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In-Stent Restenosis pada Pasien Polisitemia Vera: Sebuah Laporan Kasus

In-Stent Restenosis in a Patient with Polycythemia Vera: A Case Report

I Gusti Ayu Ratna Dewi[1], Tristi Lukita Wening[1], Sidhi Laksono Purwowiyoto[2,3]*
[1] Department of Emergency Medicine, RS Jantung Diagram Siloam, Depok, Indonesia.
[2] Department of Cardiology and Vascular Medicine, RS Jantung Diagram Siloam, Cinere, Depok, Indonesia.
[3] Faculty of Medicine of Universitas Muhammadiyah Prof Dr Hamka, Tangerang, Indonesia.

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**) Corresponding author:*
E-mail: sidhilaksono@uhamka.ac.id

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Abstract

DES has become the standard of care in clinical practice for patients undergoing Percutaneous Coronary Intervention (PCI). In-Stent Restenosis (ICR) occurs in 2-10% of a certain patient. Polycythemia Vera (PV) occurs when the body produces excessive red blood cells. It is uncommon for PV to manifest as ISR in DES that has been implanted for days. Here we present a case of a patient with PV who developed ISR shortly after PCI. We describe a 63-year-old man with polycythemia vera and an acute STEMI anterior with a history of PCI 13 days before. Coronary angiography revealed stenosis in the LCx and total ISR in LAD. We switched clopidogrel to ticagrelor and kept aspirin to prevent reoccurring ischemia occurrences. It is uncommon for PV to manifest as ISR in DES that have been implanted for days, even though PV and coronary artery disease (CAD) are linked. The treatment goal is to prevent thrombotic events. Patients with a history of PCI procedures have a higher risk of stent thrombosis, so besides Aspirin, another anti-platelet such as ticagrelor, should be used after. We can conclude that ISR in PV patients who underwent a PCI with DES is still a challenging clinical problem. Because of intimal proliferation and blockage brought on by enhanced platelet aggregation and increased shear stress due to elevated hematocrit, the PV makes the circumstances worse.

***Keywords**: DES; ISR; Polycythemia Vera*

Introduction

The most frequent cause of death globally is myocardial infarction (MI). Traditional risk factors for MI include smoking, dyslipidemia, hypertension, diabetes, and a family history of early coronary heart disease (CHD) (Barbui et al., 2018). A very uncommon type of blood cancer called polycythemia vera (PV) occurs when the body produces excessive red blood cells. PV has problems that could be fatal if left untreated. A 40% to 60% morbidity and mortality rate are caused by this condition is characterized by increased bleeding and thrombotic blockage of the coronary arteries (Barbui et al., 2018).

Complications are more likely to occur in patients with a history of arterial thrombosis and older (> 60 years). According to statistics, men are more likely than women to get PV (2.8 per 100,000 men against 1.3 per 100,000 women). 2.30/1,000,000 people each year is the overall incidence. The number of thrombotic problems has dramatically decreased thanks to cytoreductive therapy such as phlebotomy or chemotherapy and antiplatelet medication such as low-dose aspirin, which has also significantly increased survival (Barbui et al., 2018).

Case Report

A 63 y.o male was diagnosed with NSTEMI. He underwent a coronary angiogram, suggesting single-vessel disease (80% stenosis in the proximal part of the left anterior descending artery [LAD]). He got an early percutaneous coronary intervention (PCI) with a drug-eluting stent (DES) of Resolute 2.5 x 30 mm in osteal to the proximal part of LAD. The first stent was inflated to 18-20 atm (original size was 2.5 mm so it was about 3.0 mm after being expanded to 20 atm). Good TIMI 3 flow results were obtained. The patient was given the prescriptions for dual antiplatelet (DAPT), ARB, high-intensity statin, and insulin following the procedure and discharged afterward.

Thirteen days later, he returned to the emergency department and was referred to our hospital due to STEMI Anterior for intervention therapy. He presented with sudden chest discomfort and 7.5 hours of diaphoresis. He has a protracted history of smoking, diabetes, and hypertension. Normal physical examination. His Electrocardiography (ECG) on admission revealed Left Axis Deviation, marked elevation of ST-segment, and Q wave found in V2-V5 + Q wave in II, III. Compared to ECG from referring hospital we note that ST segment elevation

