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Case Report

Symptomatic Bradycardia In CAD Patient: Which One First To Treat?

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ABSTRACT

Background: The incidence of sinus node dysfunction (SND) increases with age. Likewise, the incidence of coronary artery disease (CAD) has increased from year to year in Indonesia. When doctors are faced SND patients with CAD, it can be confusing in determining initial treatment options.
Objective: This study aimed to describe the diagnosis and management of SND in CAD patient.
Case Presentation: We will discuss a 75 years old male who had schedule to management of bradycardia symptomatic related to SND. Five month before admission, he had acute coronary syndrome, and had 2 DES implantation at left main (LM) to proximal left anterior descendent (LAD) artery and mid LAD. Two months after PCI he felt near syncope with bradycardia. Evaluation with ambulatory EKG was performed with result of SND, and correction of reversible cause related to SND already done. Eventually, symptom still exist and PPM insertion was decided to perform.
Conclusion: Patients with SND and CAD have a higher risk of complications and death. Correction of reversible factors, one of which is CAD, can be done as an initial step in the treatment of SND. When symptomatic signs still appear after correction of reversible causes, PPM implantation is the modality of choice in management.

1. Introduction

Sinus node dysfunction (SND) is a condition with heart rate < 50 bpm and/or a sinus pause > 3 seconds.[1] SND is one of classification of bradycardia, instead of atrioventricular block. The electrocardiographic findings in patients with SND are varied.[2] Sinus node dysfunction is caused by intrinsic/idiopathic factors (49%), treatable extrinsic factor (51%) or mix factor.[3] Incidence of SND with coronary arterial disease (CAD) is increasing with age.[2,4] There are about 0.03% patient with SND in UK, and much more common in elderly.[3] Data showed that SND with CAD account for 10 - 15%.[2] In 2013, prevalence of coronary disease in East Java is 1,3% people (375.127) and 0,5% (883.447) nationally.[5] While, elderly population in Indonesia is increasing each year.[6,7] With increasing incidence of coronary heart disease and increasing of elderly population in Indonesia, the incidence of SND could be increasing either.

Patient with SND tend to have high mortality rates, high risk of heart failure, and atrial fibrillation (AF).[2,8,9] This situation can reduce quality of life. Therefore, good early management can make a good prognostic to patient. In situation with symptomatic bradycardia related to SND and with existing CAD, physician may get confuse which one to be treated first? Do we need to do early pacemaker insertion or revascularization? We realize that proper treatment and good decision can maximize the outcome.

2. Case Illustration

Male 74 years old came to Saiful Anwar Hospital scheduled with complaints of weakness and near syncope with slow heart rate that happen since two months before admission. This situation happen approximately three - twice a week for less than 10 minutes, and said disturbed his daily activity. The symptom was often preceded by palpitation, but not triggered by an angry or emotional state, not because of urinating, nor coughing. The patient was also not experiencing diarrhea. No complaint of sleep apnea from his family while patient sleeping at noon or night. After the symptom relieved by itself, there was no unilateral weakness at patient extremities. In admission, there was no chest pain, heavy chest sensation, or radiating pain.

Five months before presentation, the patient had had severe shortness of breath and felling like falling followed by chest pain, 7-8/10 VAS and cold sweats. Because the complaints did not resolve, the patient was taken to private hospital. Patient was diagnosed with acute coronary syndrome and received injection at the abdomen. He was treated for 4 days in the ICU. After discharge the patient was routinely controlled to cardiologist and was planned for elective cardiac catheterization at the Hospital.

Five months before presentation, the patient had had severe shortness of breath and felling like falling followed by chest pain, 7-8/10 VAS and cold sweats.

