CASE REPORT / OLGU SUNUMU

Development of Coagulopathy and Pancreatitis Due to Saw Palmetto Used for Urinary Symptoms

Üriner Semptomlar İçin Kullanılan Saw Palmettonun Neden Olduğu Koagülopati ve Pankreatit Gelişimi

Muhammet Şencan [1], Nurettin Özgür Doğan [1]

ABSTRACT

Aim: Serenoa repens, commonly known as saw palmetto, is a widely used herbal supplement for lower urinary tract symptoms. However, data regarding the toxicity of this dietary supplement is limited. In this study, it is aimed to emphasize that herbal extracts such as saw palmetto can cause coagulation disorder and pancreatitis.

Case Presentation: In this case report, we present a 60 year-old male patient using saw palmetto extract for urinary stone disease and urinary tract symptoms. The patient had widespread ecchymoses on the tip of the tongue, trunk and extremities. The coagulometric tests of the patient, who did not use any anticoagulant drugs, were prolonged; renal failure had also developed. Vitamin K and fresh frozen plasma were used to treat the coagulopathy. The patient, who also developed acute pancreatitis in the days following hospitalization, was discharged on the 15th day without any additional complications.

Conclusion: Herbal supplements are widely used in medical practice. Saw palmetto extracts may have different adverse effects including abdominal pain, headache, hepatotoxicity, coagulopathy, and pancreatitis. Patients using these supplements should be aware of these effects of saw palmetto.

Keywords: Saw palmetto extract, serenoa, blood coagulation disorders, pancreatitis, emergency department

ÖZ

Amaç: Yaygın kullanımıyla saw palmetto olarak bilinen serenoa repens, alt üriner sistem semptomları için sıkça kullanılan bir bitkisel takviyedir. Bununla birlikte, bu besin takviyesinin toksisitesine ilişkin veriler sınırlıdır. Bu çalışmada, saw palmetto gibi bitkisel ekstrelerin pıhtılaşma bozukluğu ve pankreatite yol açabileceğinin vurgulanması amaçlanmaktadır.

Olgu Sunumu: Bu vaka raporunda, üriner taş hastalığı ve idrar yolu semptomları için saw palmetto ekstresi kullanan 60 yaşında bir erkek hasta sunulmaktadır. Hastanın dil ucunda, gövde ve ekstremitelerinde yaygın ekimozları mevcuttu. Herhangi bir antikoagülan ilaç kullanmayan hastanın koagülometre testleri uzamış; böbrek yetmezliği de gelişmişti. Pıhtılaşma bozukluğunu tedavi etmek için K vitamini ve taze donmuş plazma kullanıldı. Tedavisini takip eden günlerde akut pankreatit de gelişen hasta ek komplikasyon gelişmeden tedavisinin 15. gününde taburcu edildi.

Sonuç: Bitkisel takviyeler tıbbi uygulamada yaygın olarak kullanılmaktadır. Saw palmetto ekstrelerinin karın ağrısı, baş ağrısı, hepatotoksisite, koagülopati ve pankreatit gibi farklı yan etkileri olabilir. Bu takviyeleri kullanan hastalar, saw palmettonun bu etkilerinin farkında olmalıdır.

Anahtar Kelimeler: Saw palmetto ekstresi, serenoa, kan pıhtılaşma bozuklukları, pankreatit, acil servis

Received: 3 May 2023 Accepted: 23 October 2023

[1] Department of Emergency Medicine, Kocaeli University Faculty of Medicine, Kocaeli, Türkiye.