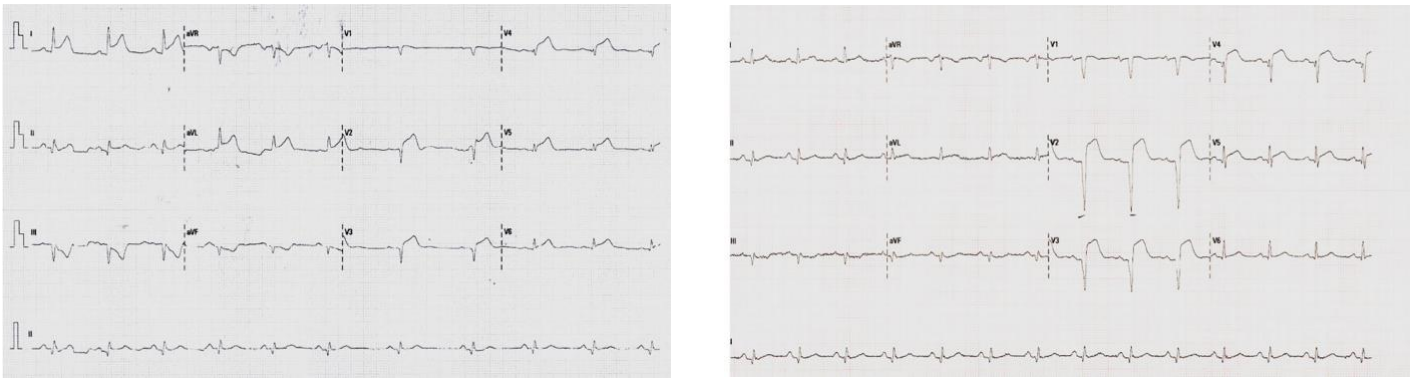

Figure 1. Compared to ECG from referring hospital (right) note that ST segment elevation in I, II, aVL with reciprocal III, aVR, aVF.

in I, II, aVL with reciprocal III, aVR, aVF (Fig 1). The Troponin I was slightly high at 0.03 (normal range below 0.02), and it was getting higher to 24.7 after we did a serial in our emergency department. Other laboratory results showed he had polycythemia vera and hyperglycemic stress [Hb 19.1, Ht 51.1, Leu 23.410, Tr 747.000, Erythrocyte 6.10 x 10^6/uL, GDS 311]. Other laboratory tests revealed normal electrolytes, serum urea, and creatinine. His son is known to have phlebotomy periodically for his polycythemia vera.

He had coronary angiography, which revealed two significant stenoses in LAD (total occlusion in the proximal part) and left circumflex (LCx). Also, total in-stent restenosis (ISR) in LAD. [Fig. 2]. Previously patient was implanted stent in the ostial and proximal LAD with Resolute 2,5x30 mm. PPCI was done in proximal to mid-LAD with Supraflex Cruz 3.0x40 mm drug-eluting stent (DES), with good results with TIMI 2 flow. The ICCU patient was administered dobutamine 5mcg/kg/mnt for perfusion support, and echocardiography showed an ejection fraction of 40% with wide apex akinetic to the septal base. A few days later the patient had new-onset atrial fibrillation (AF). The internist recommended taking hydroxyurea, but his family refused for no significant reason. After being hospitalized for 7 days, the patient was discharged.

Discussion

In-stent restenosis (ISR) is commonly found in a bare metal stent (BMS), and DES has become more popular in recent years and has decreased the incidence of ISR. DES has become the standard of clinical practice for patients undergoing PCI. Despite the use of modern DES, ISR may still occur in 2-10% of certain patients. The timing presentation of DES-ISR mostly has a long period until several years after stent implantation. Compared to BMS-ISR, DES-ISR lesions have more focal patterns while BMS-ISR characteristics are diffuse (Shlofmitz et al., 2019). A study showed that DES-ISR is more likely to present as a recurrence of angina symptoms or an acute coronary syndrome (ACS). Many factors influence the development of ISR, including biological, mechanical, and operator-related factors. Drug components of stents, hypersensitivity that caused local inflammation, under-expansion stent, type 2 diabetes, and barotrauma outside the stents are some of the reasons which caused ISR. Restenosis progressively starts hours after the barotrauma from the percutaneous coronary intervention (PCI) (Bahbahani et al., 2015). Myointimal trauma induced by PCI triggered a vessel injury that led to sequence processes and increased the inflammatory process by causing vasoconstriction and early endothelial dysfunction, shown by a rise in C-reactive protein (CRP) or MCP-1. The migration of myofibroblasts from tunica adventitia and smooth muscle cells from tunica medium to tunica intima is stimulated by wall stress in the tunica intima. DES technology added an antiproliferative drug and a polymer to the stent structure. Increased neointimal proliferation caused by the stent is balanced by this improvement (Buccheri et al., 2016; Shlofmitz et al., 2019).

Polycythemia vera (PV) mostly happens in people around 40-60 years old, mostly in men rather than women (2:1). It is reported 2.3 every 100.000 population every year in America.

