CRCP Case Reports in Clinical Practice

Case Report

Journal Homepage: http://crcp.tums.ac.ir

Herbal Fertility Remedies Leading to Massive Pulmonary Embolism: A Case Report

Iman Bhia[1], Aryan Seraj[1], Toktam Alirezaei[2]*

1. Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. Men's Health and Reproductive Health Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Use your device to scan and read the article online

Citation Bhia I, Seraj A, Alirezaei T. Herbal Fertility Remedies Leading to Massive Pulmonary Embolism: A Case Report. Case Reports in Clinical Practice. 2024; 9(2): 74-78.

Running Title A Trigger for Pulmonary Embolism

ABSTRACT

The rising use of herbal medicines raises concerns about their safety and effectiveness. This case report involves a 55-year-old male who developed shortness of breath and chest discomfort after using herbal substances and sildenafil for erectile dysfunction and infertility. He was diagnosed with a massive acute pulmonary embolism (PE) via CT angiography and treated with alteplase, followed by oral apixaban after discharge. The herbal substances included carob, ginger, red ginseng, and others. This case highlights the need to investigate how herbal remedies may affect hormone balance and contribute to cardiovascular risks, particularly PE.

Article info:
Received: March 12, 2024
Revised: March 24, 2024
Accepted: April 18, 2024

Keywords:
Pulmonary embolism; Herbal medicine; Testosterone; Infertility treatment

Introduction

Herbal medicinal product use has surged globally, with over 80% of people incorporating them into healthcare. However, lacking solid evidence and limited monitoring hinders understanding of their side effects and drug interactions. Recently, case reports have linked herbal substances to pulmonary embolism (PE) [1, 2]. Herbal medicine is often used by males with age-related testosterone decline as testosterone replacement therapy (TRT). While over-the-counter testosterone-boosting supplements are popular, they are poorly studied and loosely regulated. Despite TRT's benefits, its cardiovascular risks, like increased polycythemia, are frequently underreported [3].

PE occurs when a clot obstructs the pulmonary artery, causing right ventricular failure and potentially leading to death [4, 5]. Risk factors for PE include long flights, obesity, surgery, pregnancy, contraceptives, hormone therapy, cancer, and thrombophilia [6, 7]. Most patients (85%) report sudden or worsened resting dyspnea. This case involves a saddle PE linked to an infertility treatment package provided by a traditional medicine practitioner.

Case presentation

A 55-year-old patient, known to have uncontrolled type 2 diabetes and grade 2 varicocele, presented

*** Corresponding Author:**
Toktam Alirezaei
Address: *Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*
E-mail: *alirezaei.toktam@sbmu.ac.ir*

at the emergency department with complaints of dyspnea and new-onset chest discomfort three days before admission. The patient did not report nausea, vomiting, cold sweats, or paroxysmal nocturnal dyspnea. Upon arrival at the emergency department, the patient had an arterial oxygen saturation of 96%, a pulse rate of 68, a blood pressure reading of 116/86 mm Hg, and normal distal pulses.

The patient's medical history includes a diagnosis of type 2 diabetes mellitus 12 years ago, which was not being treated, resulting in the patient's blood sugar levels consistently exceeding 300 mg/dL. Additionally, the patient was diagnosed with varicocele 18 years ago. There is no prior history of ischemic heart disease, habitual alcohol or tobacco use, or drug abuse.

After taking the patient's medical history, the patient denied any typical risk factors for PE. He emphasized that he is physically active, avoids alcohol and smoking, and has not had any prior history of diseases aside from diabetes and varicocele. However, the patient mentioned seeking alternative treatment from a traditional medicine practitioner for his varicocele, erectile dysfunction, and infertility issues. Consequently, the patient had been taking sildenafil 100 mg daily for the past 40 days, in addition to a combination of herbal substances commonly used in Iran for treating infertility or erectile dysfunction. These herbal substances were initiated on July 12, 2023, and included the following:

1. Carob (Ceratonia siliqua) herbal tea and syrup infused with ginger and heart of palm (Palmito) syrup.

2. Red ginseng capsules.

3. Varicocele paste composed of royal jelly (RJ) and pollen.

4. Alfalfa herbal tea enriched with barley yeast.

5. A distillate referred to as blossom distillate, containing Fumaria indica, chicory, and purslane.

6. Aphrodisiac powder (carob, saffron, natural black seed, honey, ginseng with almond).

The patient followed this specific regimen: blossom distillate (50 cc, three times a day); varicocele paste (twice a day); carob herbal tea (containing 5 cc of carob, twice a day before taking the varicocele paste); carob syrup (consumed before breakfast along with 50 cc of ginger syrup and heart of palm syrup); red ginseng capsule (taken at night); alfalfa herbal tea enriched with barley yeast (50 cc).