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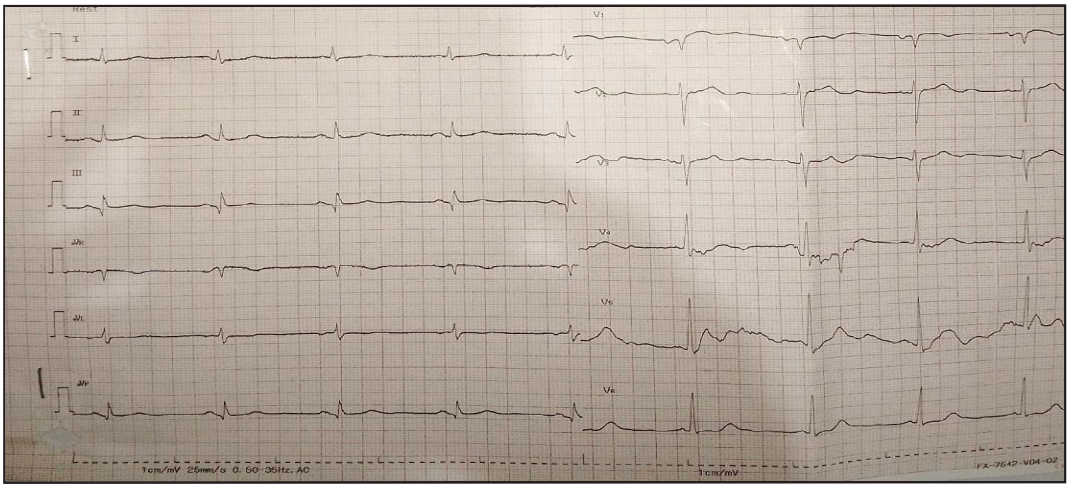

Figure 1. ECG on admission showed Sinus rhythm, HR 55 bpm, FA N, HA N, QRS 80ms ST Change (-) pathological q at III; T inverted aVL with conclusion : Sinus bradycardia.

Because the complaints did not resolve, the patient was taken to private hospital. Patient was diagnosed with acute coronary syndrome and received injection at the abdomen. He was treated for 4 days in the ICU. After discharge the patient was routinely controlled to cardiologist and was planned for elective cardiac catheterization at the Hospital.

A month after that, patient had catheterization with diagnose CAD 3VD post 2 DES implantation in Mid LAD and Proximal LM-LAD. After catheterization, patient felt better activity with less shortness of breath. Patient was planned to do next catheterization for distal LAD and RCA.

Two months before admission, the patient complained of chest palpitations with slow heart rate, accompanied by weakness and near syncope. There were no emotional state change prior to palpitation nor urinating or coughing. This sensation was never happen before. Holter procedure was performed with the results : basic sinus rhythm with frequent episodes of sinus arrest (conclusion: SND, suggestion of permanent pacemaker).

Patient also complained of swelling at both feet with pitting +2 at ankle level. Patient was diagnose with new onset CKD and underwent hemodialysis twice a week.

One month before admission, patient still complained of chest palpitation with slow heart rate that happened intermittently. Patient was performed catheterization at mid-distal LAD. Percutaneous trans luminal coronary angioplasty (PTCA) was done at chronic total occlusion (CTO) RCA. There was no event during procedure. No further revascularization was needed and medical optimization was suggested.

Patient had hypertension since 35 years ago. He didn't regularly take medication before, but had started consuming medication regularly since 20 years ago. No history of diabetes or stroke. Patient had hemodialysis (HD) since 1 month ago for newly diagnose chronic kidney disease and had been scheduled twice per week.

Patient regularly consumed Aspilet 0-0-80mg, Clopidogrel 75mg-0-0, Atorvastatin 0-0-20mg, Lansoprazol 1x30mg, Valsartan (Diovan) 0-0-160mg, Spironolactone 0-25mg-0, ISDN 3x10mg. Previously, patient had Bisoprolol 2,5mg for his heart failure medication, but already stopped since palpitation with slow heart rate occurred two months ago.

Patient was retired from local government civil servant. The patient can perform light daily activities independently.

From family history, his father died at age of 80 due to complications from kidney stones and had history of hypertension (HTN). The his mother died at age of 56 due to heart disease and had history of HTN. The patient is the first among 10 siblings. His sister (6th child) has HTN and cardiovascular disease that already done catheterization. All patient's siblings have HTN.

On physical examination we found GCS E4 V5 M6, BP: 139/75 mmHg, HR: 45 x/minute regular-strong pulse, RR: 20 x/minute, SpO2 : 98% on RA. Body weight: 60 kg, height: 169 cm, BMI: 21.0 kg/m2 (normo-weight), urine output: 800cc/24Jam, fluid balance: +50cc/24 hours on routine hemodialysis (HD) for twice per week.