Our patient was discovered incidentally after a routine blood investigation, the PV workup based on diagnostic criteria for the Polycythemia Vera Study Group (PVSG) set into two categories (Bahbahani et al., 2015).

Criteria for Category A:

1. In women, The total red blood cell mass is less than 32 or 36 mL/kg.
2. A 92% arterial oxygen saturation
3. Splenomegaly

Criteria for Category B:

1. Platelet count > 400,000/L with thrombocytosis
2. Leukocytosis, defined as a white blood cell count of more than 12,000/L.
3. Leukocytosis, defined as a white blood cell count of more than 12,000/L.
4. Serum vitamin B12 concentration or binding capacity of greater than 900 pg/mL.

The presence of either all three major requirements or just the first major criterion and the minor criterion is required for PV diagnosis criteria under the 2016 updated World Health Organization (WHO) recommendations (Barbui et al., 2018):

Major criteria:

1. Red cell mass >25% over mean normal projected value, or hemoglobin >16.5 g/dL in males and >16 g/dL in females, or men's hematocrit >49% and women's hematocrit >48%

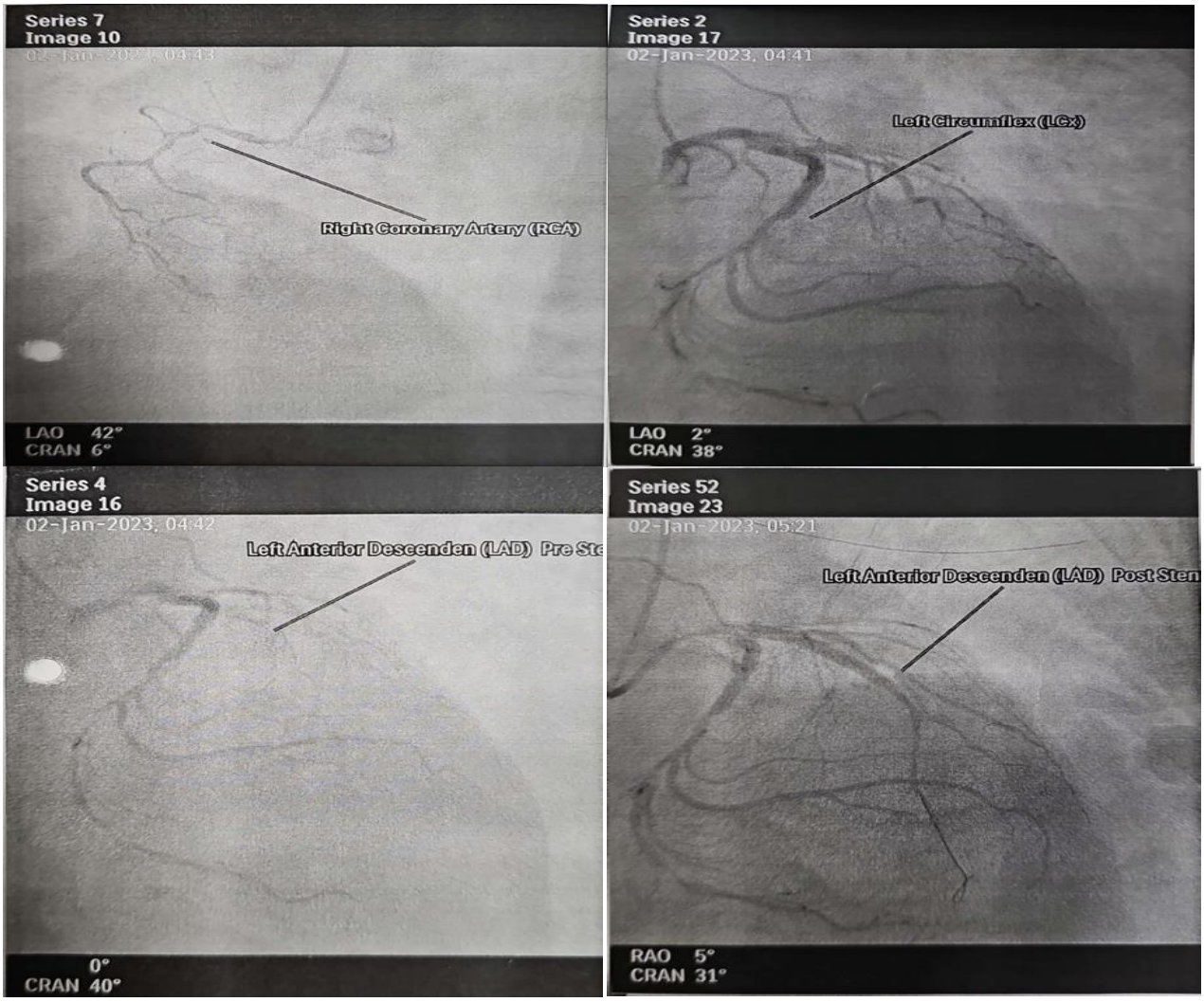

Figure 2. Cath report shows pre-stent and post-stent LAD

2. A pleomorphic adult megakaryocyte (differences in size) is found in an aging bone marrow biopsy along with trilineage growth (panmyelosis), significant erythroid, granulocytic, and megakaryocytic proliferation.
3. The presence of JAK2V617F or a mutation in JAK2 exon 12