Upon arrival at the emergency department, the initial laboratory findings revealed the following values: a blood sugar level of 398, urea at 38.6, creatinine at 1.14, creatine phosphokinase (CPK) at 68, Creatine Kinase MB (CK-MB) at 13.8, a white blood cell count of 12.8, hemoglobin at 16.9, platelet count at 202, sodium level of 140, potassium at 4.4, troponin at 0.06, and a pro-brain natriuretic peptide (pro-BNP) level of 3270. The patient's electrocardiogram was also taken during hospitalization, as shown in (Figure 1).

The patient was admitted to the cardiac care unit (CCU) for a comprehensive evaluation. A transthoracic echocardiogram showed moderate right ventricle (RV) enlargement, mild RV dysfunction, mild mitral regurgitation (MR), mild to moderate tricuspid regurgitation (TR), and a pulmonary artery pressure (PAP) of 55 mmHg. Additionally, the patient's inferior vena cava (IVC) was dilated and collapsed <50%, with an ejection fraction (EF) of 55%. The patient's PE was confirmed by computed tomographic pulmonary angiography (CTPA), which reported saddle PE (Figure 2).

Due to the patient's stable hemodynamics and the findings in both CTPA and transthoracic echocardiogram, the patient was diagnosed with submissive PE. Thus, the patient was a candidate for receiving 100 mg of alteplase. Two days after receiving alteplase, the patient underwent a repeat transthoracic echocardiogram, which revealed normal RV size and function. Additionally, the transthoracic echocardiogram indicated mild MR, mild TR, a PAP within the range of 20-25 mmHg, an EF of 55%, and no evidence of PE. The patient also underwent an endocrinology consultation and began receiving subcutaneous insulin NPH twice daily. Following this, the patient was discharged with a prescription for oral apixaban tablets at a 10 mg dosage to be taken every 12 hours for 7 days, then 5 mg every 12 hours, along with a recommendation to return to the emergency department if any symptoms were to reoccur.

Discussion

The patient underwent herbal therapy to address his infertility, with some ingredients potentially causing hormone imbalances, a known risk factor for PE [6]. Therefore, to fully assess the remedy's effects, the properties of each herbal medicine must be understood.