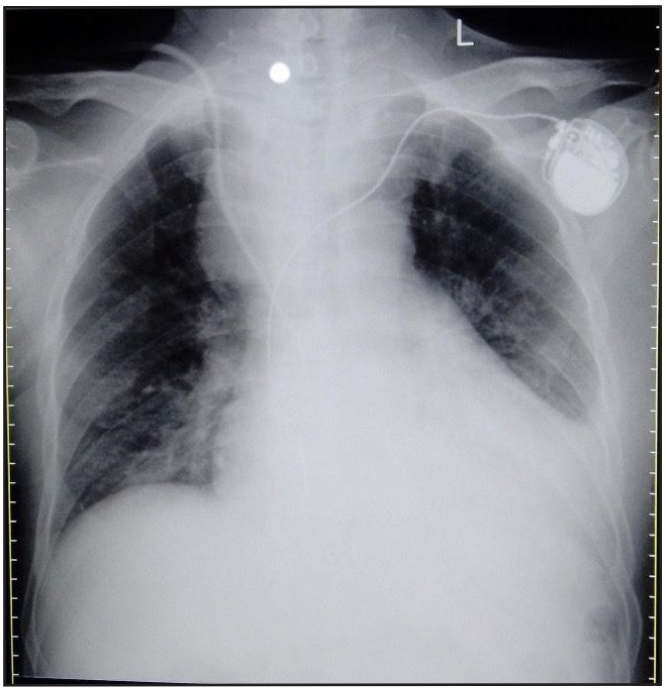

Figure 2. Chest X-Ray post PPM implantation

Table 1. Laboratory finding at admission

	Value		Normal Range
Hb	8,40	g/dL	13.4 – 17.7 g/dL
Leukocytes	4,26	/μL	4300-10300/μL
Hematocrit	27,80	%	40 – 47 %
Thrombocytes	133	/μL	142000-424000/μL
MCV	94,60	fL	80 – 93 fL
MCH	28,60	pg	27 – 31 pg
MCHC	32,20	g/dL	32-36 g/dL
Differential count	9,2/0,2/51,9/22,3/16,3		0-4/0-1/51-67/25-33/2-5 %
Random Blood Sugar	77	g/dL	<200 mg /dl
Urea	155,8	mg/dl	16.6 – 48.5 mg/dL
Creatinine	7,26	mg/dl	16.6 – 48.5 mg/dL
eGFR (CKD-EPI)	6,718	mg/dl	136 – 145 mmol/L
Sodium (Na)	140	mmol/L	3.5 – 5.0 mmol/L
Potassium (K)	3,49	mmol/L	98 – 106 mmol/L
Chloride (Cl)	106	mmol/L	3.5 – 5.5
Albumin	3,51	g/dL	Non reactive
Anti SARS COV-2	Non reactive		9.4-11.3
PPT	10,70	sec	24.6-30.6
APTT	28,10	sec	<1.5
INR	1,03		136 – 145 mmol/L

Head and neck examination showed conjunctiva pale +/+, icteric sclera -/- , JVP R+2 cmH2O (45deg), no palpable mass around neck examination. Thorax examination showed cardiac: ictus cordis invisible, palpable at ICS V 2 cm lateral MCL left, S1 S2 , murmur (-) and gallop (-) left, S1 S2 , murmur (-) and gallop (-). Pulmonology auscultation within normal limit, abdomen soefl, bowel sound normal, extremities warm acral, CRT < 2 seconds, with leg edema +/+ at level of ankle.

On ECG examination we found sinus rhythm, HR 55 bpm, frontal axis normal, horizontal axis normal, QRS 80ms ST Change (-), q pathologies at III, T inverted at aVL. Laboratory finding showed normocytic normochromic anemia and increased renal function test related to CKD. Serum electrolyte was within normal limit. Other finding was within normal limit. CXR at postero-anterior view examination showed cardiomegaly with CTR 64%, flattening cardiac waist, and apex embedded.
Echocardiography on June 12th 2021 showed mild MR, moderate TR, reduced LV Function with EF 47%, with RMWA hypokinetic at anterior segment.

4. Discussion

4.1 Differential Diagnosis

The patient came to the Saiful Anwar hospital after previously experiencing a near syncope accompanied by slow heart rate. Prior to feeling of near syncope, the patient did not complain of any emotional changes, diarrhea, or standing for a long time. As a first step in evaluating the patient, we re-evaluate whether the patient is hemodynamically stable or not.[10] Signs of hypotension, loss of consciousness, shock, ischemic chest pain, and acute heart failure were absent at presentation. The patient does not complain of typical chest pain, and palpitations was relieved in < 10 minutes. In this case, the patient is in a stable condition. Syncope or near syncope is included in the Transient Loss of Consciousness (TLOC) group, which is defined as a state of actually passing out or about to lose consciousness. The clinical picture can be amnesia during periods of unconsciousness, abnormal motor control, loss of responsiveness, and happen in a short period of time. Initial screening for TLOC was divided into 2 groups: those caused by head trauma or non-trauma.[11] In patients, nearly syncope are caused by non-trauma.

