

A Rare Cardiac Side Effect of a Herbal Medicine; QT Prolongation Due to *Hypericum Perforatum*: Case Report

Bitkisel Bir İlacın Nadir Bir Kardiyak Yan Etkisi;
Sarı Kantaron Kullanımına Bağlı QT Uzaması

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ABSTRACT Medicinal herbs are widely used all over the world. In particular, *Hypericum perforatum* is commonly used to treat depressive disorders. Our paper examines the development of a long QT interval resulting from *Hypericum perforatum* usage. A 39-year-old female patient was admitted to our hospital with palpitations and syncope after using *Hypericum perforatum* for one week. Electrocardiography (ECG) demonstrated a marked QT prolongation. The patient was hospitalized, and the etiology of the potential cause of the prolonged QT were evaluated. A coronary angiography revealed normal coronary anatomy. We also performed a 24-hour rhythm monitorization and found a frequent ventricular premature complex (VPC) with marked QT prolongation. VPCs were mostly monomorphic and isolated; however, couplet and triplet VPCs were seen frequently. Three weeks after discontinuing the herbal medication, symptoms subsided and ECG results returned to normal.

Key Words: Hypericum; long QT syndrome

ÖZET Bitkisel ilaçlar tüm dünyada yaygın olarak kullanılmaktadır. Sarı kantaron bitkisi başta depresyon olmak üzere sıklıkla kullanılmaktadır. Bu yazıda sarı kantaron kullanımına bağlı gelişen uzun QT ve sonuçları tartışıldı. 39 yaşında kadın hasta sarı kantaron kullanımından 1 hafta sonra çarpıntı ve senkop ile hastanemize başvurdu. Fizik muayenenin ardından çekilen elektrokardiyografide (EKG) QT uzaması saptandı. Hasta yatırıldı ve QT uzamasına neden olan tüm faktörler değerlendirildi. Laboratuvar testleri yanında koroner anjiyografi de yapıldı. Koroner arterler normal saptandı. Hastaya 24 saat ritim holter monitorizasyonu yapıldı. Ritim holterde uzun QT yanında sık ventriküler erken atımlar (VEA) izlendi. VEA'lar çoğunlukla monomorfik ve izole olmakla birlikte sık ikili ve üçlü atımlar olarak dikkati çekti. Bitkisel tedavinin kesilmesiyle şikayetlerinde tamamen kaybolma ve 3 hafta sonraki kontrolde EKG'de düzelme tespit edildi.

Anahtar Kelimeler: Hiperikum; uzun QT sendromu

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Medicinal herbs are widely used in Europe and the Middle East. *Hypericum perforatum*, commonly known as St. John's wort, is one of the oldest, most well-known herbal treatments (Figure 1). St. John's wort products are primarily used to treat depressive disorders.¹⁻³ *Hypericum perforatum* is comprised of naphthodianthrones and phloroglucinols.⁴ Previous research has investigated the antidepressant properties of St. John's wort extracts. St. John's wort has been shown to work by inhibiting the reuptake of neurotransmitters such as serotonin, dopamine, and norepinephrine from the synaptic gap into the neuron.⁵ In addition, Hypericum

extracts are potent activators of cytochrome P450 3A4 (CYP3A4).⁶ This activation of cytochrome P450 3A4 poses the greatest risk in *Hypericum perforatum*'s interactions with other drugs. The usage of *Hypericum perforatum* is generally safe with few side effects. However, rare and serious side effects can occur with drug interactions.³ Cardiac side effects haven't been reported.

CASE REPORT

A 39-year-old female patient with a history of depression decided to treat it with *Hypericum perforatum*. One week later, she suffered from palpitations and syncope. The patient was successfully evaluated by the emergency service of our hospital. A physical examination revealed cardiac arrhythmia. The patient's history showed no other drug usage. The electrocardiogram showed QT prolongation with T-wave inversions. The QT was 580 msec, and the QTc was 630 msec (Figure 2). The patient was hospitalized and evaluated carefully for syncope and QT prolongation. Her echocardiograph was completely normal. A 24-hour Holter monitorization demonstrated frequent ventricle premature beats, including couplets and triplets (Figure 3). Various etiologies of QT prolongation, including drug usage, hypokalemia, hypomagnesemia, thyroid disorders, and structural heart disease were investigated. A laboratory examination yielded the following results: hemoglobin: 13.7 g/dL; hematocrite: 41.7%; blood urea nitrogen: 10.2 mg/dL;



FIGURE 1: *Hypericum perforatum*.

