in high-risk patients with essential thrombocythemia [7]. The new agent Anagrelide has recently been introduced for the treatment of essential thrombocytosis. However, recent studies showed that Anagrelide is not significantly more effective than traditionally used Hydroxyurea. [6]. We made diagnosis on the basis of exclusion criteria in which we excluded all causes of reactive thrombocythemia by appropriate investigations. We followed the revised diagnostic criteria for essential thrombocytosis which were proposed in 2005 [19] and WHO (World Health Organization) updated diagnostic criteria for essential thrombocytosis 2016 [11].

4. CONCLUSION

As essential thrombocythemia complicated with acute myocardial infarction is a very unusual. In our patient was treated from Acute Myocardial Infarction and incidentally found out the diagnosis of essential thrombocythemia was made. This case is reported because it is not a common disease and to demonstrate that routine examination of blood complete picture is very crucial. Routine investigation like blood complete picture is often missed. We incidentally diagnosed the cause of Acute Myocardial Infarct as thrombocythemia.

This case report depicts that thrombocythemia can present with mild (headache) to severe (stroke and gangrene) sign and symptoms and rarely with Acute Myocardial Infarction. Headache should not be considered as a casual symptom. Proper work up is essential to prevent under-diagnosis and complications of this scarce problem. So in conclusion, young patients or middle age with no known CVRF (cardiovascular risk factor) who present an acute coronary syndrome, the ET should be taken into account as a possible etiology of the process.

CONSENT AND ETHICAL APPROVAL

Informed consent was taken from the patient and also obtained ethical clearance from the Institution Research Ethics Committee.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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