Etiologically, syncope/near syncope can be divided into 3 groups, such as reflex (neurally mediated syncope), orthostatic hypotension, and cardiac syncope. These three groups have their own characteristics. In our patient, the symptom was not preceded by emotional changes, eating activities, excessive physical activity, urinating, or standing for a long time. The patient felt palpitations when about to pass out. The patient had a history of acute coronary syndrome who underwent catheterization and stent implantation at LM to proximal LAD coronary artery and mid LAD. On physical examination, the patient showed bradycardia and the ECG showed sinus rhythm, HR 55 bpm, frontal axis normal, horizontal axis normal, QRS 80ms, ST Change (-), q pathologies at III, T inverted at aVL . From the history and physical examination, it can be concluded that the syncope/near syncope experienced by the patient tend most likely to a group of cardiac syncope.[11]

Table 2. Reversible Cause inducing SND1

Factors	Description
Acute myocardial ischemia or infarction	
Athletic training	
Atrial fibrillation	
Cardiac surgery	Valve replacement, maze procedure, coronary artery bypass graft
Drugs or toxins	Toluene, organophosphates, Tetrodotoxin, Hypoglycemia
Heart Transplant	
Hypervagotonia	Therapeutic hypothermia (exp. post cardiac arrest) Environmental exposure
Hypothermia	
Hypothyroidism	
Hypovolemic shock	
Hypoxmeia, hypercarbia, acidosis	Sleep apnea, respiratory insufficiency (suffocation, drowing), stroke, drug overdose
Infection	Lyme disease, Legionella, Psittacosis, Thypoid fever, thyhus, listeria, malaria, leptospirosis, dengue fever, viral hemorrhagic fever, Gullain-Barre
Medication	Beta blocker, non-dihidrophyridine calcium channel blockers, digoxin, antiarrhythmic drugs, lithium, methyldopa, risperidone, cisplatin, interferon.

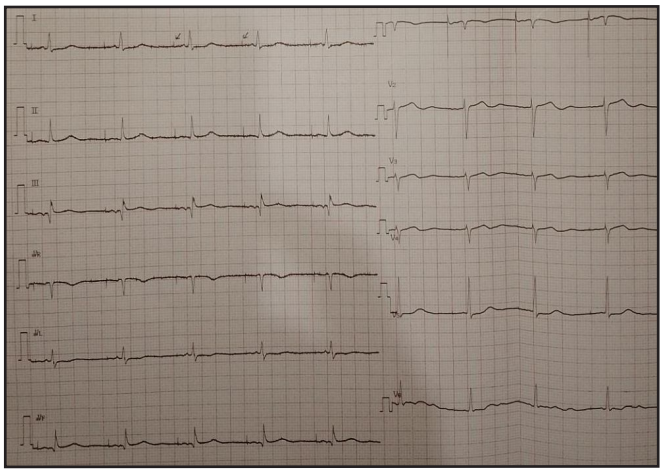

Figure 3. EKG after PPM insertion showed Pacing rhythm, HR 60 bpm, FA N, HA CWR, QRS 80ms.

In addition to conduction problems, other cardiac causes that can cause syncope include structural problems (e.g. valvular heart disease, myocardial heart disease, pericardial disease) and vascular causes. The patient had mild mitral regurgitation (MR) and moderate tricuspid regurgitation (TR), accompanied by decreasing left ventricular ejection fraction (LVEF) 47% which was probably caused by coronary heart disease.

