Clinical Case Report

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Wellens syndrome in HIV-infected patients

Two case reports

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Abstract

Background: Wellens syndrome is a pattern of electrocardiographic (ECG) changes in the context of unstable angina characterized with deep inverted T-waves or biphasic T-waves in the precordial leads. These specific ECG changes are highly suggestive of stenosis in the left anterior descending artery (LAD), which can result in acute myocardial infarction, left ventricular dysfunction, or death. Human immunodeficiency virus (HIV) infection is known as an independent risk factor for the cardiovascular disease.

Case Report: The first case is a 61-year-old African American female with a history of HIV infection who presented with chest pain for 8 h. Electrocardiogram (ECG) showed deep T-waves inversions in leads V3–V6. Emergent cardiac catheterization showed 99% stenosis in the mid-LAD and a drug-eluting stent (DES) was subsequently placed. The second case is a 49-year-old African American female with a medical history of type 2 diabetes mellitus, HIV, active cigarettes smoker admitted for intermittent substernal chest pain of 1-day duration. ECG showed biphasic T-wave in V2 and deep T-waves inversion in V3–V4, coronary angiography showed 95% stenosis in the proximal LAD and a DES was placed.

Conclusion: Wellens syndrome has characteristic ECG changes that indicates LAD stenosis. Early recognition of this syndrome, especially in HIV-infected patients who are high risk for cardiovascular disease, will help to avoid impending myocardial infarction.

Abbreviations: ART = antiretroviral therapy, CVD = cardiovascular disease, DES = drug-eluting stent, ECG = electrocardiographic/electrocardiogram, ER = emergency room, HIV = human immunodeficiency virus, LAD = left anterior descending artery, MI = myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-Elevation Myocardial Infarction, TTE = transthoracic echocardiogram.

Keywords: acute coronary syndrome, HIV infection, Wellens syndrome

1. Introduction

Wellens syndrome is a pattern of electrocardiographic (ECG) changes of deeply inverted T-waves (75%) or biphasic T-waves (25%) in the precordial leads. It was first described by de Zwaan et al in 1980s[1] and is also referred as left anterior descending artery (LAD) coronary T-wave syndrome. These ECG changes, if developed in the setting of unstable angina, are highly specific for the critical stenosis in proximal LAD. The ECG changes usually occur in a pain free state, but the patient may suffer extensive anterolateral myocardial infarction (MI) or cardiac arrest in the coming days or weeks if no interventional therapy is performed.[1] Wellens syndrome is "equivalent" to ST-elevation myocardial infarction (STEMI) in terms of necessitating emergent invasive therapy.

Cardiovascular disease (CVD) has become one of the major causes of death in human immunodeficiency virus (HIV)-infected patients as patients live longer in the post-antiretroviral therapy (ART) era. There is approximately a 1.5-fold increase in cardiovascular events including acute MI, other ischemic heart diseases, and coronary atherosclerosis in HIV-infected patients compared with the uninfected population.[2] The long-term use of ART also contributes to the increase of CVD by the side effects of fat distribution, lipoatrophy, and metabolic abnormalities.[3] Wellens syndrome is "equivalent" to ST-elevation myocardial infarction (STEMI) in terms of necessitating emergent invasive therapy. To the best of our knowledge, this is the first report about Wellens syndrome in HIV-infected patients. The patients gave informed consent for all the information discussed here.

2. Case report

2.1. Case 1

A 61-year-old African-American female came to the emergency room (ER) of Brookdale Hospital with the chief complaint of acute-onset chest pain for about 8 h. She started to experience mid substernal pressure-like chest pain since early that morning after she woke up from sleep. The pain radiated to the left side of her

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The case report is approved by institutional review board of Brookdale University Hospital and Medical Center. The informed consent is obtained from both patients.