Carob boasts a range of properties, including anti-

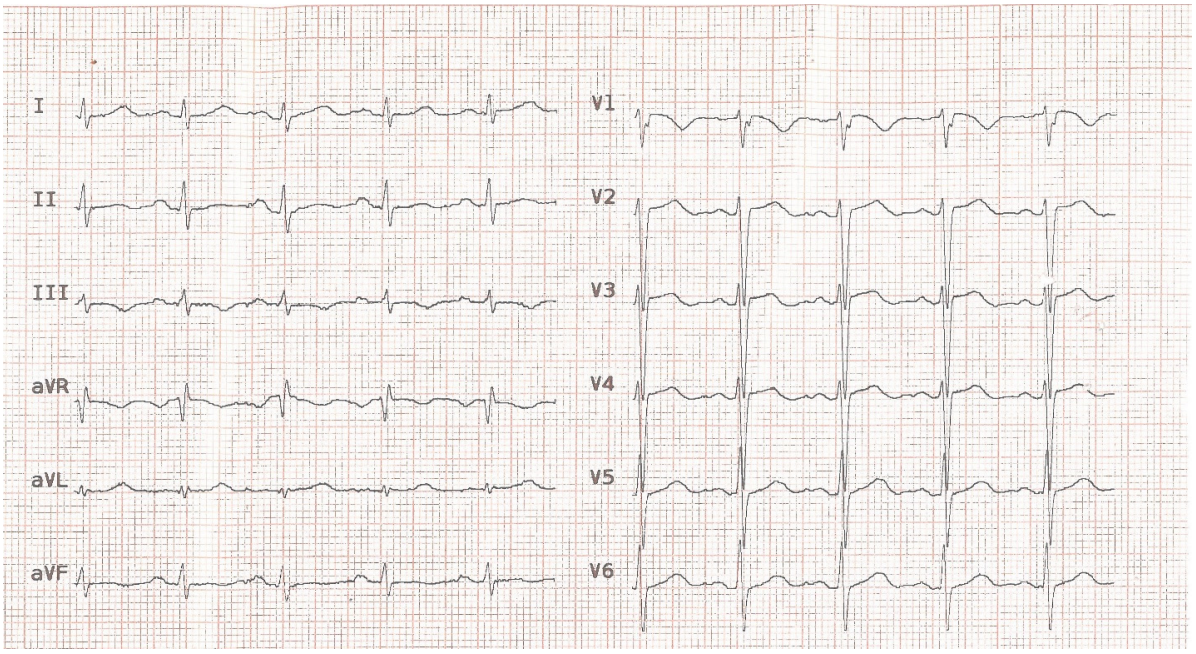

Fig. 1. The patient's electrocardiogram during his hospitalization reveals a sinus tachycardia rhythm, along with mild ST-segment elevation in V1-V3.

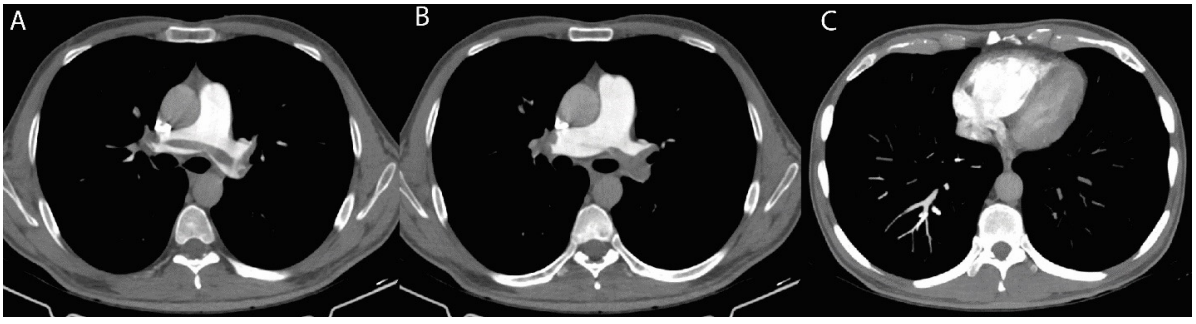

Fig. 2. Patient's CTPA which in (A) and (B) we can see clear evidence of saddle PE. (C) shows RV enlargement.

inflammatory effects through the reduction of TNF-alpha and IL-6, anti-lipid activity, antioxidative properties, and beneficial effects on glycemia in individuals with type 2 diabetes [8]. A recent clinical trial also found it improves sperm count, motility, and morphology without alterations in hormonal parameters [9]. In contrast, ginger has been reported not only to enhance semen quality but also to impact hormonal parameters [10]. Dokhanchi et al. and their colleagues explored the effects of palmito on the reproductive organs of Sprague-Dawley rats, ultimately concluding that it led to a significant decrease in testosterone and estradiol levels [11].

Red ginseng is renowned for its anti-fatigue, anti-inflammatory, anti-cancer, antioxidant, and anti-obesity properties [12]. A study reported that it significantly enhances sperm concentration, motility, morphology, and viability without affecting hormone levels [12]. Another ingredient was RJ, which has shown positive effects on human fertility by improving hormonal balance, and sperm and ovule quality. In men, it increases semen volume, sperm count, motility, and seminal fructose, along with boosting serum testosterone levels [13]. Alfalfa plants have antioxidant and anti-inflammatory properties. Their hydroalcoholic extract, rich in phytoestrogens and oxidative stress control effects, may enhance ovarian activity in adult rats [14].

Fumaria indica increases sperm count, testosterone levels, sperm density, and Leydig cell count, while also boosting the weight of the testis and epididymis [15]. As for chicory leaves, Dorostgoal et al. concluded that they enhance male rat reproductive parameters [16]. Moreover, purslane holds the capacity to reduce intracellular ROS and protect mitochondrial membrane function, resulting in enhanced sperm motility and mitochondrial membrane potential in boars and goats [17]. Lastly, aphrodisiac powder ingredients, including

saffron, improve semen morphology in men [18], while natural black seeds increase testosterone levels in male mice [19].

