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OMEPRAZOLE INDUCED GYNAECOMASTIA- A CASE STUDY

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Abstract : Gynecomastia is the presence of subareolar breast tissue that is palpable and has a diameter of 2 cm or more. The frequency rises with age, obesity and is typically silent, undetected by patients. Gynecomastian is assumed to be caused by an altered balance between oestrogen and androgen effects. A 66 years old male patient had diagnosed with ulcer and omeprazole tablet should be taken in 3 months. Then after 3 months cardiologist confirmed this patient had omeprazole induced gynecomastia. After that omeprazole tablet should be stopped and alternatively ranitidine tablet 150 mg twice daily should be given.After two weeks patient symptom was subsided and he recovered.

IndexTerms - Omeprazole, Gynecomastia, Estrogens, Androgens.

INTRODUCTION

Gynecomastia is currently defined as the presence of subareolar breast tissue that is palpable and has a diameter of 2 cm or more. The frequency rises with age, obesity and is typically silent, undetected by patients. Although the exact cause is unknown, Gynecomastia is assumed to be primarily caused by an altered balance between oestrogen and androgen effects as a result of an absolute increase in oestrogen production, a relative decrease in androgen production, or a mix of both[1,2]. Because oestrogen serves as the breast's growth hormone, excess estradiol in men causes breast expansion by causing ductal epithelial hyperplasia, ductal elongation and branching, periductal fibroblast proliferation, and vascularity[2].Despite the fact that gynecomastia is typically asymptomatic and frequently unnoticed by patients, common complaints among those who have it include social anxiety that may cause aesthetic worries and discomfort from localised soreness and sensitivity[3]. Gynecomastia has a variety of physiological and pathological causes, and these can be used to differentiate between idiopathic and related gynecomastia when making a differential diagnosis[4]. Due to the use of various assessment techniques and the examination of males of various ages and lifestyles, the incidence of gynecomastia was reported a range from 32 to 65%, while postmortem data suggest a prevalence of 40%[2].

The Simon BE classification of gynecomastiadivides into three degrees, is the one that is most frequently used for patients

Level 1: Slight breast growth, particularly close to the areola, without extra skin or a fatty chest; typically disappears on its own.

Level 2: There is considerable breast volume expansion, a more obese chest, and no margins are present. Level 2A, where there is no excess skin, and Level 2B, where there is excess skin, are separated in parallel. Basic liposuction typically involves surgery.

Level 3: Simulates a woman's breast; as a result, there is a rise in breast volume and extra skin that must be removed. Adults who are tall are typically affected.

However, in pathologies, the likelihood of an endocrine origin must be determined, for which morning serum testosterone levels (9 a.m.), sex hormone binding globulin (free testosterone), estradiol, thyroid hormones (TSH), gonadotropic hormone, luteinizing hormone, follicle stimulating hormone, and prolactin are used. If aberrant ratios are found, endocrinology should be consulted for the patient. Moreover, the functionality of the kidneys, liver, and occasionally the karyotypes or tumour markers are evaluated. When atypical gynecomastia occurs, ultrasound of the breast's soft tissues should be done to rule out the presence of any tumours or other injuries. Mammography, fine needle aspiration biopsy (FNAB), or TRU-needle CUT in elderly patients should also be done to rule for neoplasms. It is vital to obtain beta human chorionic gonadotropin, alpha-fetoprotein, and lactic dehydrogenase while dealing with the theory of testicular cancers[5].

