

Masked Clinical Pictures (Macroscopic Haematuria and Toxic Hepatitis) Resulting from Saint John's Wort Poisoning: Two Case Reports

Umut Yücel Çavuş*, Kadir Dibek, Ridvan Sarıkaya and Sinan Yıldırım

Department of Emergency Medicine, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey

Introduction

Herbal remedies are used commonly as an alternative to classical medical treatment in many diseases and conditions [1]. *Hypericum perforatum* is a wild herb grown in Turkey and Europe and commonly known as Saint (St.) John's Wort [2]. *Hypericum perforatum* is used as in the treatment of depression, parasitic disease and ulcers, in addition it is used as an analgesic, tranquilizer and wound reparative [3,4]. The main side effects of the consumption of St. John's Wort include: Nausea, diarrhea, insomnia, anxiety, fatigue, dryness of mouth, dizziness, headache, allergic skin reactions and paresthesia [5]. There is a lack of research about the extent of the side effects, although toxic hepatitis cases had been reported to be caused by the use of St. John's Wort. However, we had not observed any hematuria case caused by the use of St. John's Wort before the case presented in this paper [6].

Case 1

A male patient aged 29 presented to the Emergency Department, complaining of a headache and that yellowing of the whites of his eyes. The patient said that he had been drinking one spoon of dried St. John's Wort (Figures 1 and 2) in a cup of boiled water, for three days to relieve dyspepsia. There were no important indications in the patient's history. He was conscious, oriented and cooperative. His sclera and skin were icteric. Tenderness in epigastric region and right upper quadrant was found but hepatosplenomegaly was not detected. His vital signs were; blood pressure 124/78 mmHg, pulse 76/min, respiratory rate 16/min, temperature 36.6°C, oxygen saturation 99%. From the laboratory analysis of the bloods the results were; Alanine Aminotransferase (ALT) 201 u/l, Aspartate Aminotransferase (AST) 201 u/l, Gamma-Glutamyl Transferase (GGT) 510 u/l, the total bilirubin 8.6 g/dl and direct bilirubin 5.4 mg/dl. Hepatobiliary ultrasonography revealed no dilatation, mass nor gallstones. Following the diagnosis of acute hepatitis the patient was admitted to the internal medicine department of the hospital. Until he transferred to the department of internal medicine, intravenous fluid was given [100 cc/h 0.9% NaCl (Total 600 cc) and 50 cc/h 5% Dextrose (Total 300 cc)] to the patient whose oral intake has been stopped with our decision. Additional tests were performed to discover the etiology of the hepatitis, however, the tests



Figure 1: St. John's Wort.



Figure 2: St. John's Wort

for viral hepatitis, Toxoplasmosis, Rubella, Cytomegalovirus, Herpes (TORCH), syphilis and autoimmune hepatitis were negative. The pathology was thought to have evolved from the consumption of St. John's Wort. On the 7th day of the treatment, blood results were; ALT 31 u/l, AST 146 u/l, total bilirubin 1.4 g/dl, direct bilirubin 0.9 g/dl and GGT 261 u/l. The patient was discharged with cure and advised to refrain from self-medication with St. John's Wort.

Case 2

A female patient aged 33 presented to Emergency Department complaining about bloody urine. There was no illness, bleeding diathesis and usage of medication in her history. She stated that her

*Corresponding author: Umut Yücel Çavuş, Department of Emergency Medicine, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey, Tel: 0505 2648050; Fax: 0312 3186690; E-mail: acildrumut@yahoo.com

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menstrual bleeding stopped five days ago and that she had drunk three cups of St. John's Wort boiled with water for her anxiety. She complained of severe groin pain and said after urinating that the color of urine was red. The physical examination was normal except for the presence of macroscopic hematuria. Urinary tract ultrasonography was normal. There was no stone and mass. However, symptoms and signs of hemorrhagic cystitis or pyelonephritis like fever, dysuria, suprapubic tenderness, and costovertebral angle tenderness are not observed. The laboratory analysis such as platelet, aPTT-INR, hemoglobin, white blood cell, biochemistry was normal apart from the level of erythrocytes in the urine. Intravenous fluid was given [100 cc/h 0.9% NaCl (Total 1200 cc) and 50 cc/h 5% Dextrose (Total 600 cc)] to the patient. It was considered that her symptoms were due to the effect of the St. John's Wort since no pathology observed which could have cause hematuria. The patient discharged with cure and advised to refrain from self medication with St. John's Wort again.

Discussion

St. John's Wort contains biological active ingredients which conjoin neurotransmitters and prevents the re-uptake of some of them. In randomized controlled trials about St. John's Wort which is commonly chosen for its antidepressant and anxiolytic characteristics, it was proved that St. John's Wort was superior to placebo but less effective than tricyclic anti-depressants [7]. Viruses, brucellosis, salmonella, hydatid cyst, autoimmune diseases, toxins and drugs can cause acute hepatitis. Most herbal based materials have hepatotoxic potential [8]. Employing herbal treatment methods together with conventional medication in the treatment of chronic diseases can create difficulty in determining a hepatitis etiology. Many herbs such as St. John's Wort, Cascara, Chaparral, Comfrey, Kava kava and Ma-Huang may have toxic effects on the hepatobiliary system. Although it is considered that some herbs can be beneficial, others such as aloe vera, may cause toxic hepatitis. So, if there is deterioration in the liver function the emergency physician should consider the possibility that the patient has consumed herbal tea in the differential diagnosis of toxic hepatitis. If the patients have been consuming herbal tea, then have to stop this immediately [9]. In the two cases presented here, the absence of drug taking and chronic disease reinforces our opinion that the pathology is related with St. John's Wort.

Toxic hepatitis comprises 1% of chronic hepatitis and cirrhosis cases, 10% of acute hepatitis and 10-20% of fulminant hepatitis [10]. The symptoms of toxic hepatitis may appear hours, days or months after the exposure to factors. In primary treatment, the consumption of the probable toxic substance should be stopped.

St. John's Wort can cause irreversible liver injury, scar tissue, and functional failure. The first patient applied to Emergency Department on the 3th day of St. John's Wort consumption and the toxic hepatitis was resolved quickly. One of the adverse effects of the St John's Wort is photosensitivity, which is a reason why the use of St John's Wort should be questioned [11].

Hematuria is a common complaint among patients presenting to the Emergency Department and it is a cause of anxiety. Hematuria may be a primary sign for bleeding diathesis and urinary tract calculi, tumors, iatrogenic injury, trauma, hemorrhagic cystitis, anticoagulant drugs are common causes of this symptom [12,13]. There is no case

of St John's Wort causing hematuria in the literature. However, Ernst E et al. reviewed the literature and showed that platelet, bleeding and clotting disorders in 4 reports and hepatobiliary system disorders in 4 reports due to hypericum perforatum [14]. The second patient was found to have macroscopic hematuria and no pathology was found to explain this symptom. Naranjo scale [15] was applied for the second case. As a result, Score 3: Possible adverse drug reaction. This intensifies our opinion that the hematuria emerged because of the consumption of St. John's Wort. Nevertheless, a detailed research is needed for this side effect.

Conclusion

In the Emergency Department, the fact that alternative treatments can have several side effects and produce unusual symptoms should be taken into account. In the case of the differential diagnosis of acute hepatitis the physician should encourage the patient to disclose any use of herbal remedies.

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