Testosterone-induced polycythemia is one of the many side effects of elevated testosterone levels [20]. Initially, it was believed that the mechanism was solely due to kidney stimulation of erythropoietin (EPO) production. However, recent studies have shown increased hemoglobin levels without a notable rise in EPO [20]. Bachman et al. proposed that polycythemia is associated with a brief stimulation of EPO and the suppression of hepcidin and ferritin, leading to increased iron absorption, transport, and subsequent erythropoiesis [21]. Moreover, estradiol is believed to contribute to polycythemia [21]. This suggests that polycythemia results from a multifaceted interplay of factors.

Therefore, this herbal remedy leads to an improvement in semen quality and an increase in testosterone levels, which itself may lead to cardiovascular events such as myocardial infarction, polycythemia, and PE [22]. However, herbal supplements related to testosterone enhancement are not extensively researched, but they continue to be in demand among men seeking outcomes of testosterone, such as improved muscle mass, increased sexual performance, and libido [3].

Conclusion

Herbal drug use may carry a risk of vascular events like PE, though the mechanism is unclear. Some ingredients, while promoting fertility, can cause imbalances like elevated testosterone, which is linked to polycythemia and possibly explains the patient's PE. Since testosterone-boosting supplements are not well-studied, both healthcare professionals and patients should be cautious. More research is needed to ensure safety and understand these risks and benefits.

Ethical Considerations

Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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 by the Editor-in-Chief of this journal on request.

Acknowledgment

We are indebted to the patient for permitting discussion of their medical case.

Abbreviations

CCU: Cardiac care unit

CK-MB: Creatine Kinase MB

CPK: Creatine phosphokinase

CTPA: Computed tomographic angiography

DVT: Deep vein thrombosis

EF: Ejection fraction

EPO: Erythropoietin

IVC: Inferior vena cava

MR: Mitral regurgitation

PE: Pulmonary embolism

Pro-BNP: Pro-brain natriuretic peptide

RJ: Royal jelly

RV: Right ventricle

ROS: reactive oxygen species

TR: Tricuspid regurgitation

TRT: Testosterone replacement therapy

References

[1] Ebhohon E, Miller D. Moringa Oleifera leaf extract induced pulmonary embolism-a case report. Int J Emerg Med. 2022;15(1):16. https://doi.org/10.1186/s12245-022-00419-3

[2] Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. Front Pharmacol. 2014;4:177. https://doi.org/10.3389/fphar.2013.00177

[3] Nguyen SM, Ko Ko N, Sattar AS, Gucuk Ipek E, Ali S. Pulmonary Embolism Secondary to Testosterone-Enhancing Herbal Supplement Use. Cureus. 2017 Aug 6;9(8):e1545. https://doi.org/10.7759/cureus.1545

[4] Greyson C, Xu Y, Lu L, Schwartz GG. Right ventricular pressure and dilation during pressure overload determine dysfunction after pressure overload. Am J Physiol Heart Circ Physiol. 2000 May;278(5):H1414-20. https://doi.org/10.1152/ajpheart.2000.278.5.H1414

[5] Lyhne MD, Kline JA, Nielsen-Kudsk JE, Andersen A. Pulmonary vasodilation in acute pulmonary embolism - a systematic review. Pulm Circ. 2020 Mar 4;10(1):2045894019899775. https://doi.org/10.1177/2045894019899775

[6] Kostadima E, Zakynthinos E. Pulmonary embolism: pathophysiology, diagnosis, treatment. Hellenic J Cardiol. 2007;48(2):94-107.

