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Hydroxychloroquine Induced Cardiomyopathy

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Hydroxychloroquine Induced Cardiomyopathy

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Abstract

Hydroxychloroquine (HCQ) is one of the immunomodulatory medications used in treatment of autoimmune diseases. Rarely, HCQ can cause serious complications, such as cardiotoxicity. We present a rare case of HCQ-induced cardiomyopathy. 60-year-old female patient with a medical history of SLE on chronic HCQ therapy for 28 years, preexisting non-ischemic cardiomyopathy and heart failure with reduced ejection fraction for 7 years, and complete heart block status post pacemaker insertion presented with acute chest pain and severe weight loss. Patient underwent coronary angiogram that showed normal coronaries and right-sided heart catheterization that showed acute heart failure. Echocardiogram showed LVEF of 30% with global hypokinesis. Patient was started on dobutamine with an improvement of her symptoms. As HCQ-induced cardiomyopathy was suspected, patient underwent an endomyocardial biopsy that revealed a pathognomonic finding of myocyte vacuolization, consistent with HCQ-induced cardiomyopathy. HCQ was discontinued immediately. However, patient was a poor candidate for heart transplantation and durable mechanical circulatory support due to severe malnutrition secondary to end-stage heart failure. Patient accepted hospice care and passed away peacefully. This case highlights the need for high index of clinical suspicion, careful medication reconciliation for patients with non-ischemic cardiomyopathy, and tissue biopsy with careful histopathological examination to diagnose this rare complication.

Keywords

Hydroxychloroquine, Cardiomyopathy, Endomyocardial biopsy, Histopathology, myocyte vacuolization.

Conflict of Interest Statement

Conflict of Interest: None

Authors

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CASE REPORT

Hydroxychloroquine Induced Cardiomyopathy

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Abstract

Hydroxychloroquine (HCQ) is one of the immunomodulatory medications used in treatment of autoimmune diseases. Rarely, HCQ can cause serious complications, such as cardiotoxicity. We present a rare case of HCQ-induced cardiomyopathy. 60-year-old female patient with a medical history of SLE on chronic HCQ therapy for 28 years, preexisting non-ischemic cardiomyopathy and heart failure with reduced ejection fraction for 7 years, and complete heart block status post pacemaker insertion presented with acute chest pain and severe weight loss. Patient underwent coronary angiogram that showed normal coronaries and right-sided heart catheterization that showed acute heart failure. Echocardiogram showed LVEF of 30% with global hypokinesis. Patient was started on dobutamine with an improvement of her symptoms. As HCQ-induced cardiomyopathy was suspected, patient underwent an endomyocardial biopsy that revealed a pathognomonic finding of myocyte vacuolization, consistent with HCQ-induced cardiomyopathy. HCQ was discontinued immediately. However, patient was a poor candidate for heart transplantation and durable mechanical circulatory support due to severe malnutrition secondary to end-stage heart failure. Patient accepted hospice care and passed away peacefully. This case highlights the need for high index of clinical suspicion, careful medication reconciliation for patients with non-ischemic cardiomyopathy, and tissue biopsy with careful histopathological examination to diagnose this rare complication.

Keywords: Hydroxychloroquine, Cardiomyopathy, Endomyocardial biopsy, Histopathology, Myocyte vacuolization

1. Introduction

Hydroxychloroquine (HCQ) is an immunomodulatory medication used in autoimmune diseases such as systemic lupus erythematosus (SLE).[1,2] Usually, HCQ is well tolerated.[2] However, cardiotoxicity is a rare and serious complication of HCQ.[3] The most common form of HCQ-induced cardiomyopathy (CM) is hypertrophic and restrictive CM.[4] HCQ rarely causes cardiac dysfunction with normal left ventricle (LV) dimensions.[5,6] We present a rare case of HCQ-induced CM with normal LV dimensions.

2. Case

A 60-year-old female patient with a medical history of SLE on chronic HCQ therapy for 28 years (with an average daily dose of 5.5 mg/kg), pre-existing non-ischemic cardiomyopathy for 7 years causing heart failure with reduced ejection fraction (HFrEF) with LVEF 30%, complete heart block status post biventricular pacemaker insertion, severe malnutrition (with recent unintentional weight loss of 45 lbs over 6 months, 27.3% of total body weight), and chronic kidney disease (CKD) who presented to our hospital with acute, retrosternal chest pain, accompanied with fatigue, nausea, and loss of appetite. Regarding outpatient HFrEF treatment, patient was only on metoprolol succinate 100 mg daily due to intolerance to standard components of the guideline-directed medical therapy (GDMT) due to progressive CKD and symptomatic hypotension.

