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CASE REPORT

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Rhabdomyolysis in an unsuspecting patient

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ABSTRACT

Vitex is an herbal supplement marketed towards women to help regulate menstrual cycles, alleviate some symptoms of premenstrual syndrome, and boost fertility. It is non-FDA regulated and can be purchased from many different places including online and in health stores.

We report a case of a 36-year old African American female with no past medical history who developed severe bilateral thigh pain and swelling four days after starting Vitex. This occurred only after mild to moderate exercise that was no more intense than the patient's typical routine, and she stated to be well hydrated that day. After appropriate labs and workup, she was diagnosed with rhabdomyolysis and admitted to the hospital for close observation and IV fluids. This report is designed to raise the concern that Vitex may potentiate muscle damage with exertion during routine exercise.

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Vitex; herbal; supplement; rhabdo; rhabdomyolysis; exercise

1. Introduction & case description

A 36-year old African American female presented to the emergency department with two days of increasing bilateral thigh pain and swelling. She stated that her thighs began bothering her shortly after a spin class that she attended two nights prior to admission, although she denied an excessive or increased intensity of training. She had exercised for less than 45 minutes at a moderate pace with frequent breaks, and she had been routinely attending this class for several months. She denied having any significant past medical or family history. She also denied alcohol, tobacco, and drug use as well as taking any prescription medications. When asked about any supplement use, however, she admitted having begun taking the herbal supplement Vitex 2 days prior to the onset of her pain (4 days prior to admission). She stated that her periods had been decreasing in frequency over the course of a year and someone at a local herbal shop recommended the supplement to her. She had not sought medical attention for her oligomenorrhea. On physical exam, her thighs were noticeably swollen and diffusely tender to palpation. No erythema or petechiae were noted and no induration or masses were palpated. Labs were remarkable for a CK of 72K and AST/ALT 834/210. Of note, her renal function was preserved. Patient denied fever, chills, gastrointestinal symptoms, decreased UOP, peripheral edema or weight gain.

Over the course of her 4 night hospital stay, she was treated for rhabdomyolysis with generous IV fluids. Nephrotoxins and hepatotoxins were avoided. Her CK gradually trended down from 72K to 17,942 and her pain and swelling resolved with supportive treatment. Her AST and ALT, on the other hand, only showed modest improvement and were 577/194 respectively upon discharge. Her phosphorous was normal throughout her stay and 3.4 when last checked. She demonstrated no symptoms of hypothyroidism, so it was not checked during her stay. We had no reason to believe that she had an underlying myopathy as she had never had muscle pain or weakness before, exercised routinely, and had no suspicious skin findings. Her pregnancy test, acetaminophen assay, hepatitis panel, and Urine Drug Screen were all negative. A right upper quadrant ultrasound demonstrated no acute findings other than a simple right renal cyst.

After treatment, the patient felt well and was eager to get back to work as an accountant. She was discharged and asked to follow up with her primary care physician to continue to monitor lab work for normalization of CK and LFTs after stopping the supplement. The patient agreed to discontinue the supplement and she presented the medical team with the bottle for further examination. The product was advertised as Nature's Way Vitex Fruit. The ingredient list included vitex, plant-derived capsule (modified cellulose), magnesium stearate, and silica.

2. Discussion

Rhabdomyolysis is the rapid destruction of skeletal muscle via necrosis leading to release of intracellular

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constituents resulting in elevated CK levels and release of myoglobin. It is well documented that LFTs also rise in rhabdomyolysis, with AST being more significant. Rhabdomyolysis is most commonly caused by traumatic (compression) or exertional methods but may also be induced by certain drugs or infections [1]. Although our patient may have displayed an exertional component, it seems that rhabdomyolysis may have been potentiated by the addition of Vitex.

Vitex is an herbal supplement marketed towards women as it is advertised to help regulate menstrual cycles, to reduce the severity of menopausal symptoms, and to increase fertility [2]. There is little to no scientific evidence to support these claims. This non-FDA approved supplement is widely sold at herbal stores, supplement shops, and multiple online websites.

This case report details an example of rhabdomyolysis that occurred with only mild to moderate exercise intensity in the setting of Vitex initiation. It was verified that the spin class and as well as level of and duration of exertion were nothing new to the patient and she stated to have been well hydrated that day. It is interesting to note that the event was preceded by the first exercise that she had done since starting the herbal supplement Vitex. There are no documented case reports of this supplement causing rhabdomyolysis in a thorough literature search [2].

Vitex (formally Vitex angus castus) is composed of a variety of compounds and has several documented side effects including intermenstrual bleeding, diarrhea, nausea, acne, weight gain, and headache. According to a study published in NCBI, 'A new labdane-diterpene, viteagnusin I, together with 23 known phytoconstituents were isolated from the fruits of *Vitex agnus-castus* L. The known compounds include ten flavonoids, five terpenoids, three neolignans, and four phenolic compounds, as well as one glyceride.' [3] Another report out of NCBI states, 'Several dietary plant polyphenols and flavonoids including curcumin, quercetin, resveratrol, and red wine polyphenols, appear to be efficacious in RM and ischemic AKI in animal models.' [4] Further, a study out of Karger describes the beneficial effects of flavonoids in rhabdomyolysis stating 'Daily administration of flavonoids from red wine reduced blood CPK as well as catalase, glutathione peroxidase, and superoxide dismutase expression in a rat model of rhabdomyolysis.' [5]. These reports raise concern that other compounds in vitex may be potentiating muscle injury greater than the protective effect of flavonoids.

Two reviews by American Society of Nephrology in 2007 and 2018 found that many herbal supplements have been linked to rhabdomyolysis and include absinthium (wormwood oil), G. glabra (licorice), niacin (especially when used in conjunction with statins), creatine monohydrate, and E. sinica (ephedra/ma huang) particularly with MAOIs [6,7]. Other specific supplements that may cause or be associated with rhabdomyolysis through drug-drug interactions include hemlock, nux, vomica, guggul, kratom, red yeast rice, coca, Ignatius bean, higenamine, kava, excessive caffeine, anise, jimson weed, intramuscular vitamin B6 (pyridoxine) injections, cranberry, pomegranate (when used simultaneously with statins), blue-green algae, chromium, gamma-hydroxybutyrate (GHB) withdrawal, guara, and Hydroxycut products [8].

As per an article from *The Lancet*, 'Associations between adverse events and ingredients are difficult to verify if a product has more than one ingredient, and because of incomplete information systems. Research into hazards and risks of dietary supplements should be a priority.' [9] These associations are especially important to be aware of when dealing with an older population, as they take more prescription and non-prescription drugs and are much more susceptible to the various side effects. Based off of an article published in *JAMA*, 'at least 1 in 25 older adults used a regimen posing a risk of a major potential drug-drug interaction; half of these potential interactions involved the use of non-prescription medications.' [10].

3. Summary

This case illustrates the association between vitex and rhabdomyolysis.

It is likely that the herbal supplement vitex predisposed the patient to developing rhabdomyolysis even with routine exercise. This case report underlines the importance of understanding rare drug interactions in the body. It is especially essential to consider non-FDA regulated supplements when evaluating older, more susceptible patients, as supplement side effects are not well recognized or documented.

Disclosure statement

No potential conflict of interest was reported by the authors.

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