Corresponding Author: Muhammet Şencan, MD. **Address:** Kocaeli University, Faculty of Medicine, Department of Emergency Medicine, 41000, Kocaeli, Türkiye. **Phone:** +905302898698 **e-mail**: muhammetsncn@gmail.com

Atıf için/Cited as: Şencan M, Doğan NO. Development of Coagulopathy and Pancreatitis Due to Saw Palmetto Used for Urinary Symptoms. Anatolian J Emerg Med 2024;7(2): 91-94. https://doi.org/10.54996/anatolianjem.1291882

Introduction

Saw palmetto (*serenoa repens*) is one of the most widely used phytotherapeutic agents for the treatment of benign prostatic hyperplasia (BPH) and lower urinary tract symptoms. It is a common phytochemical extract obtained from the dried form of dwarf palms and has a significant market share in its field (1). Since saw palmetto extract is sold without a prescription, it is difficult to determine the exact number of people who regularly use it for treatment purposes, but it is estimated to be around 2.5 million adults in the USA (2).

There are some case reports and a few studies on the efficacy and safety profile of saw palmetto (1-7). There are many hypothetical mechanisms of action of saw palmetto, but none is proven at the time of writing. Suggested mechanisms include competitive binding to androgen receptors on prostatic cells, and anti-androgenic, anti-inflammatory and anti-proliferative effects (7,8). Although previous studies have shown that the effectiveness of saw palmetto in reducing urinary symptoms is no greater than placebo, this herbal product is still widely used (7-9).

During use of the extract, the most frequently reported adverse events are abdominal pain, headache, hepatotoxicity, coagulopathy, pancreatitis, and intraoperative bleeding. However, side effects associated with bleeding complications have generally been reported as case reports (3,4). In this case report, we aimed to describe a patient who started using saw palmetto a few days prior to presentation at the emergency department (ED) due to urinary tract complaints and presented with non-traumatic ecchymoses in different parts of the body.

Case Presentation

A 60-year-old male patient with known diabetes mellitus, hypertension, and chronic kidney disease was admitted to the ED with complaints of weakness, vomiting, abdominal pain and non-traumatic ecchymoses in a number of body areas. His medical history also included ischemic stroke, bilateral carotid artery stent and surgery for kidney stone disease. He had been using acarbose, losartan, acetyl salicylic acid and trimetazidine. The patient reported that he was diagnosed with urinary tract infection three days prior to presentation and a supplement containing saw palmetto was prescribed. Abdominal pain had started two days earlier, with bloody stool and vomiting more than ten times a day.

On physical examination, the patient was conscious, had a Glasgow Coma Scale score of 15, his pupils were normoisochoric, and he had bilateral pupillary light reflexes. His vital signs were completely normal and his electrocardiogram was in normal sinus rhythm. There was widespread tenderness on abdominal examination, but no rebound was detected. There were widespread ecchymoses on the tip of the tongue, abdomen, back, right hand, left palm, both knees and both thighs, right gluteal region and sacral region, and right foot (**Fig. 1**). Preliminary differential diagnoses included acute renal failure, electrolyte disorders, disseminated intravascular coagulopathy (DIC), gastrointestinal hemorrhage, and pancreatitis.

Initial laboratory blood test results were: glucose 221 (74-106) mg/dL; urea 198 (16.6-48.5) mg/dL; creatinine 7.86 (0.7-1.2) mg/dL; aspartate aminotransferase (AST) 46.9 (<40) U/L; alanine aminotransferase (ALT) 18 (<41) U/L; gamma-glutamyl transferase (GGT) 32 (10-71) U/L; alkaline phosphatase (ALP) 88 (40-129) U/L; lactate dehydrogenase (LDH) 359 (135-225) U/L; albumin 34.3 (39.7-49.4) g/L; globulin 28.1 (11-35) g/L; total bilirubin 0.46 (0.0-1.2) mg/dL; haptoglobulin 2.31 (0.3-2.0) g/L; amylase 74 (28-100) U/L; lipase 201.2 (13-60) U/L; hemoglobin 7.50 (12.1-16.6) g/dL; sodium (Na) 125 (136-145 mmol/L; potassium (K) 5.61 (3.5-5.5) mmol/L; calcium (Ca) 8.5 (8.5-10.5) mmol/L; hematocrit 20.3% (36.9-52.9); platelet 325 (172-380) (cells x 10^3/µL); activated partial thromboplastin time (aPTT) 57.8 (17.9-31.2); international normalized ratio (INR) 77.73 (0.8-1.25); and prothrombin time (PT) 79.5 (10-14). His d-dimer level was 9.87 µg/mL (<0.55) and fibrinogen level was 574.9 mg/mL (170-420). Arterial blood gas analysis revealed pH of 7.24, pCO_2 of 30.6 mmHg, lactate level of 41 (4-20) mg/dL, HCO_3 of 13.3 (22-26) mmol/L, and anion gap of 18.8 (7-16) mmol/L.

