International Journal of Research and Review
Vol. 9; Issue: 1; January 2022
Website: www.ijrrjournal.com
Review Article *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

Wellens Syndrome: A Review Article

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DOI: https://doi.org/10.52403/ijrr.20220109

ABSTRACT

Wellens syndrome is a pre-infarct stage of coronary syndrome and a clinical condition associated with left descending proximal anterior artery stenosis. Diagnostic criteria for Wellens syndrome include clinical history, ECG changes, and laboratory results. The pathognomonic ECG of Wellens syndrome is anterior inverted T-wave in precordial leads, which can be seen during pain-free period, accompanied by isoelectric or minimally elevated ST segment (<1 mm), no precordial Q waves, and normal or slightly elevated cardiac serum markers. Early diagnosis leads to early management and a better prognosis. Early management of Wellens syndrome involves maintaining an airway, breathing, circulation, monitoring vital signs, and medical management. Still, the only definitive management is urgent cardiac angiography to prevent further myocardial ischemia. The combination of early diagnostic and appropriate management will reduce complications and mortality rates.

Keywords: Wellens Syndrome, Acute Coronary Syndromes, pre-Infarct MI

INTRODUCTION

Cardiovascular disease is the leading cause of morbidity and mortality and is responsible for one-third of all deaths in Indonesia. Data from the Indonesian Family Life Survey in 2008 found that less than a third of Indonesian with moderate to high cardiovascular risk did not receive optimal treatment.[1] Coronary heart disease is the leading cause of death and morbidity in developed countries. Although deaths from this condition have gradually decreased over the past few decades in European countries, it still accounts for about one-third of deaths in people over 35 years old. The American Heart Association (AHA) reported that 15.5 million people ≥20 years old in the United States have coronary heart disease. At the same time, the prevalence increases along with age for both women and men, and myocardial infarction occurs approximately every 42 seconds.[2]

Wellens syndrome (WS) or left anterior descending artery (LAD) syndrome was first described by de Zwaan et al. in a subgroup of patients with unstable angina who had inverted anterior on their electrocardiogram findings (ECG).[3] The classification of WS can be divided into type A marked by deep, symmetrical T-wave inversions in leads V2 and V3, often including leads V1, V4, V5, and V6 and type B, which is characterized by biphasic T-waves in leads V2 and V3 during the pain-free period. These findings are associated with stenosis of the anterior descending artery.[4] In addition to those findings, the absence of precordial Q waves, minimal elevated ST segment (<1 mm), and normal or slightly elevated cardiac serum markers can help to confirm the diagnosis.[5]

The incidence of WS ranges from 10-15% of all acute coronary syndrome cases with the exact etiology as coronary artery diseases such as atherosclerotic plaque, coronary artery vasospasm, hypoxia, and increased cardiac demand.[6] Two studies in hospitalized unstable angina, WS can be

found on 14% -18% ECG findings, and 75% of WS patients who did not undergo myocardial revascularization had an extensive anterior myocardial infarction within the first few weeks of treatment, indicating the importance of early diagnosis of this syndrome.[4] Early diagnosis of WS may be a diagnostic challenge due to difficulty interpreting ECG changes on patients with acute chest pain, which leads to late intervention and increased morbidity and mortality rate.[7] Factors that contribute to the difficulty in recognizing this syndrome were lack of physician skills in interpreting ECG, evident ischemia was not found during initial evaluation, symptoms which occurred during the pain-free period, and the same ECG findings with other conditions such as hypokalemia, intracerebral hemorrhage, pulmonary embolism, persistent juvenile T-wave inversion, or normal variant.[8]

Definition and Risk Factors

WS is a clinical condition characterized by left descending proximal anterior artery stenosis and massive myocardial infarction on the anterior wall, accounting for 10-15% of all incidences of unstable angina.[8,9] Most cases of WS involved proximal segment with the most common ECG finding was type B marked by precordial T wave inversion in V1-V5 (76%) and type A in V2-V3 (24%).[6]

Risk factors of WS include a family history of premature coronary heart disease, type II diabetes mellitus, metabolic syndrome, hypertension, smoking, hyperlipidemia, work stress, advanced age (55 ± 9 years), HIV-related cases, history of early coronary disease as well as in patients without cardiovascular risk factors.[6] The pathophysiology of ECG changes has not been clearly defined, presumably due to local edema or intermittent or unstable blood flow in the anterior descending coronary artery with significant obstruction. These changes have been demonstrated by magnetic resonance imaging.[2] WS results from temporary stenosis of the LAD coronary artery, which is usually caused by atherosclerotic plaque rupture leading to the obstruction of LAD, with significant clot lysis before myocardial infraction occurred.[3] Severe stenosis of the LAD artery caused severe complications and was called a widowmaker lesion. LAD originates from the left main coronary artery, supplying the anterior myocardium via the interventricular sulcus. Alterations in LAD blood flow caused severe left ventricular dysfunction, increased the risk of congestive heart failure and death. WS is diagnosed based on classic T-wave inversion in ECG findings for chest pain and pain-free. [10]

