Acute Effusive Pericarditis due to Horse Chestnut Consumption

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Patient: Male, 32
Final Diagnosis: Pericardial effusion related to the consumption of herbal product
Symptoms: Dyspnea
Medication: Horse chestnut (*Aesculus hippocastanum* L)
Clinical Procedure: Pericardial and pleural effusions were drained through a pericardiopleural window
Specialty: Cardiology

Objective: Unusual clinical course
Background: There are many well-known causes of pericardial effusion, such as cancer metastasis, bacterial or viral pericarditis, and uremic pericarditis; however, no reports exist in the literature demonstrating a pericardial effusion that led to cardiac tamponade following consumption of an herbal remedy.
Case Report: A 32-year-old male patient was referred to our cardiology outpatient clinic with a complaint of dyspnea. The patient's medical history was unremarkable; however, he had consumed 3 boxes of horse chestnut (*Aesculus hippocastanum* L) paste over the previous 1.5 months. His chest x-ray examination revealed an enlarged cardiac shadow and bilateral pleural effusion. On transthoracic echocardiographic examination, his ejection fraction was found to be 55% with circumferentially extended pericardial effusion that reached 3.9 cm at its maximal thickness. No growth had been detected in the pericardial and pleural biopsies or blood samples; there was no evidence of an infectious process in the physical examination. Based on this information, we diagnosed pericarditis resulting from the use of herbal remedies. This is the first report to demonstrate that herbal remedy consumption may cause this type of clinical condition.
Conclusions: Besides other well-known causes, pericardial effusion related to the consumption of herbal remedies should always be considered when treating patients with pericardial effusion caused by unclear etiologies.

MeSH Keywords: **Aesculus • Cardiotoxins • Pericardial Effusion**

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Background

Pericardial effusion occurs when the amount of fluid in the space between the heart and the pericardial sac increases. There are many well-known causes of pericardial effusion, such as cancer metastasis, bacterial or viral pericarditis, and uremic pericarditis. Herbal remedies are popular today; however, these products may cause serious adverse cardiovascular and metabolic effects, including dermatitis, arteritis, arrhythmias, chest pain, congestive heart failure, hypotension, hypertension, pericarditis, myocardial infarction, and death [1,2]. To our knowledge, there are no reports in the literature of a pericardial effusion that led to cardiac tamponade following herbal remedy use. This is the first report to demonstrate that herbal remedy consumption may cause this type of clinical condition.

Case Report

A previously healthy 32-year-old male patient was referred to our cardiology outpatient clinic with a complaint of having had dyspnea for 1 week. Physical examination revealed that the patient was tachypneic and orthopneic with bilateral rales on auscultation. He was afebrile and had a pulse rate of 88 beats/min. His respiratory rate was 22 breaths/min, and his blood pressure was 110/70 mm Hg. The patient's medical history was unremarkable, but he had consumed 3 boxes of horse chestnut (*Aesculus hippocastanum* L) paste over the previous 1.5 months.

On transthoracic echocardiographic (TTE) examination, the patient's ejection fraction was 55% with circumferentially extended pericardial effusion that reached 3.9 cm at its maximal thickness (Figures 1, 2). His chest x-ray examination revealed an enlarged cardiac shadow and bilateral pleural effusion.

Laboratory test results revealed the patient's blood level of alanine transaminase (ALT) was 245 U/L. His C-reactive protein (CRP) level was 124.3 mg/dL. Intravenous steroid therapy (40 mg/d), a perioral nonsteroidal anti-inflammatory drug, and colchicine treatments were initiated following a diagnosis of acute effusive pericarditis. The patient also stopped consuming horse chestnut.

During follow-up, the patient developed signs of jugular venous distention and hepatic congestion, and signs of cardiac tamponade were also found in his TTE. Pericardial fluid drainage was considered, and the patient was referred to the thoracic surgery department to have the pericardial and pleural effusions drained through a pericardiopleural window. The operation was performed successfully and both effusions were drained completely. The antibioclature, the biochemical assays, and the cell counts were studied in the pericardial and pleural fluid samples; pericardial and pleural biopsy samples were also sent to pathology. The pericardial fluid was found to be the exudative type. The adenosine deaminase activity had not increased in the pericardial fluid, and results of cultures taken from both the pericardial and pleural effusions did not reveal any bacterial growth. Direct examination of the pleural fluid revealed a large number of polymorphonuclear leukocytes but no bacteria. The pericardial and pleural biopsies, the cell counts and the immunohistochemical assays did not demonstrate any findings that suggested malignancy. Results of testing for rheumatologic and autoimmune disease markers (rheumatoid factor [RF], antinuclear antibody [ANA], anti-smooth muscle antibody [ASMA], antiendomysial antibody, anti-DsDNA, antineutrophil cytoplasmic antibody [ANCA], anti-mitochondrial antibody [AMA]-M2) were negative in the blood samples. Based on all these findings, consumption of horse chestnut paste was considered to have been the cause in this case of pericarditis.

Figure 1. Parasternal long-axis view demonstrating pericardial effusion and pleural effusion. (Arrow indicates pericardial effusion; asterisk indicates pleural effusion).

Figure 2. Subcostal view demonstrating pericardial effusion. (Arrow indicates pericardial effusion).