After evaluating the possibility of cardiac syncope, further evaluation needs to be done to find the etiology of syncope. From the patient's presentation, the pulse was <60 bpm when a feeling of near syncope appeared. A pulse below 60 bpm is a sign of bradycardia. The feeling of near syncope that occurs incidentally related to decreased heart rate is a picture of symptomatic bradycardia.[1,12] Bradycardia can be classified into two groups: sinus node dysfunction (SDN) and atrioventricular (AV) block. A history and physical evaluation will assist in identifying the etiology of bradycardia. It is also necessary to obtain information about the frequency of symptomatic events, their duration, severity, circumstances accompanying the appearance of symptoms, and factors that reduce the severity of symptoms. In addition, we should evaluate the routine drugs consumed by the patient regarding the possibility of induction of bradycardia. In patients with bradycardia or conduction disturbances, screening for a 12-lead ECG, screening for structural heart defects and systemic disease is recommended. ECG abnormalities at the beginning of the examination provide predictive results and the possibility of structural disorders of the heart. Echocardiography is useful in evaluating patients with symptoms suspected to be of cardiac origin, e.g. aortic stenosis, hypertrophic cardiomyopathy or heart failure. Furthermore, investigations to evaluate metabolic disorders such as acidosis, hyperkalemia, hypokalemia, hypothermia, hypothyroidism, and hypoxia and cardiac structural disorders also support the search for the etiology of the disease.[1,12,13]

In the patient, near syncope symptom with bradycardia occurred at least 2-3 times per week with duration of < 10 minutes. After the incidence, there was no weakness at one side of the body. This incidence reduced the patient's quality of life. The patient did not have any emotional changes, diarrhea, or standing for long periods of time. One of the drugs consumed by the patient is bisoprolol, which has the possibility of induction of bradycardia. However, bisoprolol was discontinued after the first symptomatic appearance.

Physical examination showed normal blood pressure and bradycardia. The temperature and saturation were within normal limit. On examination of the neck, there was no palpable mass that led to an enlarged thyroid gland. There was swelling in the right and left legs at ankle level. From laboratory finding, no hypokalemia/hyperkalemia were found. Blood gas analysis and thyroid function tests were not performed. A 12 lead ECG showed a sinus rhythm with a heart rate of 55 bpm and a pathological q in lead III and an inverted T in aVL. The CXR image showed cardiomegaly with a CTR of 64%, cardiac waist flattening, and apex embedded. Echo examination showed a mild MR and moderate TR, accompanied by an LVEF of 47% (decreased) which was probably caused by coronary heart disease. From the results of the patient's evaluation, it appeared that the heart rhythm disturbances were bradycardia without metabolic disorders and without significant structural disturbances in the heart.

In the case of patients experiencing syncope/near syncope whose etiology is unclear or in patients who have repeated palpitations, the implementation of an ambulatory ECG becomes a class I choice.[1,14–16] There are 3 types of ambulatory ECG : Holter, event recorder (loop and non-loop) and real time continuous event recorder. The consideration of choosing any type of ambulatory ECG is based on the patient's symptoms on arrival, the frequency of complaints, and the degree of suspicion of a malignant arrhythmia.[14,15] Other considerations such as the availability of equipment, the capability to use the equipment, and financial coverage should also be considered in the choice of an ambulatory ECG modality. In patients with a dominant presentation of syncope, a continuous recording or loop recording is selected to overcome the patient's inability to activate the device when syncope occurs. Meanwhile, in patients with a dominant presentation of palpitations, the choice of non-loop recording can be considered. With the relatively high frequency of occurrences in daily activities, the selection of short duration recordings is deemed adequate. However, with the frequency of complaints being rare, the choice of a longer duration should be considered. In patients with suspected malignant arrhythmias, the choice of real time recording to monitor the condition continuously is recommended.[14,15]

Our patient had a near syncope presentation accompanied by palpitations with a frequency two to three times per week and the ECG showed sinus rhythm. The selected ambulatory ECG to support diagnosis is continuous ambulatory. A Holter monitor was set for 24 hours, by stopping bisoprolol prior to examination, and advice to do activities as usual. The results of the Holter monitor showed a basic sinus rhythm, good AV node conduction, no ST-T wave changes, bradycardia episodes, a maximum heart rate of 65 – a heart rate of at least 18 bpm, with the longest sinus arrest being 5.6 seconds.