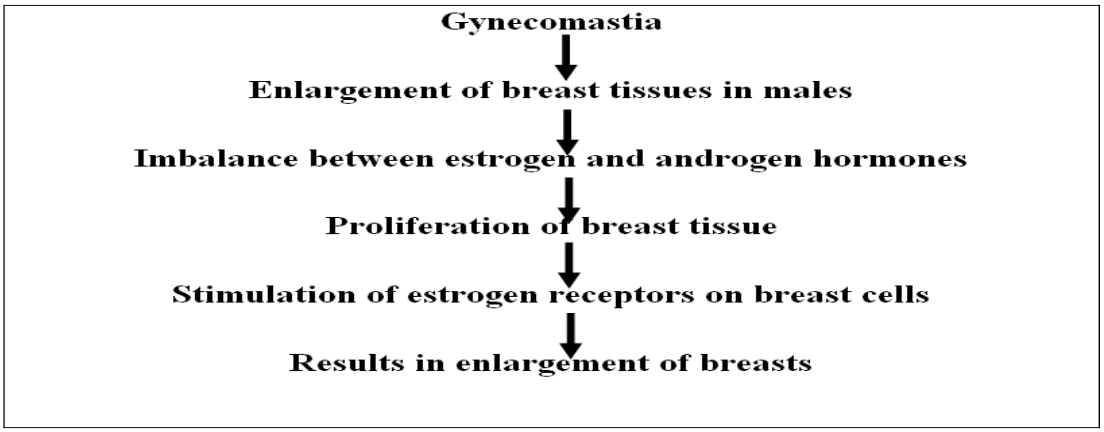
Omeprazole

Omeprazole, a proton pump inhibitor, is used to treat gastric and duodenal ulcers because it is a powerful inhibitor of acid secretion. Due to its potent inhibition of gastric acid secretion, omeprazole may interfere with the natural feedback regulation of stomach acid secretion[6]. Gynecomastia, or the growth of breast tissue in men, is one adverse consequence of PPIs that hasreceived relatively in one compactresearch.Proton-pump inhibitors frequently cause side effects such as nausea, vomiting, stomach pain, constipation, diarrhoea, flatulence, headaches, and dizziness. Gynecomastia is an ADR that is noted in the SPCs for Nexium® (esomeprazole) and Losec® (omeprazole), but not in the SPCs for the other proton-pump inhibitors[7].

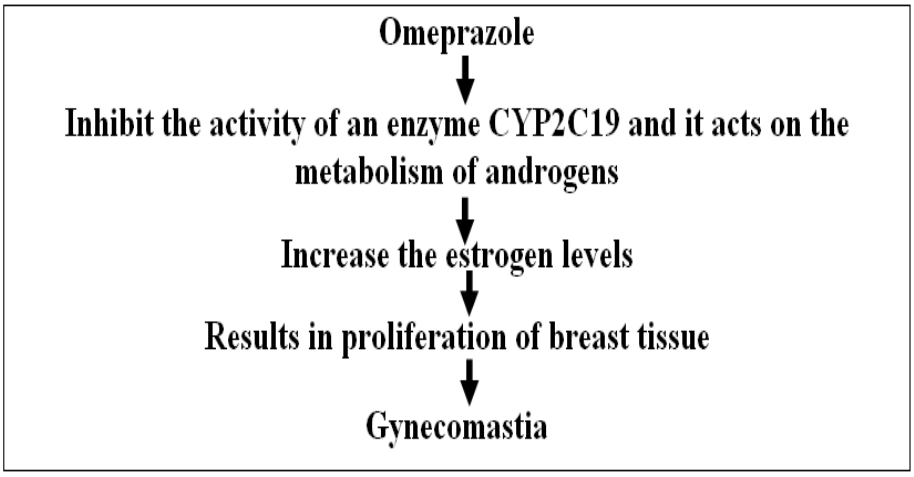
Mechanism behind omeprazole induced gynecomastia

Gynecomastia may be caused by an increase in the estrogen/androgen ratio as a result of omeprazole's inhibition of estradiol metabolism. This rise in estradiol serves as a common catalyst for the development of gynecomastia. The oxidation of estradiol, which is its main catabolic pathway, is substantially catalysed by cytochrome P450 (CYP)3A4, which is inhibited by omeprazole at high concentrations. This results in an increase in estradiol levels. Omeprazole is extensively metabolised by CYP2C19, for which more than 15 variant alleles associated with a decreased metabolism have been identified; the frequency of poor metabolizers among Europeans ranges from 1% to 6%; therefore, it is possible that such patients, when treated for long periods of time with higher doses of omeprazole, would be at particular risk for the development of gynaecomastia[7].

