

Clavis panax kullanan bir hastada gelişen akut yaygın pulmoner emboli

Acute massive pulmonary embolism developed in a patient using clavis panax

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Özet- Son yıllarda tüm dünyada ve ülkemizde, bitkisel ilaçların, bitki ekstraktları veya gıda takviyelerinin kullanımı ciddi oranda artmıştır. Bununla birlikte bu bitkisel karışımların bileşimindeki maddelerin etkin dozları, metabolizmaları ve ilaç etkileşimleri konusunda elimizde yeterli veri yoktur. Bu tür karışımların kullanılmasının yaygınlaşması ile birlikte, bunlardan kaynaklanan yan etkiler ve hayatı tehdit edici klinik tablolar bildirilmeye başlanmıştır. Bu yazıda, piyasada Clavis Panax adıyla satılan ve içeriğinde Tribulus terrestris, Avena sativa ve Panax ginseng kombinasyonu bulunan bitkisel karışıma bağlı olarak gelişen akut yaygın pulmoner embolili bir olgu sunuldu. Panax kullanan 41 yaşında erkek hasta ani gelişen nefes darlığı ve senkop şikayeti ile acil servise başvurdu. Yapılan tetkikler sonucu (kan gazları, ekokardiyografi, ventilasyon-perfüzyon sintigrafisi) akut yaygın pulmoner emboli tanısı konuldu. Hastanın panax kullanımı dışında bilinen bir hastalığı ve pulmoner emboli için herhangi bir risk faktörü yoktu. Hastaya trombolitik tedavi uygulandı. Tedavi sonrası nefes darlığı düzeldi. Hastaneden çıkış öncesi kullandığı panax adlı bitkisel karışım hakkında hasta bilgilendirildi. Varfarin başlandı ve INR kontrollerine gelmek üzere taburcu edildi.

Summary- In recent years, the use of herbal combinations, plant extracts or food supplements has increased in our country and all over the world. However, there is not enough data to determine the effective doses of these substances in the composition of herbal preparations, or their effects on metabolism and drug interactions. With the widespread use of herbal combinations, life-threatening adverse effects and clinical manifestations that arise from them have been reported. Herein, we present a case with acute massive pulmonary embolism while using an herbal combination in the context of Tribulus terrestris, Avena sativa and Panax ginseng. A 41-year-old man was admitted to the emergency department with the complaint of sudden onset of dyspnea and syncope. As a result of investigations (blood gases, echocardiography, ventilation-perfusion scintigraphy) he was diagnosed with an acute massive pulmonary embolism. The patient's use of panax did not pose as a risk factor for the pulmonary embolism. He was given thrombolytic therapy and shortness of breath improved. At the pre-discharge the patient was informed of the risks associated with the herbal combination, especially panax. Coumadin was started and he was discharged for the INR checks to come.

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Abbreviations:

AS	<i>Avena sativa</i>
PG	<i>Panax ginseng</i>
TT	<i>Tribulus terrestris</i>
TR	<i>Tricuspid regurgitation</i>

Since antiquity, herbal mixtures have been used in many diseases for therapeutical purposes. Currently, herbal mixtures in the composition of the drugs constitute the foundation of medical therapy. However, random use of officially uncontrolled herbal mixtures can cause life-threatening clinical disasters. Panax is one of the herbal mixtures which gained increasing popularity owing to the impact of printed, and visual media. It contains *Tribulus terrestris* (TT), *Avena sativa* (AS), and *Panax ginseng* (PG).

Herein, we present a case with acute massive pulmonary embolism developed secondary to intake of a herbal product containing a combination of TT, AS, and PG.

CASE PRESENTATION

A 41-year-old man was admitted to the emergency department with complaints of sudden onset of dyspnea and syncope. He hadn't any known cardiovascular disease. On physical examination his blood pressure, and pulse rate were 60/40 mmHg, and 120 bpm, respectively. His electrocardiogram demonstrated normal sinus rhythm with sinus tachycardia. Blood gas tests revealed a hypoxemic, and hypocapnic state. His echocardiograms revealed a 65 % ejection fraction {EF}, enlargement of the right heart chambers, right ventricular free wall hypokinesia (McCornell sign) not involving cardiac apex, and moderate degree of tricuspid regurgitation (TR).