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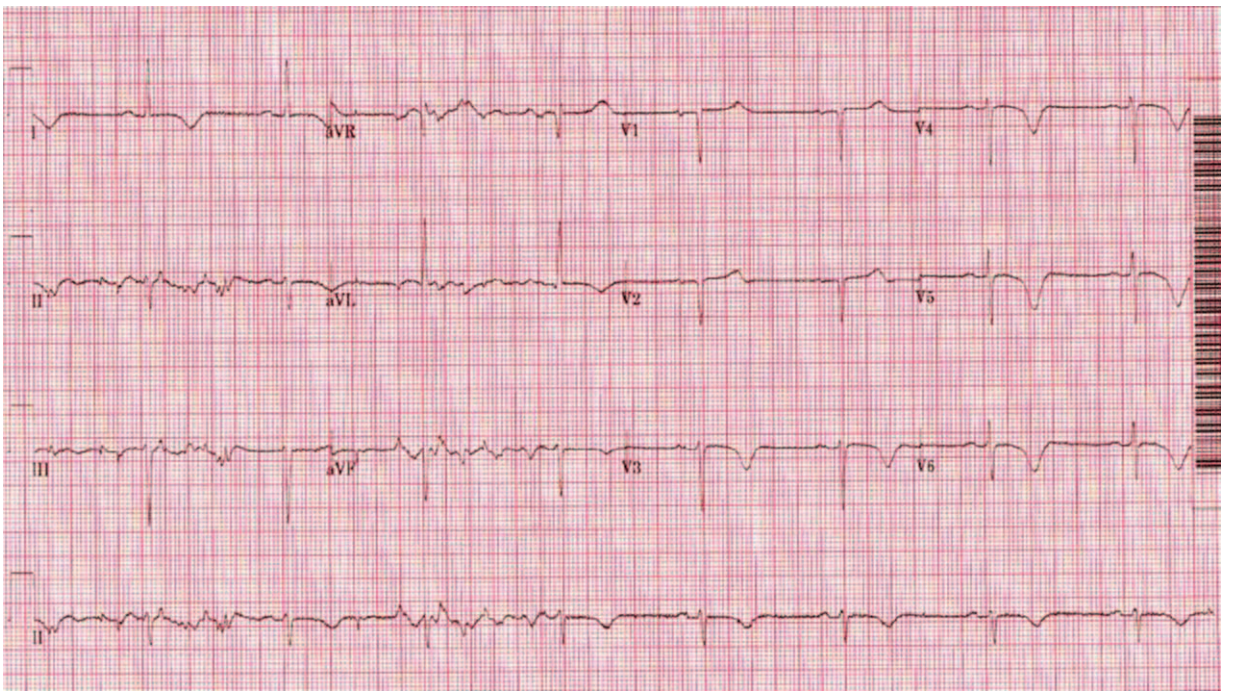

Figure 1. Case 1 electrocardiogram of the first case showed deep, symmetrical T-wave inversions in leads V3–V6, mild T wave inversions in I, II, III, avL, avF, no apparent ST depression or elevations.

neck and initially was 9/10 on intensity, constant, but gradually abated. She denied accompanied shortness of breath, diaphoresis, nausea, vomiting, or palpitations. She had one similar episode of chest pain about 6 months prior; the pain resolved spontaneously and she did not seek medical attention. Her medical history was significant for HIV infection, essential hypertension, and stage III chronic kidney disease. She was compliant with antiretroviral treatment composed of abacavir, lamivudine, and efavirenz. Her most recent CD4 count was 642 cells/μL and viral load was undetectable 3 weeks prior. She denied any history of cigarettes smoking, alcohol use, or recreational drug abuse. She denied any family history of heart disease or premature death.