During hospitalization, the patient's CRP level decreased to 54.1 mg/dL; therefore, pericardial drainage was performed and the patient's steroid therapy discontinued. However, after the discontinuation of steroid therapy, the patient's pericardial effusion worsened and his CRP level increased to 97.2 mg. Therefore, intravenous steroid therapy was restarted, at 40 mg/d. The elevated ALT level on admission and relapse of pericardial effusion after stopping steroid therapy also helped to confirm our diagnosis that the patient had acute effusive pericarditis because of his horse chestnut consumption. After restarting the steroid therapy, the pericardial effusion disappeared very rapidly. The patient had colchicine treatment, at a dose of 0.5 mg twice daily for 3 months, starting from the beginning of his hospitalization. Ibuprofen 600 mg twice daily was also continued for a total of 3 months, along with the colchicine treatment. The dosage of the steroid therapy was reduced by 4 mg per week and discontinued within 2 months. Physical examinations performed on the 45th and 90th days demonstrated no abnormalities, and the patient's CRP level dropped to its normal reference range. Pericardial effusion was not observed in the control TTE examinations.

Discussion

Herbal remedies are popular at present; nonetheless, health care professionals generally remain undecided about their risks and benefits. These medicines may become potentially harmful in a large proportion of patients. A systematic review conducted by Ernst in 2003 highlighted that life-threatening cardiovascular complications including arrhythmias, congestive heart failure, myocardial infarction, hypotension, hypertension, and pericarditis may occur in patients receiving herbal medicines [1]. In 1998, Cuncha et al. reported a 3-year-old Hong Kong girl who had been taking a traditional Chinese herbal medicinal product (*ju huang chieh tu pien*). She had been diagnosed with pericarditis, pulmonary edema, and metabolic acidosis. The reason for these conditions was attributed to the high arsenic component of this herbal product. Despite all efforts, the patient died of arsenic poisoning [3].

Horse chestnut, one of the most popular herbal remedies, is an intriguing tree unique to the Balkans. It is planted across Europe and North America. Extract obtained from the seeds is generally used for treatment; however, the bark and leaves can also sometimes be used. Its active components are aescin, phytosterol, flavonoids, tannins, and hydroxycoumarins [4]. The most active component in this herb, aescin, has anti-inflammatory and antiedematous features [5]. Although current scientific knowledge justifies the use of horse chestnut only in chronic venous failure, it has for a long time been widely used in traditional and folk medicine as a treatment and cure for various disorders [6,7]. In 1999, German Commission E accepted

the use of horse chestnut products for chronic venous insufficiency treatment [8]. In 2004, Ruffini et al. demonstrated that topical treatment containing aescin in gel form was very effective in improving skin perfusion and nutrition in patients with venous microangiopathy [9]. In 2013, Gurel et al. reported their research about an herbal cream for hemorrhoids on rats, which contained horse chestnut fruit along with some other herbs. Treatment with their herbal hemorrhoid cream demonstrated anti-inflammatory and antioxidant effects [10]. In traditional medicine, horse chestnut has been consumed to improve cough and to cure rheumatism; however, these uses are not recommended because of their potential toxicity [4].

Here we present a case of pericardial tamponade that followed pericardial effusion and was related to the consumption of horse chestnut. The 4 types of pericardial effusion are transudative (e.g., heart failure, myxedema, nephrotic syndrome); exudative (e.g., tuberculosis, empyema); hemorrhagic (e.g., trauma, ruptured aneurysm); and malignant (e.g., fluid accumulation triggered by tumor metastasis). The pericardial effusion in our case was found to be exudative. No growth had been detected in the pericardial and pleural biopsies or blood samples. Physical examination revealed no evidence of an infectious process. The patient had been consuming horse chestnut paste for 1.5 months. Based on this information, we diagnosed pericarditis resulting from the use of herbal remedies. To the best of our knowledge, cardiac tamponade following the consumption of herbal remedies has not been reported in the literature.

Causality assessment is used to demonstrate a causal relationship between a drug and a suspected adverse drug reaction (ADR). A number of algorithms have been published in the literature to determine this relationship, such as World Health Organisation Collaborating Centre for International Drug Monitoring, the Uppsala Monitoring Centre causality categories, the Vennet algorithm, and the Naranjo Probability Scale. The Naranjo Probability Scale offers an objective, reliable, and acceptable causality assessment for ADRs, and it is helpful for evaluating unexpected ADRs [11,12]. According to the Naranjo Probability Scale, our observation of acute effusive pericarditis due to horse chestnut consumption is overall scored with 6 points, corresponding to a "probable" relationship for this ADR.

Some researchers suggest that horse chestnut is a strong inhibitor of adenosine diphosphate – induced thrombocyte aggregation [13,14]. The development of pericardial effusion after consumption of horse chestnut could be due to this strong antiaggregant feature. Eating an entire horse chestnut that has not been purified is likely to have considerable side effects [5,15]. Our patient consumed unpurified, traditionally acquired horse chestnut paste. Taken this way, the antigen

amount to which the body can react increases substantially. Another possible mechanism is that the production of antibodies as an immunologic response to these antigens might progress into a clinical condition that leads to pericardial effusion. Exudative effusion, such as was seen in our case, might have occurred within this inflammatory ground. This theory is supported by the negative results for the bioculture, malignancy, and rheumatologic markers.

Our patient recovered clinically, and his laboratory test results improved with anti-inflammatory treatment.

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Conclusions

This is the first case in the literature to show that pericardial tamponade might develop after the use of herbal remedies. When approaching cases of pericardial effusion of unknown origin, it would be logical to inquire about the use of herbal remedies along with investigating for other, more common etiologies.

Statement

The authors have no financial interest to report.