SND is associated with increasing age (with the highest proportion found in the age of 70 – 80), progressive, degenerative fibrosis in the SAN and around the atrial myocardium.[1,3,17] By definition, SND can be expressed as:

1. Sinus rhythm with rate <50 bpm;
2. Atrial depolarization caused by an atrial pacemaker other than the sinus node at <50 bpm;
3. Sinoatrial block with evidence of obstruction of conduction between the sinus node and adjacent atrial tissue;
4. Sinus pause: sinus node depolarizes >3 seconds after last atrial depolarization;
5. Tachycardia-bradycardia syndrome ("tachy-brady"): sinus bradycardia, ectopic atrial bradycardia, or sinus pauses alternating with periods of abnormal atrial tachycardia, atrial flatter, or atrial fibrillation (S2.2-6). Tachycardia may be associated with sinus suppression of node automation and sinus pauses of varying duration as the tachycardia ends;
6. Chronotropic incompetence: defined as the inability of the heart to increase its rate according to increased activity, as a percentage defined as failure to achieve 80% of the expected HRR during exercise;
7. Isorrhythmic dissociation: atrial depolarization (from either the sinus node or ectopic atrial site) is slower than ventricular depolarization (from the atrioventricular node, bundle of His, or ventricle).

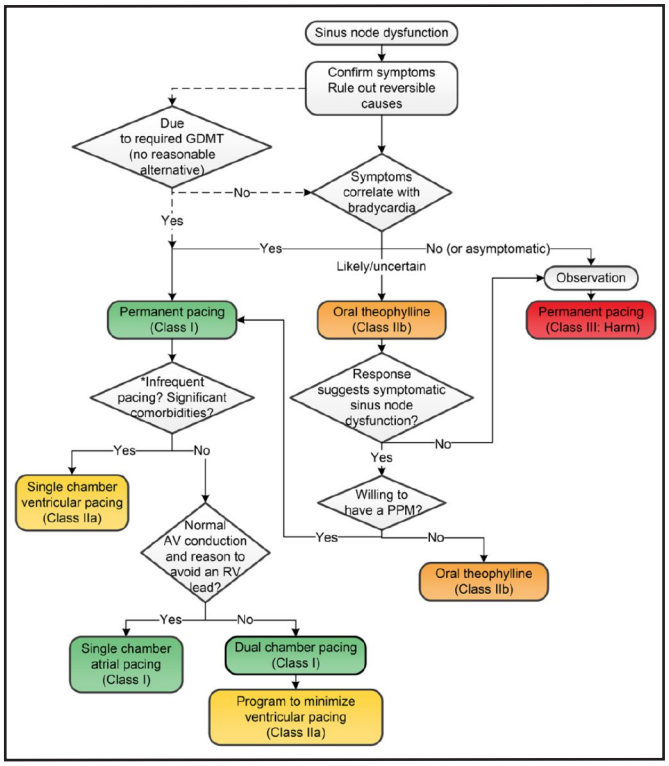

Figure 4. Diagram of Sinus Node Dysfunction management by ACC/AHA/HRS Guideline 2018. Note that different color showed different class of recommendation. First step to mention is to rule out reversible cause of SND.

From the 24-hour Holter, 74-year-old patient was found to have a sinus rhythm with a minimum rate of 18 bpm – a maximum rate of 65 bpm and a sinus arrest with a longest time of 5.6 seconds. These pictures support the diagnosis of SND in cases of symptomatic bradycardia.

4.2 Clinical Diagnosis

Sinus Node Dysfunction

The pathophysiology of SND varies from conduction problems to structural problems. Patients with symptomatic bradycardia that correlateso with SND have a high risk of cardiovascular events such as syncope, AF, heart failure and in ther hand increases the risk of cardiovascular death.[1,2,18] Clinical manifestations that often appear in patients with SND include syncope, dyspnea on effort, lightheadedness, and chronic fatigue. In SND patient with stable symptomatic bradycardia, evaluation and treatment of reversible causes is important to assess the trigger factors for reversible SND (recommended class I) such as acute myocardial infarction, atrial tachyarrhythmias, medications, electrolyte abnormalities, hypothyroidism, metabolic abnormalities and infections.[1]

The use of bradycardia-inducing drugs such as beta-blockers and calcium channel blockers has a fatal systemic toxicity effect by inducing negative chonotropic and inotropic.[1,19] The bradycardia-inducing drug that was routinely used (bisoprolol) was discontinued at the onset of the complaint of bradycardia. The patient did not have electrolyte disturbances despite having associated chronic kidney disease and had routine HD 2 times per week.