Diagnosis

The diagnosis of WS depends on clinical history, ECG changes, and cardiac biomarkers.[11] The clinical manifestation of WS consistent with an acute coronary syndrome, including chest pain or tightness or pressure-like usually induced by physical activity, relieved by rest, may radiate to the neck, jaw, or shoulder. Chest pain as a sign of myocardial ischemia was caused by total or near-total obstruction of LAD.[12] Patient usually presented during a pain-free period at an emergency department.[3] Physical examination revealed protodiastolic murmur on the third intercostal space above the midline of the left clavicle, which may be due to turbulence of direct distal blood flow to the stenotic segment, known as a Dock's murmur. The diagnosis can be confirmed by coronary angiotomography in a hemodynamically stable patient or by doubt on the initial examination. This is the most accurate and reliable noninvasive modality to exclude significant coronary artery stenosis.[6]

The diagnostic criteria for WS are as follows: deep inverted T waves in leads V2 and V3 (also seen in leads V1, V4, V5, and V6) or biphasic T waves (with initial positivity and negative terminals) in V2 and V3, absence of Q waves without loss of precordial R waves, no significant ST-segment elevation (< 1 mm), normal or minimally increased cardiac markers,

history of chest pain and T wave changes (biphasic or inverted) in the precordial leads during the pain-free period, as (shown in Figure 1) Inverted or biphasic T-waves in the precordial leads were caused by repolarization abnormalities due to reperfusion injury and myocardial edema.[13,14] It is essential to consider coronary angiograms as an initial diagnostic modality rather than any other conservative examination in a patient with an ECG pattern, suggesting the possibility of WS.[7] An example of common coronary angiography findings in WS which show obstructions in LAD (can be seen in Figure 2).[15]

Serial ECG and cardiac enzyme laboratory should be performed. Echocardiography can be beneficial in patients with atypical chest pain because it can detect any cardiac abnormality before the rise of serum troponin. Based on current guidelines, the stress test should be performed within 72 hours or admission to chest pain units for stress testing consideration.[10,16]

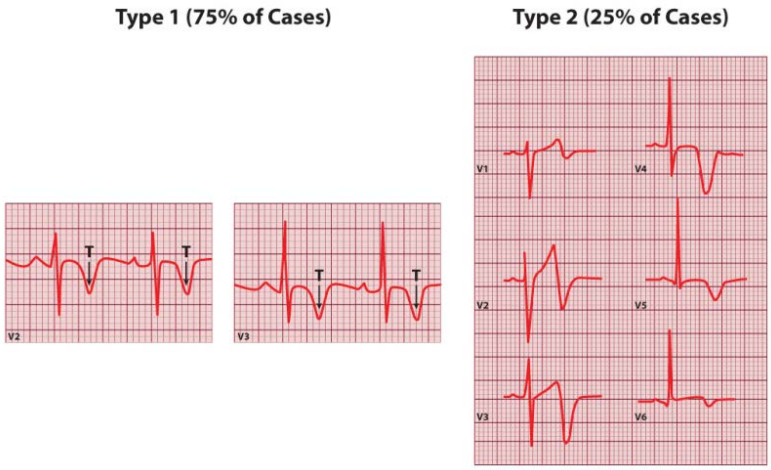

Figure 1. ECG Findings of Wellens Syndrome Type 1/B (left) and Type 2/A (right)[3]

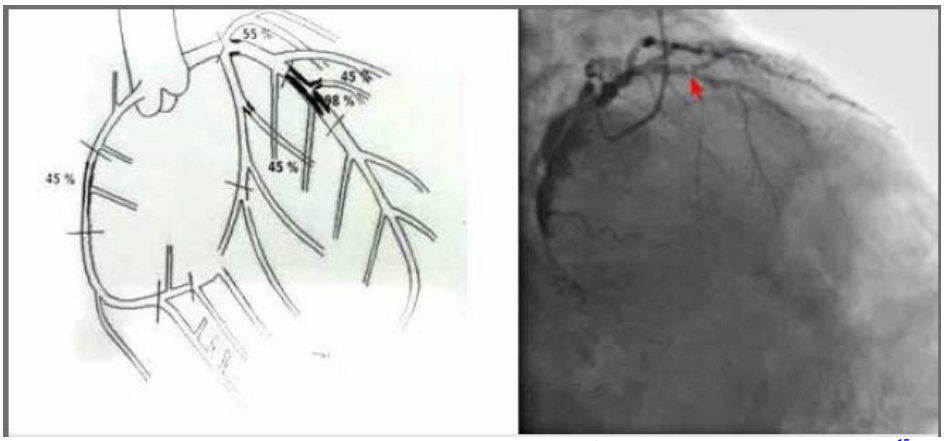

Figure 2. Coronary Angiographic Findings with Narrowing of the Medial LAD Proximal LAD.[15]

