



Compulsion for Herbal Medicine Culminating in Bilateral Gynecomastia – A Case Report

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Abstract

A 55 year old man consulted out patient department for painful bilateral breast swellings. He had been diagnosed as having Ischemic Heart Disease proved on TMT and advised for coronary angiogram. He refused for further investigations and did not take any allopathic medicine. On further review of symptoms, he reported no changes in testicular size, no history of testicular trauma, no STD, no headache, no visual changes and any change in muscular mass or strength. Initial laboratory assessment showed higher estradiol concentration (180 pg/ml) and normal testosterone level. Subsequent findings from testicular USG, CT of chest, abdomen and pelvis were normal. Because of the normal findings from the imaging evaluation, the patient was interviewed again and after taking into confidence, he disclosed a daily intake of 3 g Indian Kudzu (*Pueraria tuberosa* DC.) from last one month. He was advised to discontinue the drug which resulted in complete resolution of symptoms within 20 days. This is a first case of gynecomastia caused by ingestion of India Kudzu reported from Udaipur, Rajasthan. Health care providers should thoroughly review patient's history of ingestion of herbal product to reveal the unusual manifestation of medical conditions.

Keywords: Phytoestrogen; Daidzein; Isoflavones; *Pueraria tuberosa*; Estradiol

Introduction

Gynecomastia (breast enlargement in male individuals) is relatively common in male infants, pubertal boys and elderly men [1]. Although it is usually symmetric, it can be unilateral. Careful physical examination along with ultrasonography or radiography can help distinguish gynecomastia from excess adipose. Gynecomastia can be due to relative estrogen excess such as in the swelling of testicular failure or androgen resistance, and it can be caused by absolute higher levels of estrogen due to testicular trauma, bronchogenic carcinoma, adrenal disease, thyroid disease or liver disease.

Many drugs can cause gynecomastia, including drugs that decrease testosterone synthesis such as ketoconazole, metronidazole or cytotoxic agents and drugs that decrease testosterone action such as marijuana, cimetidine, flutamide and spironolactone. Furthermore, some drugs such as isoniazides, penicillamine, calcium channel blockers and central nervous system agents (includes diazepam, tricyclic antidepressants, reserpine, phenytin and amphetamine) can cause gynecomastia via an unknown mechanism of action [2]. Gynecomastia has also been linked to tea tree oil and lavender oil [3]. Phytoestrogens, a component of soy products, have estrogen like properties and in large amount can lead to gynecomastia [4,5].

Case Report

A 55 year old, male approached for having painful swellings in both the breasts. He had history of chest pain which was confirmed to be of cardiac origin proved on treadmill test (TMT). He was chronic smoker but left since the diagnosis of his cardiac disease three months back. He was advised for coronary angiography for further investigation and management (allopathic medicine + angioplasty). He out rightly refused for angiography and allopathic drugs. He decided to stick to life style modification. He modified his diet, started regular morning walk and yoga, stopped smoking and reduced weight. He was feeling well with all these life style modifications but still opted for addition of some natural herbal drugs which can improve the existing disease and prevent the further extension of the disease process.

He was prescribed daily intake of a powdered herbal drug in dose of 3 g by some practitioner. After one month of which he developed painful swellings in both the breasts. On physical examination, he had normal genitals and bilateral tender gynecomastia (Figure 1 and 2). He was noted to have normal concentration of β -human chorionic gonadotrophins (β -HCG), prolactin, lutenizing hormone (LH), follicle stimulating hormone (FSH) and total & free testosterone. Thyroid function, renal function and liver function test results were normal. His estradiol concentration was 180pg/ml which was higher than the reference range of 13-59 pg/ml. He had normal findings from ultrasonography of the testes, computed tomography of the chest, abdomen and pelvis.

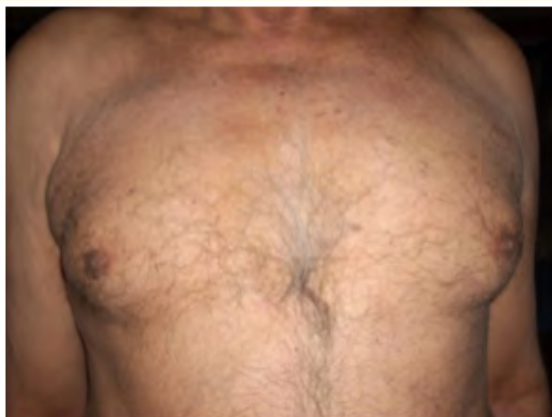


Figure 1: Bilateral gynecomastia (Front view).



Figure 2: Gynecomastia (Lateral view).

Initially, he did not reveal about the intake of herbal drug, but after repeatedly asking, he disclosed about the intake of herbal drug powder and provided the sample of the powder. As he was unaware about the ingredients of the powder, we investigated about the identity of the powdered drug through HPLC with the help of Department of Botany, Mohanlal Sukhadia University, Udaipur. The herbal drug was identified as *Pueraria tuberosa* DC. a member of family – Fabaceae; commonly known as Indian Kudzu. After identification, he was compelled and convinced that the swellings were because of the herbal powder and therefore, it was immediately stopped. The swelling subsided after one month and he was followed for another six months and did not develop any symptoms of gynecomastia.

