Acute, reversible type II (Wenkebach) heart block due to combined chloroquine and diltiazem treatment

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Introduction

International travel to malarial areas is increasingly common. Chemoprophylaxis using chloroquine is common, but can cause cardiac problems. We describe a new problem, of reversible heart block, in a patient on both chloroquine and the frequently-used calcium channel blocker, diltiazem.

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Case report

A 51-year-old man on long-term diltiazem treatment for angina travelled to India for a two-week period. He was recommended to take antimalarial prophylaxis with 200 mg proguanil daily and 300 mg chloroquine once a week. After starting the antimalarial medications and throughout his trip abroad he complained of feeling breathless. He was also aware of a slow or irregular heartbeat.

Two years earlier he had undergone angioplasty and stent insertion for a left anterior descending artery stenosis. Following this he had been able to complete 12 minutes of the Bruce protocol exercise test. He had never had conduction abnormalities and had no ongoing anginal symptoms. The only past medical history of note was ankylosing spondylitis, which had been diagnosed 25 years ago, which was quiescent. His daily medications were diltiazem LA 200 mg, aspirin 75 mg, atorvastatin 10 mg, and indomethacin-R 75 mg. He had shown no evidence of atrioventricular block prior to his malaria treatment (figure 1a).

On his return, his general practitioner referred him for cardiological assessment. In the clinic his resting electrocardiogram (ECG) showed Wenkebach type II heart block (figure 1b). Since he had travelled in rural areas with endemic malaria and remained within the 28-day incubation period for malaria, it was felt unwise to discontinue his antimalarial treatment and therefore the diltiazem was stopped. He was reviewed five weeks later, after he had completed his course of antimalarial therapy. His symptoms had completely resolved and his ECG had returned to normal (figure 1c).

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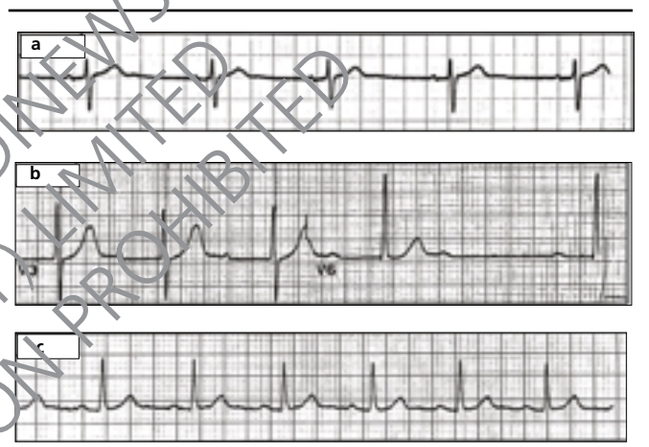
Figure 1. Electrocardiogram changes with combined chloroquine and diltiazem therapy. **a)** shows sinus rhythm whilst the patient was taking diltiazem. **b)** shows type 2 (Wenkebach) heart block whilst the patient was taking both diltiazem and chloroquine. **c)** shows a return to sinus rhythm with neither drug present



Discussion

Diltiazem, as with many calcium channel blockers, can cause varying degrees of heart block, particularly in overdose or in combination with a beta blocker.[1] It is contra-indicated in patients with high degrees of block. In this patient, however, there was no evidence of any conduction defect prior to the addition of antimalarial prophylaxis and his conduction returned to normal once he had discontinued this therapy. We therefore suspect that the transient conduction defect was due to an interaction between his chronic diltiazem therapy and one or other of the antimalarial drugs.

Proguanil has not had cardiac conduction abnormalities reported as a complication in the literature, but chloroquine has been implicated in the development of fascicular or atrioventricular block. In all cases, this had occurred as a result of long-term (ab)use of chloroquine.[2-4] In these reports chloroquine had been taken for many years before the development of heart block, which was typically irreversible and required pacemaker implant. The mechanism for this effect is unclear but long-term chloroquine use can cause skeletal myopathy

Key messages

- Diltiazem can cause varying degrees of heart block
- Chloroquine has been implicated in the development of fasicular or atrioventricular block
- Diltiazem and chloroquine taken in combination may cause profound calcium channel blockade
- This blockade is reversible

and it is suggested that conduction delay may be due to a related cardiomyopathy and fibrosis affecting the interventricular septum.

An explanation for the reversible, acute onset block seen in this patient may lie with chloroquine's actions on intracellular calcium. Chloroquine has been shown to decrease the slow calcium channel current, behaving like a calcium channel blocker. Inositol trisphosphate (IP3) is a second messenger responsible for the release of calcium into the cytosol. Chloroquine and its derivatives have been shown to prevent release of intracellular calcium after ligand-binding by blocking the IP3 receptor.[5,6] This, coupled with the direct effect of diltiazem on the calcium channel, could have resulted in sufficient slowing of action potential propagation to result in the conduction abnormality seen.

Ankylosing spondylitis has also been associated with conduction abnormalities and it is possible that this patient had minor abnormalities of the cardiac conduction system that predated his malaria prophylaxis.

In summary, we suggest that this patient's transient atrioventricular block was related to his chloroquine therapy. Rather than the irreversible block seen in long-term chloroquine therapy, this reversible block may have been due to a profound calcium channel blockade consequent on the combined therapy with chloroquine and diltiazem.

References

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