PATHOPHYSIOLOGICAL MECHANISMS OF GYNECOMASTIA



MECHANISM OF OMEPRAZOLE INDUCED GYNECOMASTIA



CASE SCENARIO:

A 66 years old male patient on Dec 2022 came to cardiac OP department with the complaint of burning sensation in the stomach followed by the diagnosis of **ulcer** and was prescribed with C.Omez (Omeprazole) 20 mg once daily in the morning before food for 3 months, he was also prescribed with other medications such as T.Clopidogrel 75 mg (OD), T.Aspirin 150 mg (OD), T.Atorvastatin 20 mg (OD), T.Atenolol 50 mg (OD), T.Enalapril 2.5 mg (OD) for the past medical history of ACS-PWMI/MODERATE LMS + CRITICAL 3 VESSEL DISEASE and MILD LV DYSFUNCTION and was called for review after 3 months. After 3 months patient came with the complaint of swollen breast tissue as the major symptom of gynaecomastia and it was conformed by the cardiologist as **omeprazole induced gynaecomastia.** So the cardiologist prescribed T.Ranitidine 150 mg Twice daily in the morning and night and stopped the drug omeprazole. The patient was advised to come for review after 2 months.

The Vital signs were found to be normal.

Table 1- Vital signs

Blood Pressure	Pulse Rate	Temperature	Spo2	Height	Weight	BMI
120/60 mmHg	69b/mt	96.5˚f	99%	166cm	64kg	25kg/m²

The Vital signs were found to be normal.

Documentation of reaction:

The **OMEPRAZOLE INDUCED GYNECOMASTIA** was reported and documented in the **Suspected Adverse drug Reaction Reporting Form** and **Naranjo Adverse drug reaction Probability scale**and the overall scoring in the Naranjo Adverse drug reaction probability scale was found to be **5 (Probable).**

Version-1.2

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

ForVOLUNTARYreportingofAdverseDrugReactionsbyHealthcareProfessionals

INDIANPHARMACOPOEIACOMMISSION (NationalCoordinationCentre-PharmacovigilanceProgrammeofIndia)Ministryof Health & Family Welfare,Government of India Sector-23,RajNagar,Ghaziabad – 201002	FORAMC/NCCUSEONLY AMCReportNo: .
ReportType ● Initial □ Followup	WorldwideUniqueNo: IN-IPC-300754104

A.PATIENTINFORMATION

1.PatientInitials	2. Age at time ofEvent or Date ofBirth:**66 Yrs**	3. **M** ● F □ Other□
Mr.T		4.Weight: **64 Kg**

12.Relevanttests/laboratorydatawithdates:

PHYSICAL EXAMINATION

B.SUSPECTEDADVERSEREACTION

5.Dateofreactionstarted(dd/mm/yyyy) **07/03/2023**

6.DateofRecovery (dd/mm/yyyy)
15/03/2023

7.Describethe reactionorproblem

OMEPRAZOLE INDUCED GYNECOMASTIA

13. Relevant medical/ medication history (e.g. allergies, race,pregnancy,smoking,alcohol abuse,hepatic/renaldysfunctionetc.)

NIL

14.Seriousness of thereaction:No●ifYes□(pleasetick anyone)

☐ Death(dd/mm/yyyy) □Congenital-anomaly
☐ Lifethreatening □Required intervention toPreventpermanent
☐ Hospitalization/Prolonged impairment/damage
☐ Disability □Other(specify)

15.Outcomes
I. Recovered [1] Recovering □ Not recoveredUnknown
II. Fatal [2] Recoveredwithsequelae□

C.SUSPECTEDMEDICATION(S)

