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Oxaliplatin-induced long QT syndrome in a patient with appendiceal adenocarcinoma

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To the Editor,

A 44-year-old woman with appendiceal adenocarcinoma presented for her eleventh cycle of oxaliplatin, folinic acid (FA) and infusional 5-fluorouracil (5-FU) (e.g., FOLFOX-4). Before the chemotherapy session began, blood pressure was 120/78 mmHg, respiratory rate was 18 per minute, heart rate was

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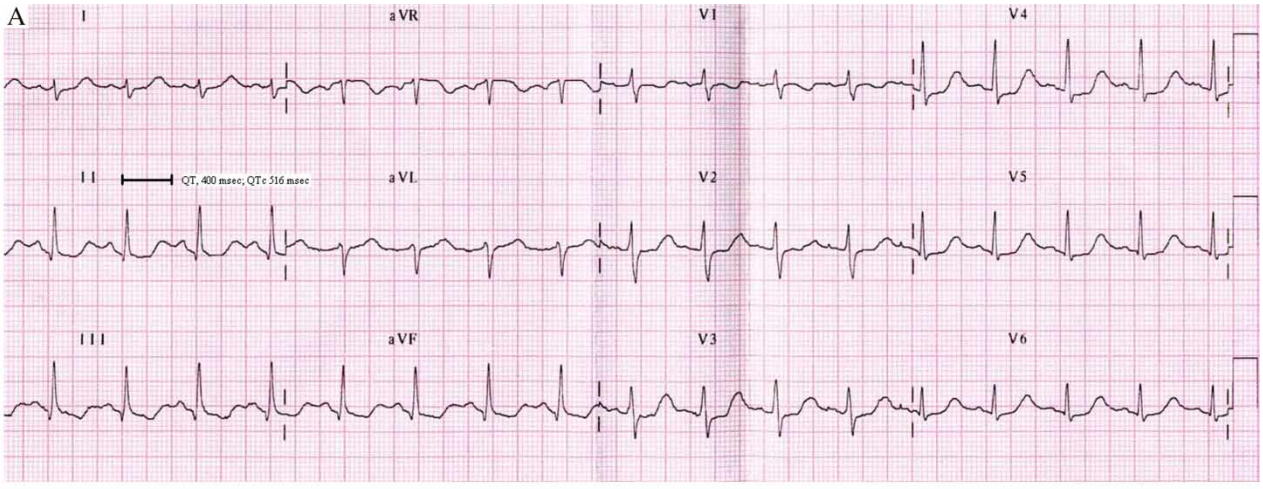
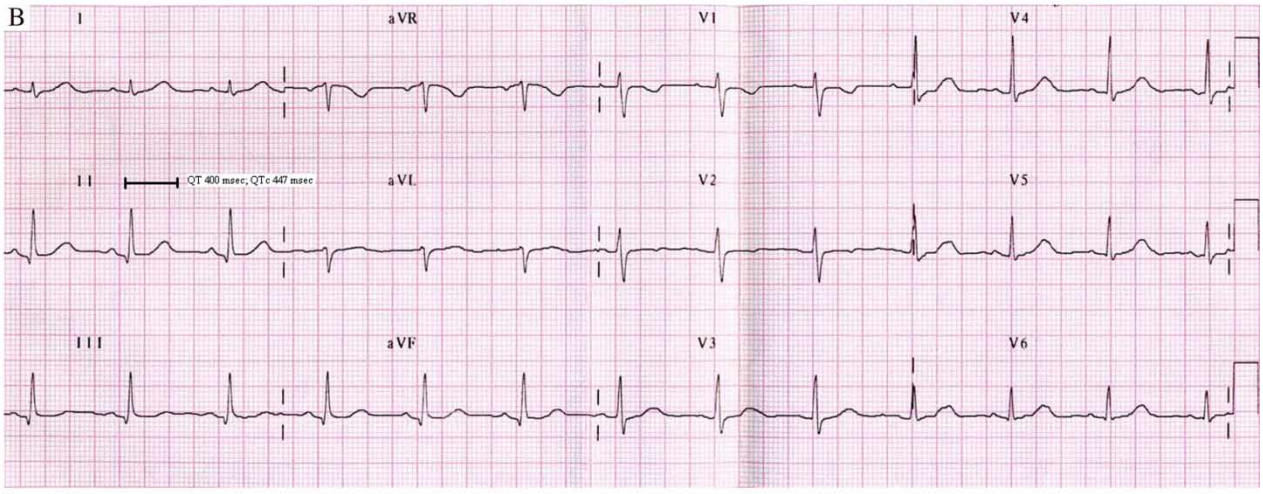
72 per minute, and temperature was 35.5°C. Roughly 30 minutes after oxaliplatin infusion was begun, she developed palpitations and dizziness followed by two episodes of syncope. Hypotension (42/20 mmHg) and bradycardia (50/min) were noted. Oxaliplatin was discontinued. Fluid resuscitation was begun, and 1 mg intravenous atropine was immediately given. Bradycardia and blood pressure recovered gradually. Later, an electrocardiogram (ECG) was performed, revealing a QT interval corrected for heart rate using the Bazett formula (QTc interval = QT interval/√R-R interval) of 516 milliseconds (Panel A) [1]. Electrolyte and enzyme data were within normal limits: sodium 141 mmol/L (135–147), potassium 4.2 mmol/L (3.5–4.9), calcium 8.7 mg/dL (8.5–10.5), magnesium 1.9 mg/dL (1.6–2.6), CPK 53 IU/L (38–174), CKMB 4.1 U/L (3–10), and troponin I 0.51 ng/mL (<0.8 ng/mL). There was neither severe headache nor focal neurologic deficit at any time. Symptoms ended within one hour; additional ECG revealed normal sinus rhythm without evidence of QT- interval prolongation (Panel B).

