中文題目：於末期腎病變病患因 hydroxychloroquine 所致急性肝衰竭及致命性心律不整

英文題目：Hydroxychloroquine(Plaquenil) induced acute liver failure and fatal arrhythmia in ESRD patient

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Introduction

Hydroxychloroquine is used to prevent and treat malaria and to manage immunological disorders such as systemic lupus erythematosus and rheumatoid arthritis as an immunomodulatory drug. Hydroxychloroquine has numerous adverse effects, necessitating vigilance on the part of the prescriber. Most commonly reported are retinopathy, hyperpigmentation, myopathy, and skin reactions and cardiotoxicity was rarely mentioned. Here we described a case of end stage renal disease patient who suffered from acute liver failure and ventricular arrhythmia after hydroxychloroquine prescribed.

Case Presentation

A 62-year-old female has the history of hypertensive cardiovascular disease with coronary artery disease, chronic hepatitis C, atrial fibrillation, and end stage renal disease with maintenance hemodialysis. One month before admission, she started to receive hydroxychloroquine 200 mg daily to treat her polyarthragia. Two weeks later, she presented with chest tightness and electrocardiogram revealed atrial fibrillation with rapid ventricular response. Amiodarone 200 mg daily was prescribed. However, she was then admitted with persisted malaise presumably secondary to impaired liver function (SGOT: 522 U/L, SGPT:588 U/L). Pertinent laboratory studies showed hemoglobin: 10.4 g/dL, serum Na: 133 mmol/L, K: 4.69 mmol/L, total calcium: 9.6 mEq/L, Mg:2.4 mEq/L, CPK: 285 U/L and troponin I: 0.02 ng/ml

On physical examination, abdominal percussion showed tympanic sound and the remainder of physical examination was unremarkable. On the 1st day of admission, she was found to be in pulseless ventricular fibrillation and Torsades de pointes (figure 1) and her arrhythmia was converted to sinus rhythm with defibrillation. After resuscitation, her electrocardiogram revealed frequent VPC and QT prolongation (Figure 2). She had suffered as many as 20 episodes of ventricular fibrillation between the first and second days necessitating repeat direct current cardioversion despite intravenous lignocaine therapy. Emergent coronary angiography was performed but there was no salient culprit lesion. On the 2nd day, refractory ventricular arrhythmia

was terminated by transvenous overdrive ventricular pacing. Furthermore, her liver function test raised gradually and the highest peak aminotransferase values were found on the 7^{th} day. Abdominal computed tomography did not show cirrhosis or abnormal dilatation of intrahepatic ducts and common bile duct. Her serum HCV RNA level was not elevated compared to previous test. After the withdrawal of hydroxychloroquine, the QT interval was significantly reduced and her liver function tests returned to normal within one week (figure 3). She remained well until six months later she died from pneumonia.

Discussion

Hydroxychloroquine (HCQ) induced cardiac toxicities include QT interval prolongation, QRS widening, Torsades de pointes, ventricular tachycardia, ventricular fibrillation and cardiomyopathy.[1-5] In our case, the refractory ventricular arrhythmia was due to QT interval prolongation with frequent ventricular ectopies and "R" on "T" pattern. During hospitalization, there was no coronary hypoperfusion or cardiomyopathy was found, as evidenced by the normal CPK isoenzyme level, troponin level, coronary angiography, and echocardiography findings. Serum electrolytes (K^+, Ca^{2+}, Mg^{2+}) were also within the normal range. Drug-induced acquired long QT interval syndrome was made on the use of hydroxychloroquine for the extended period. The key treatment for hydroxychloroquine induced acquired long QT interval syndrome relies on early recognition with prompt withdrawal, pharmacologic therapy including lidocaine, isoproterenol, and transvenous overdrive pacing to maintain hemodynamic stability because of no direct antidote for hydroxychloroquine overdose. Given its very large volume distribution, it is difficult to remove hydroxychloroquine from blood by hemodialysis. Our experience reinforces the importance of a detailed drug history and reminds physician of the chronic use of HCQ for rheumatic diseases, or as an anti-malarial drug, should be balanced against the risk of developing potentially lethal cardiac arrhythmias.