Pulmonary artery pressure calculated in consideration of TR was 44 mm Hg. Pulmonary ventilation scan detected areas of segmental/subsegmental ventilation-perfusion mismatch (massive pulmonary embolism) in both lungs. In the coronary intensive care unit, the patient was started on thrombolytic therapy with the diagnosis of acute massive pulmonary embolism. During monitorization period, hemodynamic status of the patient was improved, and his dyspnea was relieved. Subsequently, the patient was influenced by misleading advertisements in the visual media, and used herbal mixture of Panax as a performance reinforcing medicinal product for his fatigue, and malaise for 45 days, but ceased using it 3 days ago. Etiological factors of pulmonary embolism were investigated. Colour Doppler ultrasonographic examination results revealed that venous system of both lower extremities were within normal limits. Thrombophilia panel test results for Factor V Leiden G 1691A, Factor II G20210, MTHFR C677T were normal. Heterozygous MTHFR A1298C mutation was detected. It was learnt that this heterozygous mutation was relatively prevalent, and did not mean anything *per se*. The patient received anticoagulant therapy (enoxaparine sodium 0.8 ml sc 2x1) during his hospital stay.

On control echocardiograms obtained, we observed that right cardiac chambers returned to their normal dimensions, movements of the right ventricular wall improved, and pulmonary artery pressure dropped within physiologic limits. Warfarin therapy was initiated. When his INR stabilized between 2, and 3, he was discharged, and timing of control visits was arranged.

DISCUSSION

Pulmonary embolism, together with myocardial infarction, and stroke is one of the most important causes of cardiovascular mortality. Occlusion of the pulmonary artery can lead to acute, life threatening, but reversible form of right ventricular failure. In majority of the cases, pulmonary embolism is the result of deep vein thrombosis (DVT). Main risk factors of venous thromboembolism include advanced age, recent surgical intervention, trauma, immobilization, heart failure, chronic obstructive pulmonary disease, pregnancy, oral contraceptive use, obesity, metabolic syndrome, smoking, hypertension, and factor deficiencies predisposing to coagulation disorders

Recently, *clavis panax* is one of the medicinal herbal mixtures which is especially used increasingly in our country. It contains TT, AS, and PG. TT is composed of saponins which are natural glycosides. Cholesterol lowering, antiinflammatory, antimicrobial, and immune system protecting effects of saponins in animals have been demonstrated.[1-4] AS, is a herbal product derived from oat. It has favourable effects on lipid profile of men.[5] Some components of oat have reportedly improved endothelial dysfunction with their antioxidant, and antiinflammatory activities under laboratory conditions.[5] PG has been used in cardiopulmonary, and cerebrovascular diseases so as to regulate glucose metabolism, and boost physical performance, psychomotor, and sexual functions. When used as a single agent, it seems to have an improved safety profile, and scarce number of adverse effects.[6] Its most frequently seen adverse effects are headache, sleep, and gastrointestinal disorders. However its combination with ginseng can cause serious, and even

potentially life-threatening adverse effects.[6] Favourable effects of such combinations obtained in animals have not been demonstrated conclusively in humans, even their organotoxic effects, and life-threatening clinical manifestation have been reported.[7]

In the literature, many case reports on accelerated atherosclerogenesis, and acute coronary syndrome,[8] shock [9], and stent thrombosis [10] associated with *Clavis Panax* have been cited, however concurrent acute massive pulmonary embolism has not been reported so far. Our patient did not carry any risk factor related to pulmonary embolism. Genetic analysis detected normal levels of Factor V Leiden G 1691A, Factor II G20210, MTHFR C677T. A heterozygous MTHFR A1298C mutation was detected. This heterozygous mutation is quite prevalent in the community. However as it is known, it does not reportedly constitute a significant risk, unless methylation, and cytochrome mutations coexist. Our patient used this commercial herbal mixture for 45 days which is claimed to have vasodilatory, and performance-enhancing effects. Three days after withdrawal of the drug, acute massive pulmonary embolism developed in the patient due to not precisely known mechanism of action. However in this case development of acute thrombosis secondary to withdrawal of this herbal mixture might be the issue.

Promotion of herbal mixtures in our country especially as completely natural products without any adverse effects, their advertisements in printed, and visual media and accordingly their widespread use, can cause unwanted, potentially fatal clinical conditions in particularly cardiovascular patients or even in healthy individuals.

Conflict of interest: None declared

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Key words: Herbal product-drug interactions; drug interactions; myocardial infarction; panax/adverse effects; pulmonary embolism.