[7] Alirezaei T, Hajimoradi B. Is thrombotic event a side effect of oral buprenorphine abuse? Two case reports. Clin Case Rep. 2019;7(4):740-3. https://doi.org/10.1002/ccr3.2086

[8] Gioxari A, et al. Carob: A sustainable opportunity for metabolic health. Foods. 2022;11(14). https://doi.org/10.3390/foods11142154

[9] Aghajani MMR, Mahjoub S, Mojab F, Namdari M, Gorji NM, Dashtaki A, et al. Comparison of the Effect of Ceratonia siliqua L. (Carob) Syrup and Vitamin E on Sperm Parameters, Oxidative Stress Index, and Sex Hormones in Infertile Men: a Randomized Controlled Trial. Reprod Sci. 2021 Mar;28(3):766-74. https://doi.org/10.1007/s43032-020-00314-3

[10] Gholami-Ahangaran M, Karimi-Dehkordi M, Akbari Javar A, Haj Salehi M, Ostadpoor M. A systematic review on the effect of Ginger (Zingiber officinale) on improvement of biological and fertility indices of sperm in laboratory animals, poultry and humans. Vet Med Sci. 2021 Sep;7(5):1959-69. https://doi.org/10.1002/vms3.538

[11] Dokhanchi M, et al. Effects of heart of palm (Palmito) extract on reproductive system of adult male rats. Asian Pac J Reprod. 2013;2(4):272-6. https://doi.org/10.1016/S2305-0500(13)60161-X

[12] Park HJ, Choe S, Park NC. Effects of Korean red ginseng on semen parameters in male infertility patients: a randomized, placebo-controlled, double-blind clinical study. Chin J Integr Med. 2016;22(7):490-5. https://doi.org/10.1007/s11655-015-2139-9

[13] Abdelnour SA, Abd El-Hack ME, Alagawany M, Taha AE, Elnesr SS, Abd Elmonem OM, et al. Useful impacts of royal jelly on reproductive sides, fertility rate and sperm traits of animals. J Anim Physiol Anim Nutr (Berl). 2020 Nov;104(6):1798--808. https://doi.org/10.1111/jpn.13303

[14] Sistani S, Raeeszadeh M, Amiri A. The phytoestrogenic effect of hydroalcoholic extract of alfalfa on oxidative stress and follicle formation in adult female Wistar rats. J Adv Biomed Sci. 2017;7(4):447-54.

[15] Chorosho SH, Malik N, Panesar G, Kumari P, Jangra S, Kaur R, Al-Ghamdi MS, Albishi TS, Chopra H, Singh R, Murthy HCA. Phytochemicals: Alternative for Infertility Treatment and Associated Conditions. Oxid Med Cell Longev. 2023 May 11;2023:1327562. https://doi.org/10.1155/2023/1327562

[16] Dorostghoal M, Seyyednejad SM, Nejad MNT. Beneficial effects of Cichorium intybus L. extract on oxidative status and reproductive parameters in male Wistar rats: An experimental study. Int J Reprod Biomed. 2019;17(6):425-34. https://doi.org/10.18502/ijrm.v17i6.4814

[17] Torkamanpari M, Ghorbani F, Lorian K, Koohestanidehaghi Y. The effects of purslane (Portulaca oleracea) and fennel (Foeniculum vulgare Mill) hydroalcoholic extracts on the functional parameters of human spermatozoa after vitrification. Clin Exp Reprod Med. 2023 Jun;50(2):78-85. https://doi.org/10.5653/cerm.2021.04805

[18] Heidary M, Vahhabi S, Reza Nejadi J, Delfan B, Birjandi M, Kaviani H, Givrad S. Effect of saffron on semen parameters of infertile men. Urol J. 2008 Fall;5(4):255-9.

[19] Mustari A, et al. Promoting action of vitamin E and black seed oil on reproductive hormones and organ histoarchitecture of Swiss albino mice. Vet Med Sci. 2022;8(2):710-8. https://doi.org/10.1002/vms3.708

[20] Menakuru SR, Atta M, Dhillon VS, Salih A. Testosterone Usage Leading to Pulmonary Embolisms and Deep Vein Thrombosis: A Case Report and Review of the Literature. Hematol Rep. 2023 Apr 26;15(2):290-7. https://doi.org/10.3390/hematolrep15020029

[21] Bachman E, Feng R, Travison T, Li M, Olbina G, Ostland V, et al. Testosterone suppresses hepcidin in men: a potential mechanism for testosterone-induced erythrocytosis. J Clin Endocrinol Metab. 2010 Oct;95(10):4743-7. https://doi.org/10.1210/jc.2010-0864

[22] Van Buren NL, Hove AJ, French TA, Gorlin JB. Therapeutic Phlebotomy for Testosterone-Induced Polycythemia. Am J Clin Pathol. 2020 Jun 8;154(1):33-7. https://doi.org/10.1093/ajcp/aqaa019