At presentation, her blood pressure was 208/131 mm Hg and was effectively controlled by resuming her home oral antihypertensive medication consisting of nifedipine and clonidine. Physical examination was benign. Initial ECG was unremarkable and laboratory tests showed a mildly elevated troponin of 0.067 ng/mL (reference range: 0.000–0.034 ng/mL). She was transferred to observation unit for close cardiac monitoring; 5 h later repeated ECG showed significant deep, symmetrical T-wave inversions in leads V3–V6, mild T wave inversions in I, II, III, avL, avF, no apparent ST depression or elevations (Fig. 1). The patient was chest pain free at that time and repeated troponin increased to 1.920 ng/mL. Cardiology was consulted immediately and

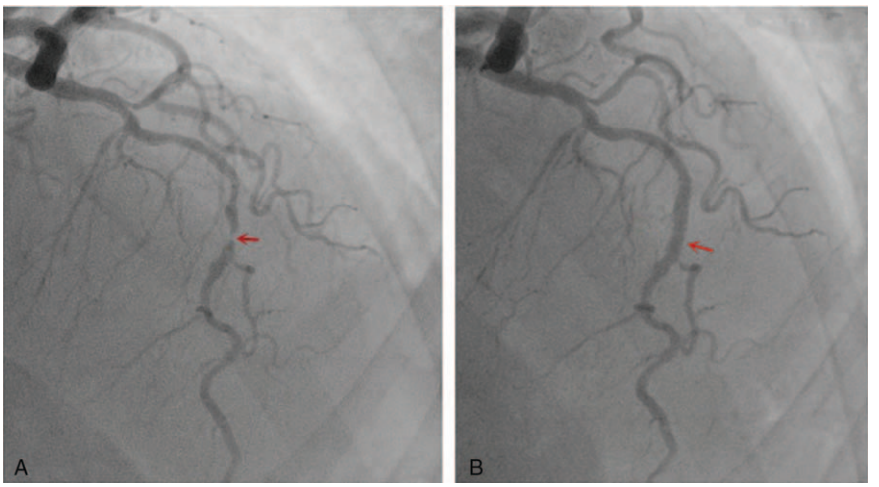

Figure 2. (A) Case 1 pre-PCI coronary angiography in the first case showed 99% stenosis in the mid-left anterior descending artery (red arrow); (B) post-PCI coronary angiography showed successful reperfusion (red arrow) after balloon angioplasty with drug-eluting stent. PCI = percutaneous coronary intervention.

STEMI code was activated. She was taken for the emergent cardiac catheterization that showed a 99% stenosis in the mid-LAD (mLAD) (Fig. 2A) and an 80% stenosis at the ostium of the 1st diagonal vessel segment. A successful balloon angioplasty and a drug-eluting stent (DES) placement were performed in the mid-LAD (Fig. 2B). The transthoracic echocardiogram (TTE) of the next day, demonstrated normal left ventricular ejection fraction with dyskinesia of the apical and lateral walls. She was symptom free after procedure and discharged home the next day.

2.2. Case 2

A 49-year-old African American female presented to the ER with the chief complaint of intermittent chest pain of 1 day duration. She started to experience chest pain while at rest at night. She described the chest pain as substernal squeezing-type pain, 10/10 in intensity that radiated to the left arm. The pain lasted about 10 to 20 min associated with dyspnea, diaphoresis, left arm numbness/"burning" sensation, and 2 episodes of vomiting. Her medical history was significant for HIV infection, type 2 diabetes mellitus, essential hypertension, systemic lupus erythematosus, and seizure disorder. She was on ART, but she was not quite adherent to treatment. She is an active smoker and smoked about 7 cigarettes/d for past 15 years. She denied any illicit drug and alcohol abuse history. There was no significant CVD or premature death in the family history.

General physical examination was unremarkable and vital signs were within normal range; heart auscultation did not reveal any murmurs or extra heart sounds. Initially ECG was insignificant and serial troponins showed a mild elevation with a peak value of 0. 496 ng/mL (reference range: 0.000–0.034 ng/mL). HIV viral load was undetectable. She was still experiencing intermittent ongoing chest pain after admission that was controlled with sublingual nitroglycerin. Repeated ECG 24 h after admission showed biphasic T-wave in V2 and symmetrical, deep T-wave inversions in V3–V4 (Fig. 3), mild T wave inversions in inferior and lateral leads (II, III, avF, V5–V6), no ST depression or elevation. Subsequently coronary angiography showed a tubular 95% stenosis in proximal LAD (Fig. 4A), balloon angioplasty was performed, and a DES was placed in the proximal LAD (Fig. 4B). TTE afterwards showed hypokinesis of the apical septum with a normal left ventricular ejection fraction (73%), she was chest pain free after the procedure and discharged home the next day.