Minor criteria

A serum erythropoietin level that is below the usual reference range

The diagnosis was established clinically, and if we refer to diagnostic criteria by the PSVG, this patient meets two criteria from category B, plus criteria A1 and A2. We can't classify this patient into the newest WHO criteria because any further laboratory examination wasn't performed. Also, his son is known to have phlebotomy monthly for his PV. A myocardial infarction occurred in 11.4% of the 149 PV patients diagnosed and followed up for ten years. Coronary events typically occur during PV. It is uncommon for PV to manifest as ISR in DES that has been implanted for days, even though PV and coronary artery disease (CAD) are linked. The frequent thromboses must make it difficult to keep a coronary artery patent (Xi et al., 2021). It is suspected that the process of neointima hyperplasia and neoatherosclerosis that occurs in ISR is related to the stimulation of platelet aggregation and thrombogenesis, the presence of leukocytosis and intimal proliferation that occurs in polycythemia vera. Research on the relationship between polycythemia vera and ISR is still underdeveloped (Bahbahani et al., 2015; Omeh & Shlofmitz, 2023).

The enhancement of total erythrocyte, increased hematocrit, caused blood hyperviscosity and lower blood velocity, and stimulated platelet aggregation and thrombogenesis, leading to thrombosis and lowering tissue oxygenation speed. High hematocrit causes higher shear stress, which causes vessel wall inflammation. Hyperviscosity is related to acute aortic occlusion. JAK2 mutation caused the activation and interaction of leucocyte and thrombocyte which caused inflammation and led to endothelial dysfunction as a marked intimal proliferation leading to occlusion. In this case, those would cause cardiovascular complications, leading to ischemia/infarction in the heart tissue (Griesshammer et al., 2019; Oktaviono et al., 2020; Shah et al., 2019). In this case, the patient had already implanted a stent in LAD from another hospital with the conclusion CAD1VD (LAD 80% proximal and LCx 50% proximal, 60% distal) successful PCI to LAD, and came to our hospital complaining of ongoing chest pain and ST-segment elevation. And his previous stent on LAD was total in-stent restenosis with LCx80% stenosis in the distal part.

The treatment goal is to prevent thrombotic events, Hematocrit levels should be lowered to 45%, and treatment and therapy for PV depend on the patient's thrombotic risk. There are two types of risk: high risk (age > 60 years or history of thrombosis) and low risk (none of the above). In addition to phlebotomy and low-dose aspirin, high-risk patients should have cytoreductive therapy, with hydroxyurea and recombinant interferon alfa as initial treatments (Xi et al., 2021). Patients with oral anticoagulants plus cytoreduction had the lowest rate of recurrences. Low-dosage Aspirin lowers the risk of nonfatal myocardial infarction, nonfatal stroke, and mortality from cardiovascular causes (Tefferi et al., 2021). PV patients with a history of PCI procedures have a higher risk of stent thrombosis, so besides Aspirin, another anti-platelet a more powerful P2Y12 inhibitor, such as ticagrelor, should be used after. Suppose DAPT cannot be used due to aspirin sensitivity. In that case, ticagrelor may be considered in certain high-risk circumstances such as those involving a high risk of stent thrombosis, complex left main stem, or multivessel stenting (Xi et al., 2021). So, we believe the patient needs regular phlebotomies and consumes hydroxyurea, aside from double anti-platelet (DAPT) since stenting is challenged by the development of stent thrombosis.

Limitation

Due to insurance policy, we cannot perform an intravascular ultrasound (IVUS) and Optical coherence tomography (OCT) examination to confirm any malposition of the stent. We also cannot perform a DAPT resistance test to rule out them as the cause of in-stent thrombosis.

Conclusion

ISR in PV patients who went a PCI with DES is still a challenging clinical problem. ISR development is difficult to treat, and optimal treatment for ACS in PV is a must to prevent further ischemic events. We presented a rare case of a male with PV who had an extremely early ISR and required a primary PCI. Because of intimal proliferation and blockage brought on by enhanced platelet aggregation and increased shear stress due to elevated hematocrit, the PV makes the circumstances worse.

Conflict of interest

The authors declare no conflict of interest.

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None

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