Biventricular Heart Failure Secondary to Hydroxychloroquine Induced Cardiotoxicity

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Introduction

The use of Hydroxychloroquine (HCQ) has the rare but severe complication of cardiotoxicity and heart failure. HCQ, an antimalarial medication developed in the 1930s, is commonly used as a disease modifying medication for the treatment of connective tissue disorders such as SLE and RA. However, its major inhibitory effect on lysosomal function represents an important cause in cardiovascular complications.

Case

60-year-old Caucasian female

PMHx:
- COPD
- Tobacco abuse
- Hypertension
- Chronic non-inflammatory degenerative joint disease, positive SS-B and ANA serologies treated with **200 mg daily** dose of **HCQ** for Eight years.

HPI:
Presented to PCP with two months:
- Progressive dyspnea with an acute decline in her respiratory status
- Confusion
- Failure to thrive

Work up:
- In-office ECG: Concerns for STEMI admitted to the hospital

Hospital Course and Beyond

- **Imaging & Interventions**:
  - **Emergent Cardiac Catheterization**: Angiographically normal coronary arteries.
  - **TTE**: Severe biventricular heart failure with LVEF 20%.
  - **Cardiac MR**: Extensive myocardial edema suggestive of acute fulminant myocarditis.
- **Inpatient Workup:**
  - Extensive non-ischemic work-up including autoimmune, vasculitis, and connective tissue disease was unremarkable.
- **Pathology**:
  - Endomyocardial biopsy: **Rare focal interstitial histiocytic** and **Lymphohistiocytic inflammatory infiltrates**
  - More prominent swelling of cardiac myocytes with **focal vacuolar** and **apparent degenerative changes.**
- **Diagnosis:** HCQ induced cardiotoxicity
- **Follow up**:
  - Regrettably, despite optimal medical therapies patients' symptoms progressed and she succumbed to her condition nearly 6 months after initial presentation.

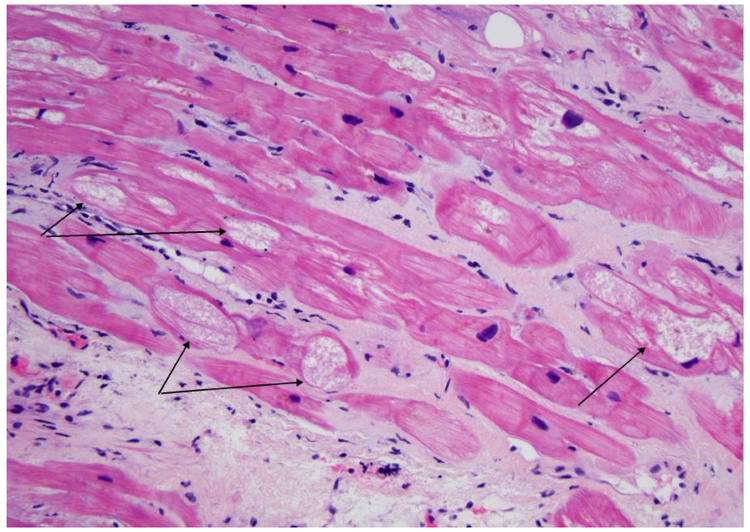

Image 1. H&E stain of the endomyocardial biopsy of the right ventricle – Arrows illustrate the swollen myocardial fibers with cytoplasmic vacuoles with a fine granular appearance of the vacuole lumen.

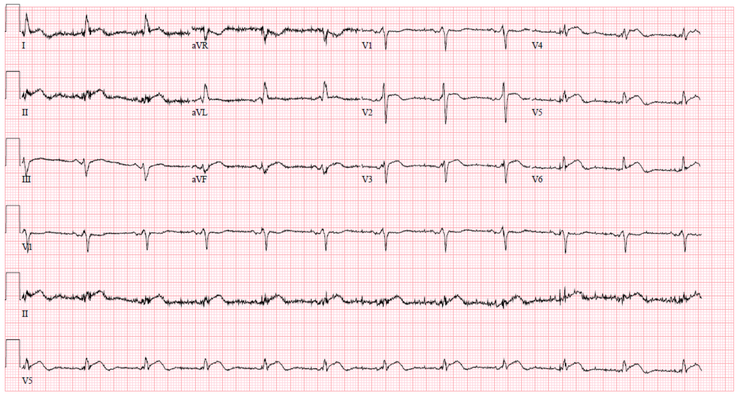

Image 2 . Initial presenting ECG – Sinus rhythm with short PR with nonspecific intraventricular conduction block and ST elevation in the anterolateral and lateral leads concerning for injury or acute infarct2

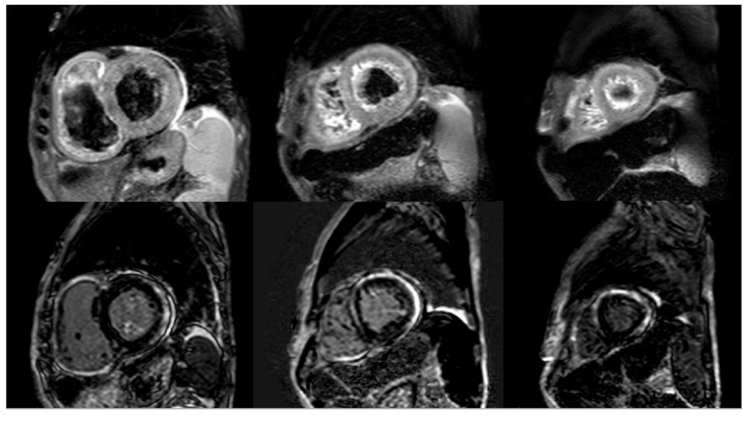

Image 3. Cardiac MRI - T2 flair with diffuse myocardial hyperintensity (top row) with corresponding late gadolinium subepicardial enhancement with heterogenous enhancement on late Gadolinium imaging (LGE) (bottom row)

Discussion & Conclusion

Anti-malarial medications used to treat autoimmune disorders carry the rare but near fatal risk of cardiotoxicity manifesting as cardiomyopathy and conduction system disease.

These therapies are commonly used within the field of Rheumatology as a disease modifying drug to slow the progression of immune mediated disease. Despite the unique serological biomarkers of this case without overt inflammatory disease we acknowledge that the adverse effect associated with these therapies are independent of the inflammatory state, biomarkers or burden.

Based on our literature review, there are limited data with isolated cases of HCQ-induced cardiomyopathy confirmed by histopathology. All documented cases involved patients with underlying SLE and/or RA. From all reported cases, there was a strong female predominance with a mean age of 58 years, accumulative dose and duration correlation with more adverse outcomes, and predominantly conduction abnormalities, closely followed by heart failure.

This case illustrates that the use of HCQ in patients with low autoimmune and inflammatory burden may potentially be more harmful and result in very serious cardiac complications in a much shorter timeframe. Early recognition and intervention are prudent for patients suffering from devastating treatment complications to prevent further irreversible cardiovascular harm.

We recommend that this subset of patients be closely monitored and selectively screened with yearly ECG and TTE. Abnormalities noted above should be followed with cMR & endomyocardial biopsy for definitive diagnosis and discontinuation of HCQ.

References

1. Yogasundaram H., Putko B.N., Tien J., Paterson D.I., Cujec B., Ringrose J., Oudit G.Y. Hydroxychloroquine-Induced Cardiomyopathy: Case Report, Pathophysiology, Diagnosis, and Treatment (2014) Canadian Journal of Cardiology, 30 (12) , pp. 1706-1715.