

SPIRONOLACTONE INDUCED GYNECOMASTIA- A CASE REPORT**Palanisamy Sharmila Nirojini^{*1,2}, Maddirevula Maneesh Kumar Reddy³, Rama Rao Nadendla⁴ and A. Pramila Rani⁵**¹Associate Professor, Department of Pharmacy Practice, Chalapathi Institute of Pharmaceutical Sciences. Research Scholar, Acharya Nagarjuna University, Guntur.²Assistant Professor, Department of Pharmacy Practice, Chalapathi Institute of Pharmaceutical Sciences.³Principal, Chalapathi Institute of Pharmaceutical Sciences.⁴Principal, University College of Pharmacy, Acharya Nagarjuna University, Guntur.***Corresponding Author: Palanisamy Sharmila Nirojini**

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ABSTRACT

Gynecomastia is proliferation male breast tissue due to an imbalance in estrogen and androgen action. Though it is rare it causes anxiety, embarrassment and physical discomfort in the affected male. This case report is of a 69-year-old male patient who presented with the symptom of painful swelling in his both breasts. He is suffering from hypothyroidism, type 1 diabetes mellitus and myocardial infarction from past few years and using Eltroxin, Atorvastatin, Aspirin, Clopidogrel, Glimipride and Metformin. He was also diagnosed with clinically controlled Congestive Cardiac Failure (CCF) for which he was prescribed Lasilactone (Furosemide 20mg and Spironolactone 50mg) and developed enlargement of his breast after 9 months of treatment and diagnosed by the physician as bilateral gynecomastia. The physician withdrawn Lasilactone and added Furosemide 40mg. but the poor prognosis of his pedal edema caused by his CCF made the patient to take Lasilactone and the symptoms of gynecomastia recurred again. Diagnosing drug induced gynecomastia and discontinuing the drug causing it will prevent the need of surgery for gynecomastia.

KEYWORDS: Spironolactone, Gynecomastia, Case report.**INTRODUCTION**

Benign proliferation of male breast glandular tissue due to imbalance between estrogen action relative to androgen action at the breast tissue level appears to be the main etiology of gynecomastia.^[1] Asymptomatic gynecomastia is more common in healthy adult male with a prevalence of 32-65% and the prevalence of symptomatic gynecomastia is lower.^[2] Though there may be several endocrine etiologies which will affect hormonal balance for gynecomastia. Its association with drugs is not fragile.^[3] Gynecomastia coexists with many pathological conditions, including chronic liver disease, which is of unquestionable epidemiological importance for the Polish population. Another common trigger for gynecomastia -inducing mechanisms may be drugs, affecting the hormonal balance.^[2] Drug-induced gynecomastia is common and might account for a quarter of all cases, including those among children.^[3] The drugs that can cause gynecomastia are listed in Table 1. Although the mechanisms by which many medications induce gynecomastia are not yet understood, some mechanisms are clear.^[4] This is a case report of 69year

old male who developed spironolactone induced gynecomastia.

Table 1: Drugs that can cause gynecomastia and their mechanism.^[4]

Drug	Mechanism
Amiodarone	Unknown
Calcium channel blockers (diltiazem, verapamil, nifedipine)	Unknown
Central nervous system agents (amphetamines, diazepam, methylodopa, phenytoin, reserpine, tricyclic antidepressants)	Unknown
Cimetidine	Androgen receptor antagonism
Cytotoxic agents (alkylating agents, vincristine, nitrosoureas, methotrexate)	Primary hypogonadism due to Leydig cell damage
Flutamide	Androgen receptor antagonism
Hormones	
Androgens	Aromatization to estrogens; other mechanisms?
Estrogens	Direct stimulation of the breast
Human chorionic gonadotropin	Stimulation of testicular Leydig cell estrogen secretion
Ketoconazole, metronidazole	Inhibition of testosterone synthesis
Marijuana	Androgen receptor antagonism
D-penicillamine	Unknown
Phenothiazines	Elevated serum prolactin
Spirolactone	Androgen receptor antagonism; at high doses, interference with testosterone biosynthesis
Theophylline	Unknown

