Elderly patient with acquired long QT syndrome secondary to Levetiracetam

Dear Editor,

Acquired long QT syndrome (ALQTS) is an alteration of ventricular repolarization characterized by a prolonged QT interval corrected for heart rate on the electrocardiogram, that is, ≥ 460 milliseconds in women and ≥ 450 milliseconds in men. ALQTS is associated with high risk, life-threatening ventricular arrhythmias, such as polymorphic ventricular tachycardia (torsade de pointes). The most common causes of ALQTS are hydroelectrical alterations, anti-arrhythmia medication, antibiotics, prokinetics, psychoactive drugs and anti-histamines.

We report the case of an 88-year old woman with a personal history of high blood pressure and a surgically treated fronto-temporal meningioma, currently on
treatment with acetylsalicylic acid and hydrochlorothiazide (Hidrosaluretil R), who came to the Emergency Room due to a switch-off episode accompanied by sucking mouth and facial movements lasting for one minute, with full recovery following the post-ictal status. Her vital signs and the clinical examination were normal and of note on the complementary testing were the haemogram and plasma biochemical analyses which included glycaemia, kidney, liver, and ion (calcium, sodium, magnesium, and potassium) profiles all within the normal range; and electrocardiogram (ECG) with sinus rhythm and a cranial computerized tomography (CT) with an area of left fronto-temporal malacia (fig. 1). During her stay in the Emergency Room, she presented another switch-off episode with automatisms, followed by tonic-clonic movements. With a diagnosis of complex partial seizures evolving into generalized seizures, treatment with levetiracetam was initiated at a dose of 500 mg IV every 12 hours. The patient was asymptomatic 24 hours later, although the ECG documented sinus bradycardia with a heart rate of 55 bpm and a corrected QT interval (Bazett’s formula) of 480 msec. An echocardiogram was ordered revealing mild tricuspid insufficiency and a 24 hour Holter documented the presence of sinus bradycardia and short spells of atrial fibrillation. In the light of these findings and without any evidence as to the cause of the QT prolongation, levetiracetam was substituted by valproic acid and the ventricular repolarization alterations were corrected within 48 hours (fig. 2).

Levetiracetam is a derivative of pyrrolidone indicated for the treatment of partial seizures with or without secondarily generalized seizures. It is characterized as being efficacious and having a good safety profile, given that it is not metabolized via cytochrome P450, thereby reducing the risk of drug-drug interactions. A previous clinical trial carried out on healthy adults reported that levetiracetam is not associated with alterations in the QT interval after a single dose.

To the best of our knowledge, this case reveals the first ALQTS possibly related to levetiracetam. It is certainly true that the patient had many risk factors associated with drug-induced ALQTS, such as being elderly and female, having high blood pressure, paroxysmal atrial fibrillation, bradycardia, and prior treatment with diuretics.

Moreover, the complexity involved in treating seizures in the elderly population is well-known, given the greater

Figure 1 Cranial computerized tomography documenting the area of left fronto-temporal malacia.

Figure 2 A: QT interval = 480 msec, recorded 24 hours after initiating treatment with levetiracetam. B: QT interval = 400 msec, recorded 48 hours after discontinuing treatment with levetiracetam.
Levetiracetam is excreted largely by the kidneys and a positive correlation has been reported between creatinine clearance and drug clearance. In fact, the elderly have been shown to require a 40% dose reduction in order to achieve the same serum concentration and also to have a greater risk of side effects even at the same serum levels in comparison with young individuals. Consequently, with this case we have wanted to illustrate that before prescribing levetiracetam in elderly patients, kidney clearance must be calculated and the dose must be titrated up gradually in order to prevent adverse events; in addition, electrocardiographic monitoring is also needed after initiating de novo treatment in patients at risk for developing QT prolongation.

References


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