S.No	8. Name(Brand/Generic)	Manufacturer(if known)	BatchNo. /Lot No.	Exp. Date(ifknown)	Dose used	Route used	Frequency(OD,BD etc.)	Therapydates		Indication	CausalityAssessment
								Datestarted	Datestopped		
I	**C.OMEPRAZOLE**				**2Omg**	**PO**	**1-0-0**			**ULCER**	**NARANJO**
Ii											
Iii											
Iv											

S.No	9.Action Taken(pleasetick)						10.Reactionreappearedafterre-introduction(pleasetick)			
As per C	Drug withdrawn	Doseincreased	Dose Reduced	Dosenot changed	Not applicable	Unknown	Yes	No	Effectunknown	Dose(if reintroduced)

I										
Ii										
Iii										
Iv										

11.Concomitantmedicalproductsincludingself-medicationandherbalremedieswiththerapy dates(Excludethoseusedtotreatreactions)

S.No	Name(Brand/Generic)	Doseused	Routeused	Frequency(OD,BD,etc.)	Therapydates		Indication
					DateStarted	Datestopped	
I	**T. CLOPIDOGREL**	**75mg**	**PO**	**0-0-1**			**CAD**
Ii	**T. ASPIRIN**	**150mg**	**PO**	**1-0-0**			**CAD**
Iii							

AdditionalInformation:

Due to an ulcer the patient has been taking **C. OMEPRAZOLE for 3 months** and after taking it for 3 months the patient was having **symptoms of gynecomastia**& the **culprit drug was withdrawn**& the patient is on recovering stage.

D.REPORTERDETAILS

16.NameandProfessionalAddress:**Aarthi A**

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Pin:**637205,**E-mail:**draarthi807@gmail.com**,

Tel.No.(withSTDcode) **6380270969**

Occupation:**Student**

Signature:**Aarthi A**

17.Dateofthisreport(dd/mm/yyyy):**13/03/2023**

Confidentiality:The patient's identityis held instrict confidence and protected to the fullest extent. Programme staff is notexpected to and will not disclose the reporter's identity in response to a request from the public. Submission of a report does notconstituteanadmissionthatmedical personnelormanufacturerortheproductcausedorcontributed tothereaction.

NaranjoAdverseDrugReactionProbabilityScale				
Questions	Yes	No	DoNot Know	Score
• Are there previous *conclusive* reports on this reaction?	+1	0	0	+1
• Did the adverse event appear after the suspected drug was administered?	+2	-1	0	0
• Did the adverse reaction improve when the drug was discontinued or a *Specific* antagonist was administered?	+1	0	0	+1
• Did the adverse event reappear when the drug was re-administered?	+2	-1	0	0
• Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	+2
• Did the reaction reappear when a placebo was given?	-1	+1	0	+1
• Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
• Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
• Did the patient have a similar reaction to the same or similar drugs in *any* Previous exposure?	+1	0	0	0
• Was the adverse event confirmed by any objective evidence?	+1	0	0	0
TOTAL SCORE:5				5

Modified from:Naranjo CA et al.A method for estimating the probability of adverse drug reactions.ClinPharmacolTher 1981;30:239-245.

SCORE : PROBABLE = 5

DISCUSSION

Gynecomastia is the most common cause of breast alteration in males and it can occurs in infants, puberty and old age. Johnson et al was suggested the prevalence rates of 60-90% in newborns, 50-60% in adolescents and 70% in men between 50 to 67 years [8]. Most of the drugs like spirinolactone, cimetidine, anti- androgens etc may cause gynecomastia. But omeprazole induced gynecomastia is a rare case report.

The corresponding authors of Luca santucci et al reported the rare case report of omeprazole induced gynecomastia and that drug may cause sexual impotence [9].

CONCLUSION:

As the patient was having swollen breast tissue as the major symptom of gynaecomastia and it was confirmed by the cardiologist as **omeprazole induced gynaecomastia.** So the causative drug was withdrawn and prescribedT.Ranitidine 150 mg Twice daily in the morning and night. The patient came for review after 2 months and it was found that the symptom was subsided. The patient was recoverd.

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