Prolongation of the QT interval is associated with a high risk of serious ventricular tachyarrhythmias, usually *torsade de pointes* (TdP) polymorphic ventricular tachycardia, although monomorphic ventricular tachycardia may also develop. Both congenital and acquired forms have been reported, acquired forms being much more prevalent. An association between human immunodeficiency virus (HIV) infection and a higher rate of dilated cardiomyopathy has also been recognized. The severity of immunodeficiency seems to influence both the incidence and severity of cardiomyopathy. A higher prevalence of QT prolongation has been reported among hospitalized HIV-positive patients with HIV infection, possibly related to drugs prescribed for such patients or to an acquired form of long QT syndrome arising from HIV infection. We report a case of QT prolongation and development of ventricular arrhythmia in one HIV patient that started with intravenous clarithromycin and cotrimoxazole therapy.

**Key words:** Long QT. HIV. Clarithromycin. Ventricular tachyarrhythmias. Torsade de pointes.

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**CLINICAL CASE**

The patient was a 30-year-old man in a methadone detoxication program with positive serology for the hepatitis C virus, without previous decompensations, and positive serology for human immunodeficiency virus (HIV), who had never received antiretroviral treatment or prophylaxis with cotrimoxazole. At the time of admission he had a viral load of 90 000 RNA copies/ml and CD4+ lymphocyte index of 36. He was hospitalized for a 10-day episode of cough, mucopurulent expectoration, pleuritic chest pain, fever, and dyspnea. The chest radiograph showed an alveolar pattern in both bases compatible with bilateral pneumonia. Laboratory tests disclosed arterial gasometry: FiO₂ 50%; pO₂ 87 mm Hg; pCO₂ 29.5 mm Hg; pH 7.46; total leukocytes, 9.1 × 10⁹/L with 7% unsegmented neutrophils; hemoglobin, 7.3 g/dL; hematocrit, 21%; MCV, 85 fl; creatinine, 2.4 mg/dL; sodium, 129 mEq/L, and potassium, 5.0 mEq/L. The ECG showed sinus rhythm with a heart rate of 100 beats/min, QRS axis 60° and corrected QT (QTc) 0.35 s. Two packs of concentrated red blood cells were transfused and kidney failure and hyponatremia were corrected by water replacement. Intravenous antibiotic treatment was be-
gun with cefepime (2 g/8 h), clarithromycin (500 mg/12 h), and cotrimoxazole (trimethoprim 240 mg+sulfamethoxazole 1200 mg/6 h). Forty-eight hours after admission, the patient presented QT prolongation (QTc 0.58 s) (Figure 1) with a cardiac rhythm disorder in the form of ventricular bigeminy (Figure 2) and a heart rate of 35 beats/min that was well tolerated hemodynamically. Twenty-four hours later he presented a self-limited episode of monomorphic ventricular tachycardia documented in two leads (V1 and V2) with a morphology of right bundle-branch block (RBBB) and QRS 0.16 ms at a rate of 150 beats/min (Figures 3 and 4). Perfusion of clarithromycin and cotrimoxazole was discontinued but treatment with cefepime i.v. was maintained. The myocardial enzyme curve (CK, CK-mass, and myoglobin) was negative. The echocardiogram revealed a slightly dilated left ventricle (left ventricular end-diastolic diameter 62 mm and end-systolic diameter 48 mm) with slightly depressed function (EF 23%). After clarithromycin and cotrimoxazole were withdrawn, no new episodes of ventricular tachycardia were registered, although the prolonged QT persisted until day four, when it normalized (QTc 0.36 s).

**DISCUSSION**

In the case of our patient the ECG at time of admission showed a normal QT. There was no personal history of syncope or a family history of sudden death, which excluded congenital causes of long QT. The electrolyte disorders, anemia, and kidney failure were corrected when the arrhythmia appeared, so that possible causes of long QT that must be considered in our patient had to have been related with HIV and the drugs administered.