On examination, vital signs showed blood pressure of 116/69 mmHg, heart rate of 77 bpm, normal temperature, and 100% oxygen saturation on room

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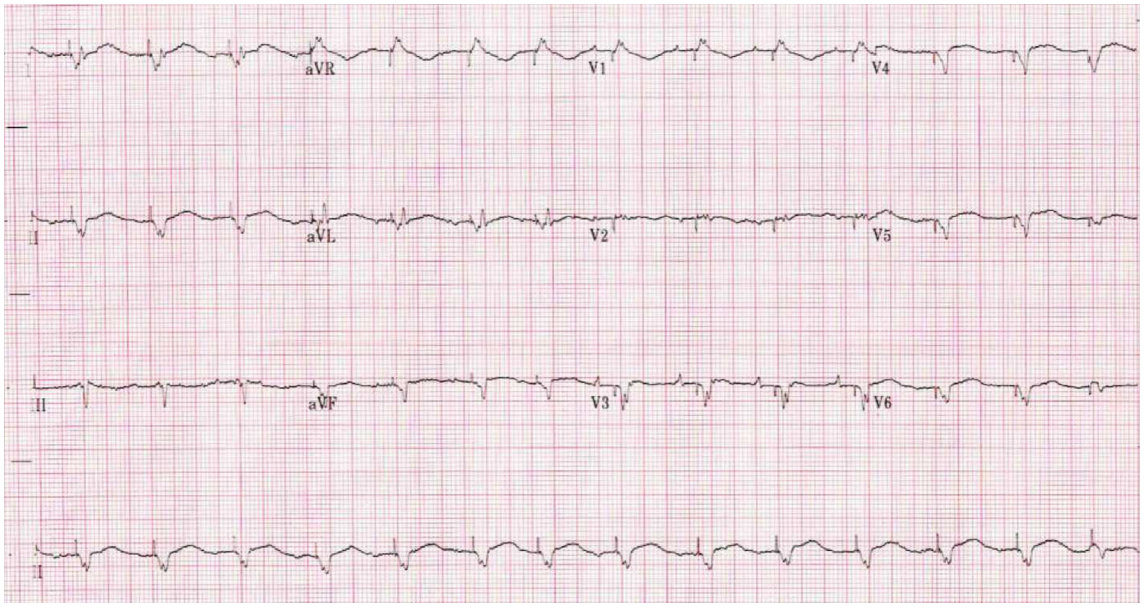

Fig. 1. EKG showing atrial sensed and ventricular paced rhythm without concerning ST segment and T wave changes for acute myocardial ischemia.

air. The patient exhibited malnourishment and bilateral lower limb edema, while the rest of the pulmonary and cardiovascular examination was unremarkable. EKG showed atrial sensed and ventricular paced rhythm without concerning ST segment and T wave changes for acute myocardial ischemia (Fig. 1). Laboratory values were remarkable for creatinine of 2.87 mg/dl (Baseline creatinine 1.8 mg/dl), NT-proBNP >35,000 pg/ml, and elevated High Sensitivity Cardiac Troponin (hsTn) with 0-h and 1-h values of 186 pg/ml and 336 pg/ml respectively. Serum Pre-albumin was <5 mg/dl, consistent with severe malnutrition.

Patient underwent coronary angiogram that showed normal coronaries (Fig. 2) and right-sided heart catheterization that showed elevated biventricular filling pressures (right atrium pressure of 10 mmHg, right ventricle systolic pressure of 28 mmHg and diastolic pressure of 8 mmHg, mean pulmonary artery pressure of 21 mmHg, and wedge pressure of 15 mmHg) with severely reduced cardiac index of 2.0 L/min/m^2. Similar to previous transthoracic echocardiogram (TTE) findings done 5 years ago, repeated TTE during this admission showed LVEF of 30% with global hypokinesis, LV end-diastolic diameter of 4.4 cm with no LV hypertrophy, and a newly diagnosed apical LV thrombus measuring 1.6 cm × 1.6 cm (Fig. 3). Patient was started on dobutamine infusion with significant improvement in cardiac index and renal function.