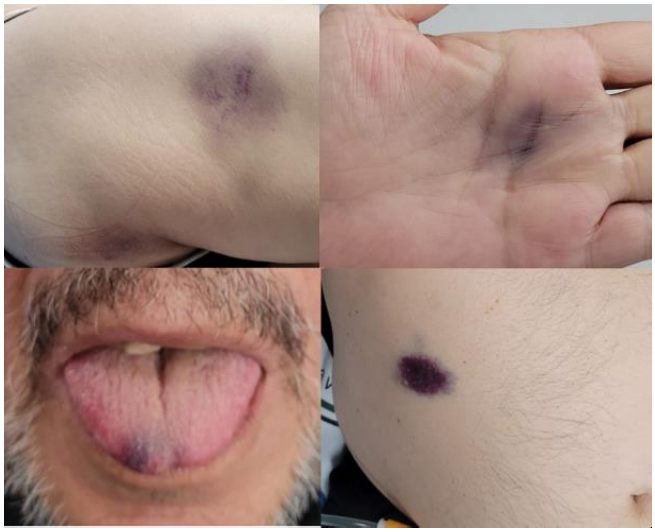

Figure 1. Ecchymoses in different parts of the patient's body

Due to the patient's current high INR and acute kidney injury (AKI), an abdominal ultrasound (USG) was planned first for intra-abdominal hematoma and postrenal pathologies. However, the radiologist recommended abdominal computed tomography (CT) for the patient's advanced age, urinary stones, renal pathologies and other pathologies that may cause postrenal obstruction. Abdominal tomography was obtained without radiocontrast material. This showed that the intrahepatic and extrahepatic bile ducts were normal, the contours of the pancreas were regular and the dimensions were normal, but the size of both kidneys was reduced. There was parenchymal calcification in the lower pole of the right kidney, but there was no obvious calculus. Dilatation and obstructive pathology in the pelvicalyceal system was not observed. However, dilatation compatible with ileus in the small bowel loops and diffuse heterogeneity in the mesentery were observed. Hemorrhagic free fluid was observed in four intra-abdominal quadrants.

The patient was consulted to the hematology clinic for coagulopathy, to the general surgery clinic for intra-abdominal hemorrhagic free fluid and ileus, and to the

nephrology clinic for acute renal failure. Due to the coagulation disorder and hemorrhagic complications identified in the ED, the patient was given 5 mg vitamin K IV, 280 milliliter of erythrocyte suspension IV, and 660 milliliter of fresh frozen plasma (FFP) IV, 0.9% sodium chloride 150ml/hour iv infusion and 50 mcg fentanyl iv. On the third day following hospitalization, the coagulometric tests completely normalized, but the lipase level increased to 1658 IU/L and the patient's abdominal pain recurred. Acute pancreatitis was considered due to the recurrence of abdominal pain, elevated pancreatic enzymes, and CT findings. The patient was followed up with appropriate supportive treatment in the following days it was thought that coagulation disorder and pancreatitis developed due to saw palmetto use. The patient, whose clinical and laboratory findings improved (glucose 91 mg/dL; urea 71 mg/dL; creatinine 2.62 mg/dL; total bilirubin 0.46 mg/dL; haptoglobulin 1.97 g/L; amylase 40 U/L; lipase 60 U/L; hemoglobin 9.5 g/dL; hematocrit 26.7%; platelet 419 (cells x 10^3/µL); aPTT 16.7; INR 0.97; and PT 10.9. His d-dimer level was 2.1 µg/mL and fibrinogen level was 430 mg/mL. Arterial blood gas analysis revealed pH of 7.35, pCO_2 of 43 mmHg, lactate level of 24 mg/dL, HCO_3 of 22.5 mmol/L, and anion gap of 9.5 mmol/L). He was discharged on the 15th day of the follow-up. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Discussion