A greater prevalence of long QT in hospitalized patients with HIV infection compared to other patients has been reported. After excluding treatment with drugs that can cause long QT, the possibility of an acquired form of long QT syndrome associated with HIV was contemplated, the causal mechanism of which could be myocarditis, a subclinical myocardopathy due to HIV, or an autonomic neuropathy.
due to the virus per se. There are no studies correla-
ting QT duration with the stage of disease due to
HIV.\textsuperscript{2,4}

The appearance of long QT in relation to different
drugs has been reported, among them class I and III
antiarrhythmics, psychotropics, antihistamines, anti-
fungals, and diverse antimicrobial agents like penta-
midine i.v., chloroquine, amantadine, erythromycin,
and cotrimoxazole. With respect to cotrimoxazole,
numerous side effects have been described, most of
which affect the skin, hematopoietic and gastrointesti-
nal systems, and the kidney. Cardiotoxicity in the
form of the appearance of long QT and torsades de
pointes has been described in a patient after the oral
administration of a tablet of cotrimoxazole (160 mg
of trimethoprim and 800 mg of sulfamethoxazole). It
has been attributed to an idiosyncratic reaction similar
to that induced in patients treated with quinidine.
The fact that the arrhythmia appeared after 72 h of treat-
ment in our patient excludes this mechanism. In a
prospective, nonrandomized study, the incidence of
QT lengthening and ventricular arrhythmias in pa-
tients with HIV treated with intravenous pentamidine
(16 patients) or cotrimoxazole (11 patients) was com-
pared. In the group treated with cotrimoxazole, no
differences in the duration of QT were observed befo-
re and during treatment. The results of this study do
not indicate an increase in ventricular extrasystoles,
nonsustained or sustained ventricular tachycardia as-
associated with cotrimoxazole treatment in patients with
HIV.\textsuperscript{6}

With regard to macrolides, the appearance of long
QT and ventricular arrhythmias in patients treated
with erythromycin has been widely described. The mecha-
nisms involved are similar to class I and III an-
tiarrhythmic agents. Erythromycin inhibits the fast po-
tassium current (\(I_{Kf}\)) in the myocyte, impeding the
outflow of potassium from the myocytes of the
ventricular myocardium and prolonging the transmem-
brane action potential (PAT) in Purkinje fibers, thus
delaying repolarization and originating QTc lengthen-
ing.\textsuperscript{7,8} The appearance of these effects is influenced
by the rate of infusion of the drug, which indicates a
relation with its plasma concentration. For that reason,
it is recommended that erythromycin be administered
very slowly.\textsuperscript{8,9} Other macrolides like roxithromycin
and azithromycin seem to be less arrhythmogenic in
comparative studies in vitro.\textsuperscript{10}

In the case of our patient the macrolide given was
clarithromycin. The cases of two patients who devel-
oped QT prolongation and torsades de pointes after
the administration of clarithromycin have been reported.\textsuperscript{11}

In Spain this complication has not been reported pre-
viously. Since the structure of clarithromycin is similar
to that of erythromycin, its arrhythmogenic properties
are similar, with the active metabolite 14(R)-hydroxy-
clarithromycin acting on \(I_{Kf}\) to prolong the QT inter-
val.\textsuperscript{11} The presence of cardiac anomalies favors the ap-
pearance of arrhythmias,\textsuperscript{12} as does the presence of he-
patic disorders, since the metabolism of the drug is
mainly hepatic and only 20\% is eliminated by the kid-
ney. In our patient the clear temporal relation between
prolongation of the QTc interval and the induction of
arrhythmia 48 h after beginning treatment, the devel-
opment of ventricular tachycardia just after finalizing
the last dose administered, and the progressive norma-
лизation of the ECG after discontinuing the drug sug-
gests that it was the trigger factor. No ventricular
arrhythmias have been identified in patients treated
with cefepime.

CONCLUSIONS

HIV-positive patients can present lengthening of the
QT interval and ventricular arrhythmias. This may be
due to the viral infection per se and could be potentia-
ted by the action of different drugs that act as triggers
of the disorder. When the causal agent is discontinued
(in our case clarithromycin), the duration of QT re-
verts to its initial state. Based on these observations,
we recommend electrocardiographic follow-up and
rection of the electrolyte disorders in patients with
HIV infection who are treated with drugs that can in-
duce prolongation of the QT interval.

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