As our patient has history of atrioventricular block, non-ischemic cardiomyopathy, and chronic HCQ use, HCQ-induced CM was suspected. Patient underwent an endomyocardial biopsy that revealed pathognomonic finding of myocyte vacuolization, consistent with HCQ-induced CM (Figs. 4 and 5)

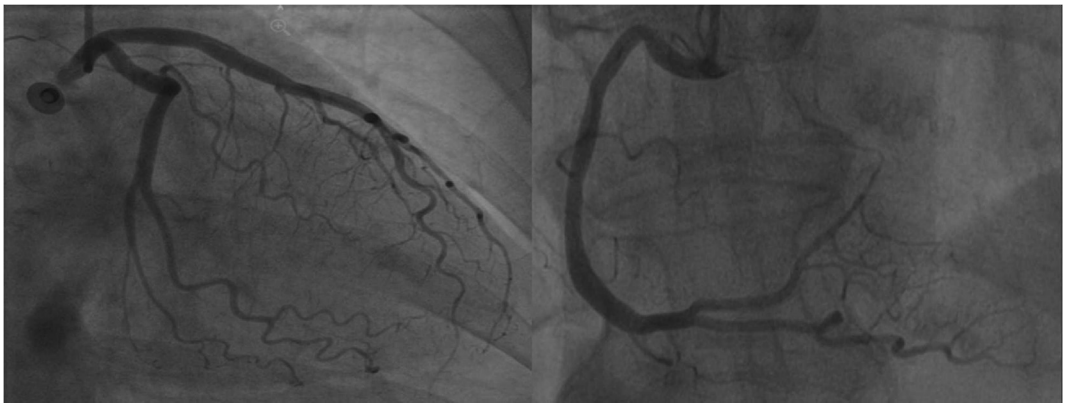

Fig. 2. Coronary angiogram showing normal Left and Right coronary arteries.

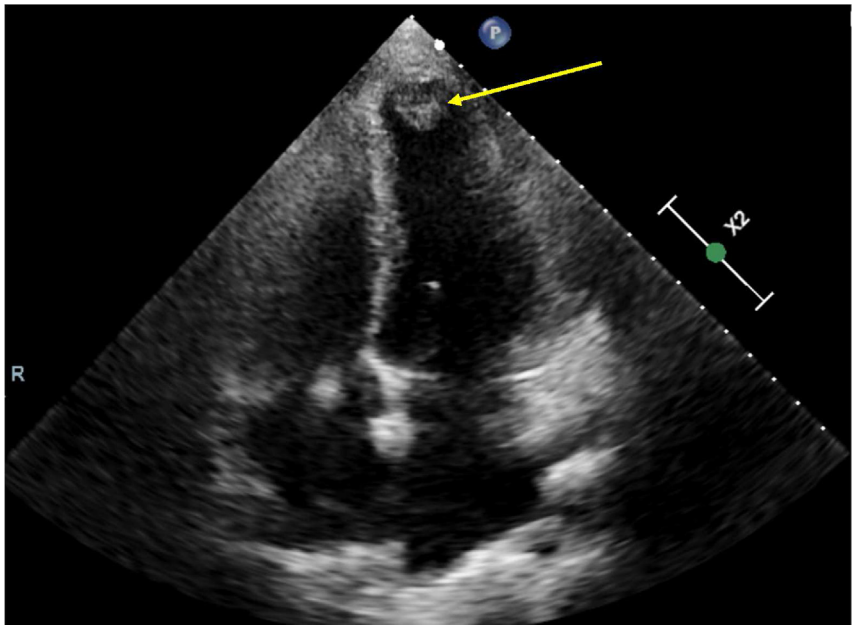

Fig. 3. TTE showing normal LV size and LV thrombus (Yellow arrow).

with no evidence of myocyte inflammation, necrosis, or vasculitis.

HCQ was discontinued promptly. However due to severe deconditioning and severe malnutrition secondary to end-stage HF, the patient was deemed a poor candidate for direct orthoptic heart transplantation (OHT) and durable mechanical circulatory support (MCS). Patient accepted hospice care and passed away peacefully.

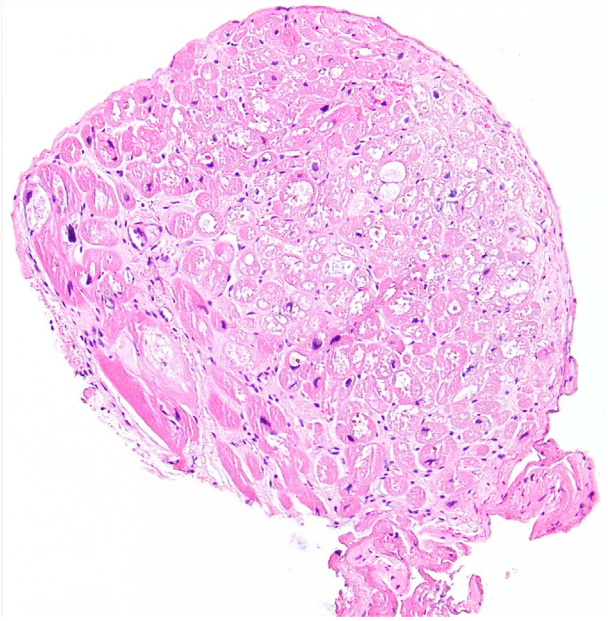

Fig. 4. Light microscopy (Hematoxylin and eosin stain with magnification ×40) of endomyocardial biopsy showing myocyte vacuolization.