The long QT syndrome (LQTS) can be congenital or acquired. Congenital LQTS is a disease of transmembranous sodium and potassium ion channel proteins. Causes of acquired LQTS include drugs, electrolyte imbalance, marked bradycardia, organophosphorus compounds, subarachnoid hemorrhage, myocardial ischemia, protein sparing fasting, autonomic neuropathy and human immunodeficiency virus disease [2]. LQTS is occasionally associated with torsade de pointes, and can cause sudden death.

In this case, congenital LQTS seemed unlikely due to lack of family history of syncope or sudden death. In addition, an ECG performed 5 months previously had shown sinus rhythm with cQT intervals of 426 milliseconds. The patient did not take any medications that are probable causes of QT-interval prolongation before the chemotherapy session in question. Although two episodes of



Panel A



Panel B

syncope occurred during oxaliplatin infusion, there were none after it was discontinued. Other probable causes such as electrolyte imbalance, ischemic heart disease and central nervous system problems had already been excluded. Given no other identifiable cause of QT-interval prolongation, it is reasonable to speculate about a possible relationship between oxaliplatin and the QT-interval prolongation observed in this patient.

Oxaliplatin is a third-generation platinum compound with activity against colorectal cancer. It has been associated with cell membrane channelopathies [3]. Adelsberger et al. suggested that oxaliplatin may alter sodium (Na^+) channel kinetics in an *ex-vivo* rat nerve preparation [4]. Because the Na^+ channel plays a central role in impulse conduction in cardiac myocytes and cells of the His-Purkinje system [5], alteration of Na^+ channel kinetics is a possible predisposing factor for arrhythmias caused by oxaliplatin. The actual mechanism is unclear and more experimental and clinical evaluations are needed to validate the correlation between oxaliplatin and LQTS. To the best of our knowledge, our patient's LQTS had oxaliplatin as its probable cause: Physicians should be aware of arrhythmias occurring immediately after oxaliplatin infusion.

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Regression of cervical spinal cord compression in a patient with chordoma following treatment with cetuximab and gefitinib

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To the Editor

A previously healthy woman born in 1932 presented in 1996 with a chordoma of the second cervical vertebra, dislocating the spinal cord. She underwent laminectomy and occipitocervical fixation. She received radiotherapy at a dose of 50 Gy in 28 fractions. In February 2006 and April 2007 she was reoperated due to deteriorating ability to walk.

The second operation did not bring about any improvement, and in August 2007 her condition worsened with incontinence, increasing right-sided weakness and her right hand became completely useless. An MRI showed spinal cord compression and a 6.5×5.5 cm large right cervical mass.

Based on a case report of successful treatment of a patient with metastatic chordoma using cetuximab and gefitinib [1], the decision was made to offer the patient treatment with these drugs. The patient was started on cetuximab weekly and gefitinib 250 mg daily. After a week she reported the return of continence and after two weeks she was able to walk using a walking frame and to use her right hand to cut while eating. At the 4-week check-up the therapy was temporally stopped due to facial acne. The therapy was resumed a couple of weeks later

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