Acute myocardial ischemia affects cardiac conduction pathways through mechanisms of abnormal autonomic tone, decreased perfusion or injury to the SAN tissue.[3] Meanwhile, in the context of chronic ischemia, the correlation with the incidence of SND is not clear. Several studies have shown that patients with a history of inferior myocardial infarction who have SAN artery stenosis >75% have lower intrinsic heart rates, longer corrected sinus node recovery times (cSNRTs) and longer sinoatrial conduction times (SACTs) compared to moderate to no stenosis (< 75%).[20,21] This is possible due to inducing of reflex cardio-inhibition phenomena caused by chemical stimulation or mechanical stretch in the ischemic dilated right heart.[21,22] Meanwhile, in another study, patients with SND rarely had sinus node artery disease, there was even severe stenosis of the sinus node artery that still showed normal SAN function. Disorders of the coronary arteries, especially the proximal RCA, increase the incidence of bradyarrhythmia and hypotension.[21–23] This is anatomically related to 61% of patients had SAN vascularization branches originating from the right coronary artery (RCA), 37% branches from left coronary artery (LCx), and about 2% from both branches (RCA and LCx). Thus, there is a high probability of impaired vascularization if there is stenosis of the proximal RCA.

From the coronary view after the first PCI procedure, with clinical signs of acute coronary syndrome (ACS) in the form of sudden weakness, near syncope and palpitation, the culprit coronary lesions were found in RCA and LAD. Catheterization and stenting were performed on the Proximal and Mid LAD with the remaining lesions on the distal LAD and CTO in the RCA. It was planned to scheduled revascularization of the residual lesion. After the revascularization procedure, the ACS complaint was relive and patient'condition was better. Complaints of palpitation with slow pulse started to appear two months after the first PCI. Holter has been performed and got results. The presence of residual coronary lesions is one of reversible cause of SND. In patients with stable hemodynamic with symptomatic, it may still be considered to correct the reversible cause through revascularization.

A month after Holter, a stent was placed in the mid-distal LAD due to diffuse stenosis. PTCA was performed on the proximal osteal portion of the RCA because CTO RCA was difficult to penetrate. It was decided that another revascularization was not necessary and medical optimization was carried out as a follow-up treatment for the patient.

From the evaluation after the second catheterization procedure, the patient still complained of near syncope with a low heart rate in almost the same frequency. Despite correction of reversible factors, electrolyte correction, discontinuation of drugs that induce bradycardia (bisoprolol), and revascularization, the patient still complained of the same symptoms. From the diagram of SND treatment, if efforts to correct the reversible cause factor have been made but the symptoms related to bradycardia are still felt, the next choice of action is the implantation of a permanent pacemaker (PPM).[1,13,24]

4.3 Clinical Procedures

Permanent Pacemaker Implantation

Permanent pacemaker Installation aims to improve the patient's symptoms, not to increase patient survival.[1,13,14] In October 2021, AAI mode PPM insertion was chosen because of good AV node function and consideration of the lower incidence of atrial fibrillation in the future. The setting of PPM AAI mode was a lower rate of 60x/minute, amplitude 3.5V, pulse width 0.04ms, sensitivity 2.8mV. The results of postoperative CXR evaluation showed the pacemaker was in the left subclavian position with the lead position in the right atrium, no signs of hematothorax and pneumothorax were found. Monitoring for 3 days in the ward showed a rate of 60 bpm with stable hemodynamics.

4.4 Follow Up

One month after the PPM installation, on evaluation and reprogramming of the PPM we found rate of 60 beat per minute with 62 atrial high-rate (AHR) events, good impression. Clinically, the symptom of near syncope was no longer felt and the heartbeat was regular. Daily activities can be done well without any problems. Patients still routinely have HD which was increased to 3 times per week. Patients also routinely control and take the drugs given.

5. Conclusion

Patients with SND and CAD have a higher risk of complications and death. Correction of reversible factors, one of which is CAD, can be done as an initial step in the treatment of SND. When symptomatic signs still appear after correction of reversible causes, PPM implantation is the modality of choice in management.

6. Declarations

6.1. Ethics Approval and Consent to participate
Not applicable.

6.3. Availability of data and materials
Data used in our study were presented in the main text.

6.4. Competing interests
Not applicable.

6.5. Funding source
Not applicable.

6.6. Authors contributions
Idea/concept: AYS, MRS. Design: AYS, MSR. Control/supervision: MSR, AR, SW. Data collection/processing: AYS, MSR. Analysis/interpretation: AYS, MSR. Literature review: MSR, AR, SW. Writing the article: AYS, MSR. Critical review: MSR, AR, SW. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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