3. Discussion

Wellens syndrome was first described by de Zwaan, Bar, and Wellens in 1982. The typical ECG pattern can be divided in 2 types: type A is characterized by biphasic T-waves in V2–V3, which accounts for 25% of Wellens syndrome; type B is characterized by deep, symmetric T-wave inversions in V2–V3, and accounts for the remainder 75%. In de Zwaan first study, 26 of 145 (18%) patients admitted for unstable angina showed these characteristic ECG patterns, 12 of 16 (75%) patients who were managed medically developed subsequently extensive anterior wall infarction within a few weeks.[1] In the following prospective study in 1988, all of 180 patients with this ECG pattern were confirmed to have LAD abnormalities, 33/180 (18%) had completed occluded LAD and 147/180 (82%) had mean degree of 85% stenosis in the LAD.[4] Failure to recognize the Wellens syndrome promptly may result in extensive anterior wall MI.[5] Both of our patients presented with unstable angina, the first case's ECG displayed typical deep, symmetrical inverted T-waves, and angiography confirmed almost occluded mid-LAD (99% stenosis). In the second case, the patient developed biphasic T-waves changes 24-h after admission and subsequent angiography showed 95% stenosis in the proximal LAD. In both cases, the

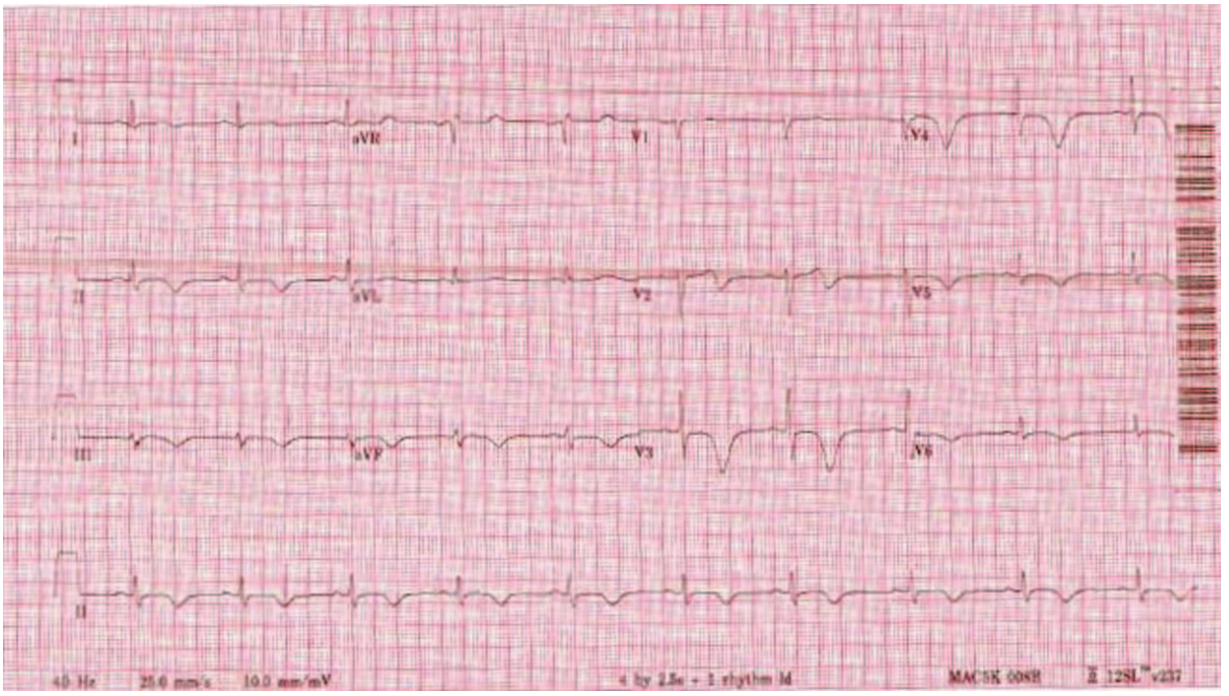

Figure 3. Case 2 electrocardiogram of the second case showed biphasic T-wave in V2 and symmetrical, deep T-wave inversions in V3–V4, mild T wave inversions in II, III, avF, V5–V6, no ST depression or elevation.