Figure 1

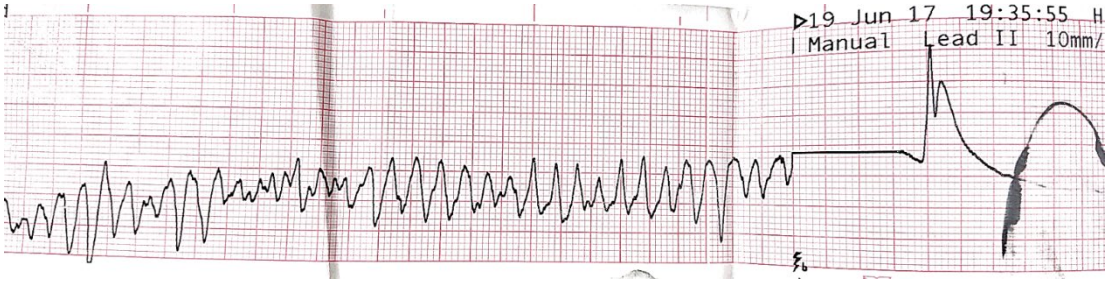


Figure 2

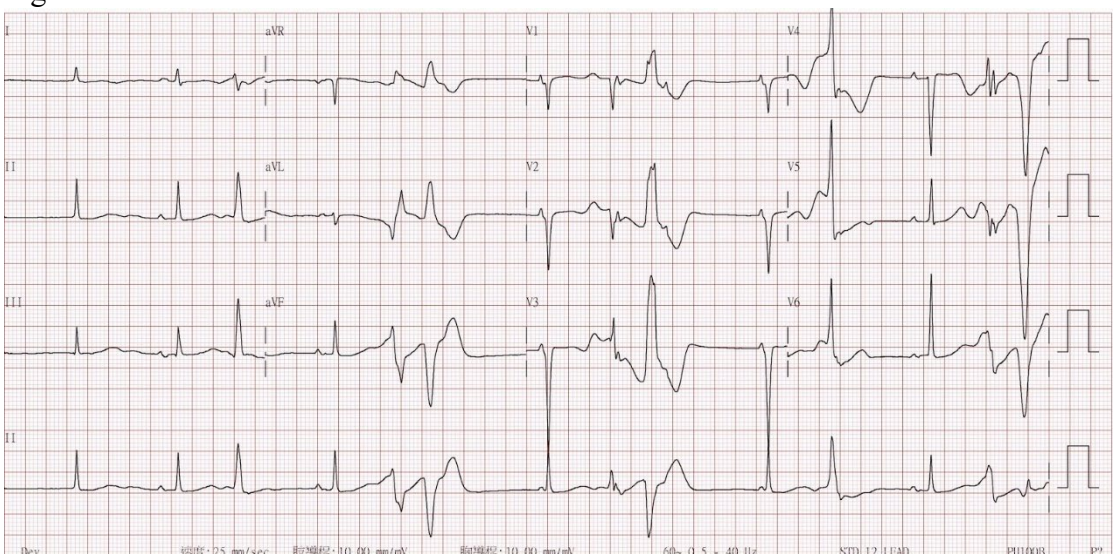
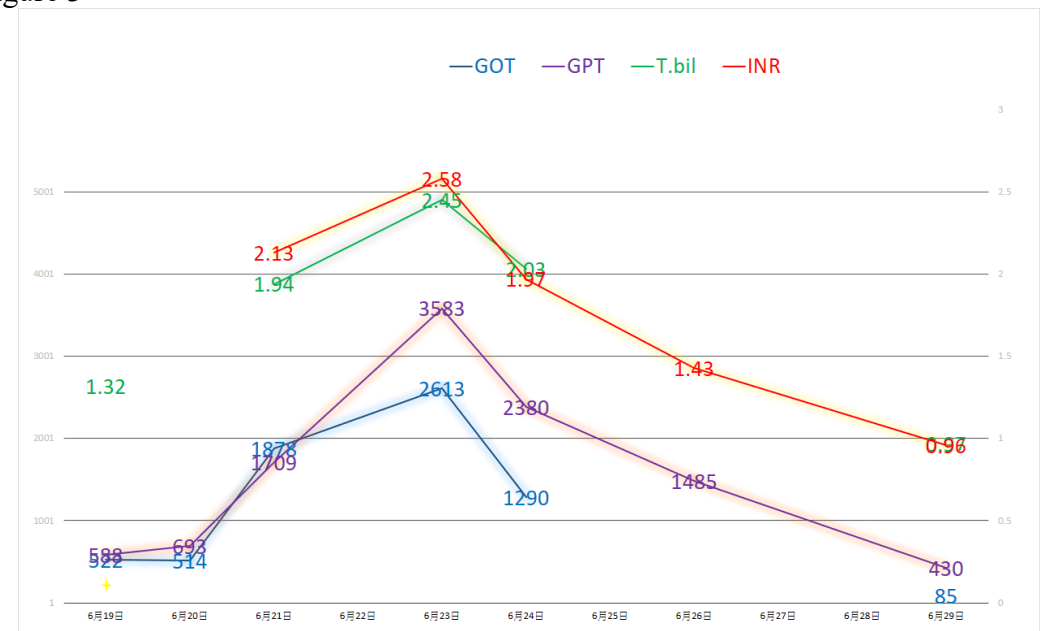


Figure 3



References

1. Yap YG, Camm J. Risk of torsades de pointes with non-cardiac drugs. Doctors need to be aware that many drugs can cause QT prolongation. Br Med J 2000; 320:1158–1159
2. Curtis LH, Ostbye T, Sendersky V, et. Al. Prescription of QT-prolonging drugs in a cohort of about 5 million outpatients. Am J Med 2003; 114:135–141
3. Marquardt K, Albertson TE. Treatment of hydroxychloroquine overdose. Am J Emerg Med 2001; 19(5):420–424
4. Jordan P, Brookes JG, Nikolic G, et al. Hydroxychloroquine overdose: toxicokinetics and management. J Toxicol, Clin Toxicol 1999; 37:861–864
5. Isbister GK, Dawson A, Whyte IM. Hydroxychloroquine overdose: a prospective case series. Am J Emerg Med 2002; 20:377–378