Saw palmetto is the fruit of a type of palm tree, a plant native to the United States, and is among the most widely used of the phytotherapeutics. There are many clinical studies of saw palmetto but few data on its potential side effects. Awins et al. compared saw palmetto preparation with placebo in 225 patients with BPH and found no significant difference between the two groups in terms of serious and non-serious side effects. However, in the same study, the authors stated that they could not exclude all potential serious side effects associated with the use of saw palmetto (2). In a systematic review published in 2009 that reported adverse events related to saw palmetto, side effects related to the preparation were generally mild and transient; abdominal pain, diarrhea, nausea, headache, decrease in libido and rhinitis were most commonly reported. This study also reported that severe adverse effects, such as death and cerebral hemorrhage, were associated with saw palmetto use at the case report level (3).

There are case reports concerning the increased risk of bleeding associated with saw palmetto. Cheema et al. reported that a patient who was operated for meningioma had severe intraoperative bleeding and the patient had a history of saw palmetto use. These authors reported that saw palmetto was found to inhibit cyclooxygenase (COX) and lipoxygenase (LOX) enzyme activity in animal studies and that the prolonged bleeding time in the reported case could be due to platelet dysfunction due to COX inhibition (10). There is a further saw palmetto-related case, in which coagulometric tests were prolonged, accompanied by hematuria (11). Similarly, coagulometric tests were impaired in our patient, but there was no identifiable reason or drug in his history likely to cause this. Therefore, we suspect that the coagulation parameters of the patient were impaired by the use of saw palmetto and the widespread ecchymotic lesions developed secondary to this.

Lapi et al. reported that a patient who presented with pain in the right hypochondrium had acute liver damage due to saw palmetto use. In this report there was no other plausible factor that could cause liver damage and, moreover, the clinical and laboratory findings of the patient improved after the preparation was discontinued (12). In our patient, aPTT, and PT/INR were high, albumin value was low, and other liver function tests were normal. It was also observed that these values returned to normal following the discontinuation of saw palmetto. We hypothesize that this preparation causes temporary liver dysfunction or acts on the coagulation cascade by an unknown mechanism.

Acute pancreatitis associated with saw palmetto have also been reported, mainly as case reports (5,13,14). Jibrin et al. reported that a patient who presented with nausea, vomiting and epigastric pain and had a history of using saw palmetto extracts due to BPH had pancreatitis, possibly related to this therapy. The patient's clinical condition improved after the use of saw palmetto was discontinued. However, his pancreatitis recurred after re-use of saw palmetto (5). Wargo et al. also stated that pancreatitis developed in a patient who used saw palmetto extract for one week due to BPH. They argued that COX inhibition due to saw palmetto triggers mechanisms leading to acute pancreatitis (13). In our case, saw palmetto was used in the context of kidney stones and urinary complaint. Abdominal pain and vomiting started one day after he started using the extract. Although our case had history of using other prescribed drugs, he had been using other drugs for a long time and it was thought that the pancreatitis might then be due to the newer use of saw palmetto.

In our case, acute renal failure due to chronic kidney disease improved with treatment. The patient's intense nausea-vomiting and prerenal causes due to acute pancreatitis may be responsible for this clinical situation. There is no previous report of a relationship between saw palmetto and nephrotoxicity.