CASE DESCRIPTION

A 69 year male, visited the physician with the chief complaint of painful swelling in his both breasts. History of present condition states that he is suffering from hypothyroidism since 12 years and he had an mild attack of myocardial infarction 17 years ago and is using Eltroxin 100mg OD (Once Daily) for his hypothyroidism, Atrovastain 40mg OD and Aspirin 325mg OD. He also diagnosed with type –II diabetes 10 years ago and using Gemer-1 (Glimipride 1mg and Metformin 500mg) BD. After 15 years of diagnosing myocardial infarction patient undergone Coronary Artery Bypass Graft he used Deplatt-CV (Atrovastain 10mg +Clopidogrel 75mg+Aspirin 75mg) OD and Atenolo 25mg OD. In his regular follow up in 2015 he was diagnosed as hypertensive and he was added with Ramipril 5 mg. 2 years back presented to the physician with bilateral pedal edema and shortness of breath. On examination his blood pressure and other vitals were normal, but he was diagnosed with clinically controlled congestive cardiac failure (CCF), then he was prescribed with Lasilactone (Furosemide 20mg and Spirolactone 50mg) per day. After 9 months of treatment, pedal oedema and shortness of breath became normal but he developed painful swelling on his both breast. The physician withdrawn Lasilactone and added Furosemide 40mg once daily, while other medications were continued as such. Due to poor progression felt by the patient he himself took Lasilactone and after 10 days again he developed painful swelling in his breast and presented to the physician.

The substantially enlarged breasts were inspected and palpated. In a sitting position with arms relaxed, a firm,

mobile lump was palpated beneath each nipple. No focal nodular thickening was palpated. High frequency ultrasound of each breast confirmed true gynecomastia with fibrous tissue predominance and diagnosed as spironolactone induced bilateral gynecomastia (fig 1). The ADR was reported to the pharmacovigilance center, Guntur, Andhra Pradesh.



Figure 1: Bilateral gynecomastia observed in the patient.

DISCUSSION

Spirolactone is a well-known cause of gynecomastia and may act by displacing androgen from the androgen receptor and sexual-hormone-binding globulin, and by causing increased metabolic clearance of testosterone and higher estradiol production.^[5] Morphologically gynecomastia was classified by simon and which was modified by Cordova-Moschella later (table 2).^[6,7]

Table 2: Morphological classification of gynecomastia.

Simon classification	Cordova-Moschella classification
I - Minor breast enlargement without skin redundancy	I - Increased diameter and slight protrusion limited to the areolar region
IIa- Moderate breast enlargement without skin redundancy	II - Moderate hypertrophy of the breast with the nipple areolar Complex above the Inflammatory fold
IIb- Moderate breast enlargement with skin redundancy	III - Major hypertrophy of the breast with glandular ptosis and nipple-areolar complex situated at the same height as or as much as 1 cm below the inframammary fold.
III- Gross breast enlargement with skin redundancy that stimulated a pendulous female breast.	IV - Major breast hypertrophy with skin redundancy, severe ptosis and the nipple areolar complex positioned more than 1 cm below the inframammary fold.

Causality was assessed using Naranjo's causality assessment scale and ADR (Adverse Drug Reaction) was found to be definite with spironolactone. Severity and preventability were assessed using Hartwig and Siegel severity and scale and Schumock and Thornton preventability scale respectively and found that the ADR is moderate and definitely preventable. Informed consent was taken from the patient to publish case report and patient alert card was also issued.

CONCLUSION

Only few reports of spironolactone-induced bilateral gynecomastia are available in Indian populations. Educating proper history and performing examination can result in correct diagnosis. If the medicine-induced gynecomastia is suspected, dechallenge should be done. Replacing to a medicine of the same class having lower incidence of gynecomastia may prevent re-emergence of gynecomastia and also to reduce patient's anxiety, embarrassment and physical discomfort. Within one month of discontinuing the causal medicine, a reduction of symptoms should occur. However, if the gynecomastia has been present for more than one year, fibrotic changes may occur, it meant for surgery. Though the informations are available on leaflet of the medication, it is not discussed with patients clearly. We can accentuate the side effects of the treatment to the patients for avoid the further complications.

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Conflict of interest

No conflict of interest involved.

Abbreviations used

CCF – Congestive Cardiac Failure, OD – Once Daily, BD – Twice Daily, ADR - Adverse Drug Reaction, ADR – Adverse Drug Reaction.

Summary

Discussing about the possible ADRs with patient will prepare him to handle the risk and also to identify those ADRs in incipient stages and helps in the management.

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