

# Acute lymphadenopathy complicating quinidine therapy

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**Summary:** A patient is described with quinidine-induced acute lymphadenopathy syndrome proven by rechallenge of the drug. Serum markers for systemic lupus were negative.

## Introduction

Lymphadenopathy is a reported complication of phenytoin therapy.<sup>1-3</sup> Quinidine bisulphate, a commonly used antiarrhythmic agent, may also lead to lymphadenopathy through the induction of lupus erythematosus.<sup>4,5</sup> We describe a patient with quinidine-induced acute lymphadenopathy syndrome proven by rechallenge of the drug and in whom serum markers for systemic lupus were negative. To our knowledge, this is the first confirmed case of direct quinidine-induced lymphadenopathy.

## Case report

A 53 year old man gave a history of paroxysmal palpitations on irregular treatment with digoxin which was stopped 1 month ago. When first seen, he was found to be in atrial fibrillation with a controlled ventricular rate of 98/min. He gave no history suggestive of thyrotoxicosis nor ischaemic heart disease, and he was a non-drinker. Examination showed a blood pressure of 120/180 mmHg, and no evidence of valvular disease. An echocardiogram showed normal mitral valve and a left atrial dimension of 3.5 cm in the long axis view. The thyroid function was normal.

An elective direct current cardioversion was planned after a course of intravenous heparin. Although external shocks of 200 J resulted in conversion into sinus rhythm, the latter was unstable and reverted back to atrial fibrillation. A course of quinidine bisulphate 500 mg b.d. and warfarin was commenced, and sinus rhythm returned after the third dose of quinidine.

He was discharged but 4 days later he developed fever, skin rash and tender lymphadenopathy. The left supraclavicular lymph node was enlarged to

1.5 × 2 cm, and painful 2 × 2 cm large lymph nodes were found in both axillae. Multiple tender inguinal lymph nodes (< 1 cm) were palpable. A maculopapular rash developed over the trunk which spread to the upper limbs. There was no hepatosplenomegaly. Investigations showed normal haemoglobin, white cell count, differential and platelet count. The renal and liver function tests were normal. Antinuclear factor was negative and complement 3 and 4 levels were within the normal limits. Serology tests for Epstein-Bar virus, rubella virus, cytomegalovirus, adenovirus and toxoplasma were negative. The rash and lymphadenopathy subsided 4 days after discontinuation of quinidine.

In view of the possibility of an intercurrent viral infection as the cause of the lymphadenopathy, the patient was admitted for repeat treatment with quinidine. A similar skin rash and fever developed within 12 hours of 500 mg of quinidine, without lymphadenopathy. The medication was stopped immediately and the patient was subsequently controlled on flecainide acetate.

## Discussion

Apart from reactions to drugs, lymphadenopathy can complicate infection, serum sickness and connective tissue disease. The hypersensitivity reaction to phenytoin is well known, with lymphadenopathy occurring either at the start of drug treatment<sup>3</sup> or developing after months of therapy. While self limiting, cases of fatal lymphomas have been reported to occur months after cessation of treatment.<sup>6</sup>

To our knowledge, there is only one previously published report of an association between lymphadenopathy and quinidine.<sup>7</sup> The patient concerned developed anaemia and lymphadenopathy after 3 years' treatment with quinidine sulphate which subsided on withdrawal of the medication. Rechallenge was not performed in that study.

although a lymph node biopsy showed reactive, atypical follicular hyperplasia. However, a direct causal relationship between quinidine and lymphadenopathy in that study was questioned.<sup>8</sup> The symptoms and signs reported were suggestive of drug-induced systemic lupus erythematosus, of which quinidine is a well recognized cause,<sup>3,4</sup> which was not excluded by relevant serological data in that study. In our patient the serological tests for lupus were negative on both occasions when

quinidine was prescribed. Although lymphadenopathy was not detected in the rechallenge after one dose of quinidine, the typical acute febrile illness and skin rash were remarkably similar to the first occasion, and we felt that further treatment with quinidine could not be justified.

Thus an acute lymphadenopathy syndrome can occur after quinidine therapy. The reactions appeared to be self limiting and did not require the induction of lupus erythematosus.

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