Discussion

The evaluation of gynecomastia must include a thorough dietary and drug history and physical examination, including testicular examination. Baseline laboratory tests should include liver function and renal tests and assessment of thyroid and sex hormones (β -HCG, LH, FSH, testosterone and estradiol). Ultrasonography (USG) of the testes is recommended in case of hypo β -HCG/or increased estradiol concentration. If USG findings of the testes are normal, abdomen and chest Computerized Tomography (CT) should be performed to evaluate bronchial carcinoma or germ cell tumors. If CT findings are also normal, the different diagnosis include high aromatase activity producing high

endogenase source of estrogens v/s other exogenous source of estrogen [6,7]. Conversion of andostenedione and testosterone via aromatase produces most of the circulatory estradiol and estrone in men. Testosterone, estradiol and estrone are bound to sex hormone-binding globulin, in circulation. Because testosterone has a hyper affinity for sex hormone binding globulin, increases in sex hormone binding globulin GII form more free estradiol and estrone than testosterone [8].

Kudzu has been extensively studied for its possible beneficial effects in human health. It has shown to enhance fibrinolysis in coronary heart disease, decrease cholesterol levels and prostate cancer as well as improve menopausal symptoms, and bone density. The isoflavone extracted from Kudzu are daidzein, daidzin, genistein and puerarin. Isoflavones are plant chemicals that have estrogenic and antioxidant effects. They may lower heart rate and regulate heart rhythms. Animal studies have shown that puerarin may promote the formation of new blood vessels around area of heart tissue damaged by heart attacks or low blood supply (Ischemia) [9-11].

Phytoestrogens are reported to reduce cholesterol, triglycerides, blood sugar, blood pressure and thereby help in prevention of cardiovascular diseases. Besides, phytoestrogens also possess many health beneficial effects such as improving immune system, cognitive functions, bone, skin and reproductive health [12]. In view of that, taking Indian Kudzu was a right choice. Gynecomastia has been reported with ingestion of herbal supplements containing phytoestrogens [5,13] besides other reasons [14]. The isoflavones in Kudzu belong to a large chemical group known as phytoestrogens. In the human body, phytoestrogens may exhibit weak estrogenic effect. The type of Kudzu that grows in North America may not have enough phytoestrogens to provide natural hormone replacement [10]. However, the side effects of taking herbal medicine should always be kept in mind. Earlier, a study has reported that consumption of *P. tuberosa* tuber powder caused gynecomastia in 11.75% of study subjects [15].

Kudzu is available in a number of different dosage forms, most commonly as raw fresh root (usually called crude root), as tablets made from dried powder root, or as a root extract. Extract are concentrated liquid preparations usually made by soaking chopped or mashed plant parts in a liquid such as alcohol and then straining

out the solid part. For Kudzu tablets, 10mg is the approximate equivalent of about 1500 mg (1.5g) of crude Kudzu root. Commonly recommended daily doses are: Kudzu root 9000 mg to 15,000 mg (9g to 15g). Kudzu tablets – 90 mg to 360 mg divided in to 2 to 3 doses, Kudzu extract – 300mg to 900mg divided into three doses. Small study on menopausal women has shown that Kudzu was mildly effective in relieving hot flashes and other symptoms of menopause. Studies also suggest that Kudzu phytoestrogens may help to protect against bone loss for individuals with osteoporosis. In addition to this, Kudzu's phytoestrogens may help to lower cholesterol levels [16,17].

Therapeutically, phytoestrogens from Kudzu may be combined with other herbals such as soy, which are believed to exert estrogen like effects through different methods. Soy milk phytoestrogens are known as the isoflavones genistein and daidzein, which are structurally and functionally similar to 17 β -estradiol, but with weaker bioactivity than estradiol. Ingested isoflavone undergo biotransformation by the intestinal microflora followed by absorptive and enterophagatic recycling, which can result in high circulatory concentrations. This is one reason why estradiol levels were delayed in returning of the reference range. There is much variability in absorption of isoflavones from one individual to another. Soy isoflavones probably interfere with the Cyp enzymes that assist in the metabolism of estrogen. However, there are some risks involved with consumption of isoflavones and therefore, precautions should be taken before consumption of herbal treatment [18-25].

Conclusion

Herbal medicines are effective, safe and natural but not always free from side effects. In fact, no medicine whether Allopathic, Ayurvedic or Homeopathic is not without side effects unless used judiciously under expert guidance. Tubers of Indian Kudzu are edible and possess many cardio-beneficial properties. However, precaution is required with its intake as due to its high phytoestrogen content, potential side effect of gynecomastia can happen. This case report highlights the importance of taking history of the patient carefully for correct diagnosis of the disease.

Conflict of Interest

None.

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