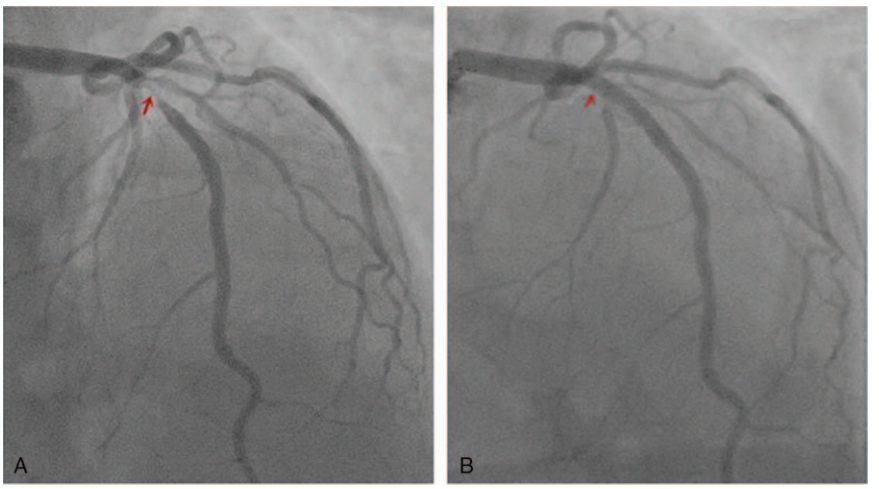

Figure 4. (A) Case 2 pre-PCI coronary angiography in the second case showed tubular 95% stenosis at the origin of D1 in proximal left anterior descending artery (red arrow); (B) post-PCI: reperfusion after balloon angioplasty and drug-eluting stent placement (red arrow). PCI = percutaneous coronary intervention.

ECG also demonstrated ischemia changes in the inferolateral leads (mild to moderate T wave inversions), these can be explained that the distal LAD may cross over the apex and provide blood supply to the inferior or lateral myocardial walls. Due to the prompt invasive therapy, no further anterior wall MI complications were identified in both of these patients and left ventricular function was preserved.

T-wave inversions in electrocardiogram are fairly common and could be related to a wide range of clinical diseases from the life-threatening conditions including acute coronary ischemia, pulmonary embolism, acute myocarditis, and central nerve system injury, to benign conditions like juvenile T-wave pattern, left ventricular hypertrophy with repolarization abnormalities, digitalis effect, bundle branch block, and pre-excitation syndrome. The accurate diagnosis of Wellens syndrome is based on the characteristic ECG pattern of deep, symmetric inverted T-wave or biphasic T-wave in the precordial leads with the isometric or minimal elevated (<1 mm) ST segment and absence of pathologic Q wave in the same lead,[6] as well as clinical history of chest pain (within hours to days), but now in painless state and with laboratory tests showing normal or slightly elevated cardiac enzymes.[7]