The differential diagnosis of precordial T-wave inversion includes pulmonary embolism, cerebral hemorrhage, left ventricular hypertrophy, cocaine or morphine-induced coronary vasospasm (pseudo-Wellens syndrome), chronic pulmonary thromboembolic hypertension, interruption or transient left bundle branch block, or Wolff-Parkinson-White pattern (WPW), persistent juvenile T wave pattern, late-stage pericarditis, digitalis effects, and Takotsubo cardiomyopathy. The differences between those conditions and WS are presented in Table 1.[3,6]

Table 1. Differential diagnosis of WS.[6]

Differential Diagnosis	Laboratory	ECG	Echocardiography	X-ray	*Computed Tomography* (CT) *scan*
Takotsubo	✓	✓	✓	✓	
Cocaine vasospasm	✓	✓	✓		
Myocardial infarction	✓	✓	✓	✓	
Myocarditis	✓	✓	✓		
Pulmonary embolism	✓	✓	✓		✓
Cerebrovascular stroke	✓	✓	✓		✓
WPW		✓			

Treatment

WS is the pre-infarct stage of acute coronary syndrome; therefore, recognizing this syndrome can be a life-saving diagnosis.[17] T-wave changes in WS are usually observed in asymptomatic patients. Although these patients may initially respond well to medical management, they ultimately have poor outcomes with conservative therapy and require a revascularization strategy.[18] The early management of WS in the emergency department was referred to the nearest hospital for further evaluation and management, airway patency, maintenance of breathing and circulation, oxygen supplementation and monitoring for a vital sign, intravenous access, administration of aspirin, clopidogrel, nitrate, beta-blocker, and morphine if needed, serial ECG examination, laboratory examination including cardiac marker (troponin I or T) and chest X-ray. Because the definitive treatment for WS is procedural or interventional, as soon as the diagnosis of WS is confirmed, consult an interventional cardiologist, and coronary angiography should be performed. This is beneficial for evaluating further management, such as angioplasty or coronary artery bypass procedures.[10] Symptomatic patients should be monitored in the intensive care unit, and cardiac catheterization should be performed in an emergency setting. Stress test which can induce acute myocardial infarction and sudden death is contraindicated in WS patients who had severe stenosis of LAD.[3]

Delayed coronary revascularization can also lead to left ventricular dysfunction and death due to extensive acute myocardial infarction of the anterior wall. Treatment with multiple antiplatelet (acetylsalicylic acid and clopidogrel), thrombolysis, blood pressure, glucose control, and statin therapy alone did not reduce complication rates and mortality. Therefore, it requires holistic management, including medical and intervention management.[6,19] According to the recent meta-analysis, ticagrelor is associated with a higher risk of significant bleeding than clopidogrel in patients with acute coronary syndrome in East Asia.[20]

Subsequent studies on WS with a follow-up period for 18 months showed that the mortality rate was very high in conservatively treated patients compared to patients treated with cardiac catheterization (26.67% vs. 0.88%). All invasive procedures such as cardiac catheterization should be considered during the 2019 coronavirus disease (COVID-19) pandemic. Based on the patient's risk, conservative therapy may be sufficient for non-ST-segment elevation myocardial infarction (NSTEMI) patients with COVID-19. WS patients with COVID-19 and stable hemodynamic are recommended to be treated conservatively in an isolated hospital ward. Several reports show an association between COVID-19 infection and cardiovascular complications, including myocardial injury, myocarditis, deep vein thrombosis (DVT), and pulmonary embolism (PE).[20]

Based on the Indonesian Heart Association recommendation, conservative care in isolated hospital wards should be considered if the WS patients are positive for COVID-19 and have stable hemodynamic to reduce the risk of transmission of COVID-19, especially when special standard facilities are not available. These recommendations align with Chinese Society of Cardiology guidelines, which recommend that NSTEMI high-risk patients be hospitalized and treated conservatively.

The American College of Cardiology suggests that in patients with stable NSTEMI, conservative therapy may be sufficient based on the patient's risk.[20]

CONCLUSION

WS is a clinical condition with significant stenosis of the proximal LAD artery marked by inverted T waves in precordial leads and usually occurred in a pain-free period. WS diagnosis can be confirmed by WS diagnostic criteria derived from clinical history, ECG changes, and cardiac biomarkers. Early diagnosis leads to early referral to designated hospital, management and intervention, so mortality and morbidity rates can be reduced.

Acknowledgment

Those who contributed to the work are listed as authors of the article.

Conflict of Interest Statement

The authors have no conflicts of interest to declare about this article.

Funding Sources

The authors received no financial support for the research, authorship, and publication of this article

Authors' Contributions

All authors contributed to the study design. Based on discussions, Dr. Sahitra Tamaray drafted the manuscript, which all authors revised.

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How to cite this article: Tamaray Sahitra, Fuadi Haizil. Wellens syndrome: a review article. *International Journal of Research and Review*. 2022; 9(1): 59-64. DOI: *https://doi.org/10.52403/ijrr.20220109*

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