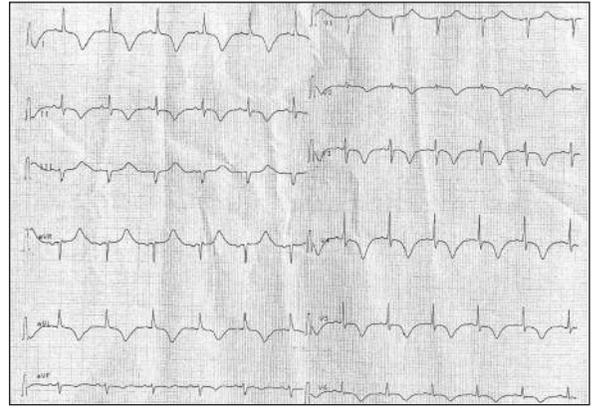


FIGURE 2: Baseline ECG with marked QT prolongation.



FIGURE 3: 24 holter records demonstrating Long QT with ventricular ectopic beats and couplets.

TSH: 0.91 μ IU/mL; blood calcium level: 9.2 mg/dL; potassium: 4.0 mmol/L; magnesium: 2.5 mg/dL; troponin I: <0.010 ng/mL; brain natriuretic peptide: 24 pg/mL. A coronary angiography was performed to exclude coronary artery disease. A vertebrobasilar system and carotid Doppler ultrasonography were performed to indicate whether vertebrobasilar insufficiency and carotid artery stenosis were present. However, the Doppler ultrasonography was completely normal, with a total 215 mL/min flow volume. The patient was referred to a neurology specialist, where neurogenic syncope was evaluated. The neurological examination, cranial magnetic resonance imaging, and electroencephalography excluded neurogenic syncope. The

herbal medication was discontinued, and the patient followed up weekly. Three weeks later, the ECG revealed a marked recovery. QT was at 410 msec, and QTc was at 430 msec without palpitation or syncope (Figure 4).

DISCUSSION

Herbal medicines are widely used among patients, and St. John's wort is one of the best known. The most common side effects of St. John's wort are gastrointestinal symptoms, allergic reactions, dry mouth, dizziness and sedation.^{7,8} Higher doses are associated with photosensitivity.⁹ In the literature, side effects of this herbal extract are commonly observed with concomitant usage of drugs. Drug interactions can be primarily explained by the activation of CYP3A4. Concomitant drug usage may be life-threatening. Bayramicli et al. declared a case presenting with upper gastrointestinal bleeding with concomitant usage of warfarin and St. John's wort.¹⁰ In the case we presented, a prolonged QT interval with a repolarization abnormality resulted from usage of *H. perforatum*. QT prolonga-

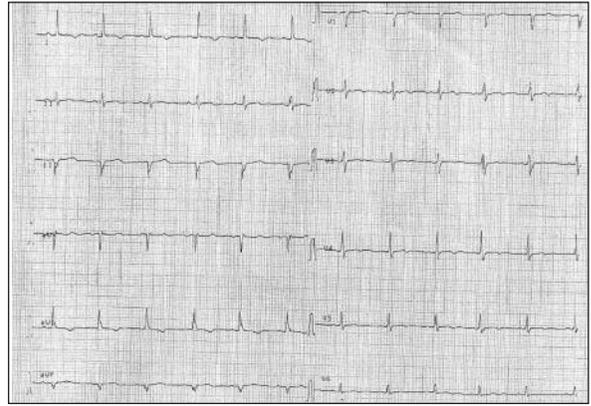


FIGURE 4: Three weeks ECG after discontinuation of herbal medicine.

tion may cause torsades de pointes, which presents a possible etiology for syncope. However, we could not demonstrate malign arrhythmias except for frequent ventricle premature beats. The reason for syncope in our patient was unclear, but it is clear that a long QT is associated with life-threatening arrhythmias. As a result, herbal medication may be harmful when used without prescriptions, presenting unexpected side effects.

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