Numerous studies have shown that HIV infection is an independent risk factor of CVD in the post-ART era.[2,8,9] CVD has emerged to be a leading cause of mortality and mobility in the HIV-infected patient nowadays. The prevalent subclinical atherosclerosis leading to CVD in HIV-infected patients may involve the inflammation and immune dysregulation of HIV infection itself[10]; increased prevalence of traditional risk factors like hypertension, diabetes mellitus, and smoking in HIV-infected population[9]; and the contribution of ART by inducing lipoatrophy, fat accumulation, and metabolic disturbances.[3,11] The HIV-infected patients who develop acute coronary syndrome are younger, more frequently male and have higher prevalence of risk factors than non-HIV-infected patients. They are also more likely to present with ST elevation myocardial infarction instead of non-ST elevation myocardial infarction or unstable angina.[12] In our first case, the patient was a female, nonsmoker her entire life, her only identified risk factors were essential hypertension and possible mild chronic kidney disease. The role of HIV infection contributing to CVD was uncertain, but definitely could not be neglected. For the second case, our patient was an active daily smoker, diabetic, and had a history of lupus. Even though she was only 49 years old, all these risk factors, with HIV infection, made her very high risk for coronary artery disease. In a moderate-sized analysis of 76 HIV-infected patients having coronary artery disease, the LAD was involved in 47 (62%) patients while the left circumflex and right coronary arteries were involved in 34 (45%) and 38 (50%) patients, respectively.[13] The relatively high prevalence of LAD involvement in CVD of HIV-infected patients may explain the incidence of Wellens syndrome in HIV-infected patients.

Wellens syndrome so far has not been reported in the HIV-infected patient; however, considering the high prevalence of CVD in HIV-infected patients, it shall never be overlooked. More data about the epidemiology of Wellens syndrome in HIV-infected patients should be further investigated.

4. Conclusion

Clinicians, especially in the HIV-infected population, should always recognize Wellens syndrome in the setting of angina pectoris and urgent invasive treatment should be pursued to avoid the subsequent anterior wall MI. The clinical significance of Wellens syndrome in HIV-infected population needs further investigation.

References

[1] de Zwaan C, Bär F, Wellens H. Characteristic electrocardiographic pattern indicating a critical stenosis high in left anterior descending coronary artery in patients admitted because of impending myocardial infarction. Am Heart J 1982;103:730–6.
[2] Currier J, Taylor A, Boyd F, et al. Coronary heart disease in HIV-infected individuals. J Acquir Immune Defic Syndr 2003;33:506–12.
[3] Barbaro G, Barbarini G. Highly active antiretroviral therapy-associated metabolic syndrome and cardiovascular risk. Chemotherapy 2006;52:161–5.
[4] de Zwaan C, Bär F, Janssen J, et al. Angiographic and clinical characteristics of patients with unstable angina showing an ECG pattern indicating critical narrowing of the proximal LAD coronary artery. Am Heart J 1989;117:657–65.
[5] Canpolat U, Kaya EB, Aytemir K, et al. Delayed therapy for Wellens' syndrome resulted in acute myocardial infarction. Kardiol Pol 2012;70:1316.

[6] Rhinehardt J, Brady W, Perron A, et al. Electrocardiographic manifestations of Wellens' syndrome. Am J Emerg Med 2002;20: 638–43.
[7] Ozdemir S. Wellens syndrome: report of two cases. Turk J Emerg Med 2016;15:179–81.
[8] Triant V, Lee H, Hadigan C, et al. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. J Clin Endocrinol Metab 2007;92: 2506–12.
[9] Saves M, Chene G, Ducimetiere P, et al. Risk factors for coronary heart disease in patients treated for human immunodeficiency virus infection compared with the general population. Clin Infect Dis 2003;37: 292–8.
[10] Kelesidis T, Kendall M, Yang O, et al. Biomarkers of microbial translocation and macrophage activation: association with progression of subclinical atherosclerosis in HIV-1 infection. J Infect Dis 2012; 206:1558–67.
[11] Durand M, Sheehy O, Baril J, et al. Association between HIV infection, antiretroviral therapy, and risk of acute myocardial infarction: a cohort and nested case–control study using Québec's Public Health Insurance Database. J Acquir Immune Defic Syndr 2011;57:245–53.
[12] Perelló R, Calvo M, Miró O, et al. Clinical presentation of acute coronary syndrome in HIV infected adults: a retrospective analysis of a prospectively collected cohort. Eur J Intern Med 2011;22:485–8.
[13] Mehta NJ, Khan IA. HIV-associated coronary artery disease. Angiology 2003;54:269–75.