Conclusion

Although the adverse effects thus far described and ascribed to saw palmetto are generally benign and transient, more data are needed on the dosing and potential adverse effects of this readily available over-the-counter preparation. In our case, hemorrhagic complications regressed spontaneously, and acute pancreatitis improved. Saw palmetto may affect the coagulation profile of some patients directly or indirectly, and multiple drug interactions should be taken into account. Therefore, in such cases, the use of herbal supplements in addition to prescribed drugs should be carefully investigated.

Conflict of interest : The authors declared no conflict of interest

Financing Disclosure: There is no specific funding related to this case report.

Authors' contributions: Each author contributed significantly to preparation of the manuscript. All authors reviewed and approved the final version of the manuscript for submission.

Informed Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review in this journal.

References

1. Singh YN, Devkota AK, Sneeden DC, et al. Hepatotoxicity potential of saw palmetto (Serenoa repens) in rats. Phytomedicine 2007;14:204-8. doi: 10.1016/j.phymed.2006.03.024.
2. Avins AL, Bent S, Staccone S, et al. A detailed safety assessment of a saw palmetto extract. Complement Ther Med 2008;16:147-54. doi: 10.1016/j.ctim.2007.10.005.
3. Agbabiaka TB, Pittler MH, Wider B, et al. Serenoa repens (saw palmetto): a systematic review of adverse events. Drug Saf 2009;32:637-47. doi: 10.2165/00002018-200932080-00003.
4. Avins AL, Lee JY, Meyers CM, et al. Safety and toxicity of saw palmetto in the CAMUS trial. J Urol 2013;189:1415-20. doi: 10.1016/j.juro.2012.10.002.
5. Jibrin I, Erinle A, Saidi A, et al. Saw palmetto-induced pancreatitis. South Med J 2006;99:611-2. doi: 10.1097/01.smj.0000215642.76198.44.
6. Wang CZ, Moss J, Yuan CS. Commonly Used Dietary Supplements on Coagulation Function during Surgery. Medicines (Basel) 2015;2:157-185. doi: 10.3390/medicines2030157.
7. Andriole GL, McCullum-Hill C, Sandhu GS, et al. The effect of increasing doses of saw palmetto fruit extract on serum prostate specific antigen: analysis of the CAMUS randomized trial. J Urol 2013;189:486-92. doi: 10.1016/j.juro.2012.09.037.
8. Barry MJ, Meleth S, Lee JY, et al. Effect of increasing doses of saw palmetto extract on lower urinary tract symptoms: a randomized trial. JAMA 2011;306:1344-51. doi: 10.1001/jama.2011.1364.
9. Bent S, Kane C, Shinohara K, et al. Saw palmetto for benign prostatic hyperplasia. N Engl J Med 2006;354:557-66. doi: 10.1056/NEJMoa053085.
10. Cheema P, El-Mefty O, Jazieh AR. Intraoperative haemorrhage associated with the use of extract of Saw Palmetto herb: a case report and review of literature. J Intern Med 2001;250:167-9. doi: 10.1046/j.1365-2796.2001.00851.x.
11. Villanueva S, González J. Coagulopathy induced by saw palmetto: a case report. Bol Asoc Med P R 2009;101:48-50.
12. Lapi F, Gallo E, Giocaliere E, et al. Acute liver damage due to Serenoa repens: a case report. Br J Clin Pharmacol 2010;69:558-60. doi: 10.1111/j.1365-2125.2010.03618.x.
13. Wargo KA, Allman E, Ibrahim F. A possible case of saw palmetto-induced pancreatitis. South Med J 2010;103:683-5. doi: 10.1097/SMJ.0b013e3181e1e3ee.
14. Bruminhent J, Carrera P, Li Z, et al. Acute pancreatitis with saw palmetto use: a case report. J Med Case Rep 2011;5:414. doi: 10.1186/1752-1947-5-414.