3. Discussion

As present in our case, HCQ-related cardiotoxicity includes cardiac conduction abnormalities, such as atrioventricular block, and cardiomyopathy.[2,4] The most common form of reported HCQ-induced CM is hypertrophic CM with restrictive physiology.[5,6] Rarely, HCQ can cause cardiac dysfunction with normal left ventricular dimensions, like in our case.[5–7]

The prevalence of HCQ-induced cardiomyopathy (CM) is poorly defined in literature.[4,5] Risk factors for developing HCQ-induced CM include longer duration of therapy (>10 years), higher cumulative dose of HCQ, older age, females, and renal impairment.[4,5,8] According to Naddaf et al., the average cumulative dose of HCQ at the onset of cardiomyopathy is 1830 g, with an average daily dose of

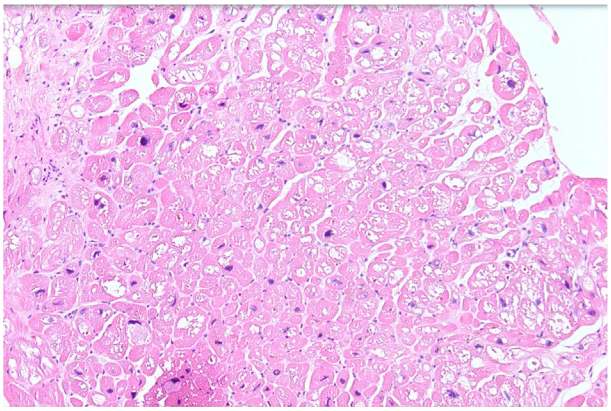

Fig. 5. Light microscopy (hematoxylin and eosin stain with magnification ×100) of endomyocardial biopsy showing myocyte vacuolization.

5.85 mg/kg.[9] HCQ inhibits lysosomal hydrolases enzymes causing accumulation of pathological metabolites (glycophospholipids) inside the lysosomes and cytoplasm of the cells and leading to cell dysfunction and damage.[5,6] Due to the accumulated glycophospholipids, histopathological findings of HCQ toxicity include vacuolar myopathy, defined as enlarged and vacuolated cardiomyocytes.[3,5,6]

Patients with HCQ-induced CM remain clinically silent for a long time until the development of typical symptoms of decompensated HF.[10] Rarely, non-specific chest discomfort may be a presenting symptom, like our patient.[3] TTE findings, such as biventricular thickening and restrictive pattern with or without ventricular systolic dysfunction, are non-specific but can raise suspicion for HCQ-induced CM in patients on HCQ therapy.[7] Advanced cardiac imaging, such as Cardiac magnetic resonant imaging (CMR) and ^{99m} technetium-labeled pyrophosphate scan (^{99m}Tc-PYP), are non-specific and not diagnostic for HCQ-induced CM. CMR may show non-specific concentric ventricular hypertrophy with a restrictive pattern.[11] CMR can be useful in assessment of ventricular function, exclusion of other infiltrative cardiomyopathies, and degree of myocardial fibrosis which can have prognostic value.[7] ^{99m}Tc-PYP can be falsely positive in HCQ-induced CM as ^{99m}Tc-PYP can be also positive in other infiltrative CM, most importantly cardiac amyloidosis.[12] Therefore, high clinical suspicion along with endomyocardial biopsy and histopathological evaluation by experienced pathologists are essential for diagnosing HCQ-induced CM.[6,13]

There is no specific medication or treatment for HCQ-induced CM.[6] Management includes immediate HCQ discontinuation and management of heart failure with GDMT.[3] Prognosis of HCQ-induced CM varies from complete recovery if HCQ is stopped early enough, to partial or no recovery, if irreversible cell injury happens.[6,7] Permanent cardiac damage may necessitate advanced therapies such as durable MCS or OHT.[10] Monitoring for recovery can be done by repeating TTE or endomyocardial biopsy within 6–12 months after stopping HCQ.[3,14]

4. Conclusion

HCQ can rarely cause non-ischemic cardiomyopathy. Main risk factors include longer duration of therapy and higher cumulative dose of HCQ. Patients remain asymptomatic for a long time and then present with symptoms of acute heart failure. High index of clinical suspicion and careful medication reconciliation are crucial for diagnosis. The main diagnostic test is endomyocardial biopsy and histopathological examination showing myocyte vacuolization. Management includes immediate discontinuation of HCQ and GDMT for heart failure.

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Conflicts of interest

None.

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