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Gynecomastia in a Patient Taking Meloxicam—A Case Report

Steven L. Rosas[1], Mark E. Deyo-Svendsen[1], Rachel Z. Oldfather[2], Michael R. Phillips[1], T. Andrew Israel[3], and Emily R. Weisenbeck[1]

Abstract

Gynecomastia is benign enlargement of glandular tissue in the male breast. It occurs due to an imbalance of estrogen and testosterone. It may be unilateral or bilateral. Physiologic gynecomastia commonly occurs in infants and during puberty and is self-limited. Gynecomastia may affect up to 50% of adult men over age 50 years old and can be related to underlying medical illness or caused by certain medications. Known causative agents include anti-androgenic and estrogenic drugs. Probable agents include alcohol and anti-ulcer, psychoactive, and antiretroviral medications. Non-steroidal anti-inflammatory drugs (NSAIDs) are not commonly associated with the development of gynecomastia. This case presents an instance in which the NSAID, meloxicam, was the only identified variable in a patient who developed unilateral gynecomastia. His breast tenderness and abnormal exam resolved spontaneously within 4 weeks of cessation of meloxicam therapy.

Keywords

NSAIDs, primary care, unilateral gynecomastia, reversible gynecomastia

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Introduction

Gynecomastia occurs when an imbalance of estrogen and testosterone causes benign proliferation of glandular breast tissue in men.[1] The diagnosis is made clinically by the finding of palpable enlargement of breast tissue in a male. Pseudogynecomastia, which is excess adipose rather than glandular breast tissue, can be ruled out by exam.[1,2] The most common causes of gynecomastia across all ages are physiologic (25%), idiopathic (25%), medication or substance abuse related (10-25%), hepatic cirrhosis (8%), primary hypogonadism (8%), hormone-secreting testicular or adrenal tumors (3%), and thyrotoxicosis (2%).[2-5] Male breast cancer is rare but should be considered in cases with unilateral gynecomastia.[2] A male with concerning signs such as a discrete, palpable breast mass, retraction of skin or bloody discharge warrants evaluation for carcinoma[6,7]

Physiologic disruption of sex-hormone imbalance can occur in the neonate, during puberty, and in older men.[1,2,4] Neonatal gynecomastia is likely due to transplacental maternal estrogens and spontaneously resolves within the first year of life.[2,4] Gynecomastia affects roughly 50% of young men during puberty, with 90% of cases resolving within 2 years of onset.[2] During early puberty, it is thought the testes may produce more estrogen relative to testosterone than during the late pubertal and post pubertal state when testosterone predominates.[1]

Men over age 50 may develop gynecomastia due to decreasing circulating androgens with resultant sex-hormone imbalance.[4]

Medication-induced gynecomastia has been associated with many different drug classes and is responsible for the majority of gynecomastia in adult men.[2,4] Krause[8] conducted a systematic review published in 2012 to categorize drug classes based on their likelihood to cause gynecomastia. Class A medications have a proven causal link to altering sex-hormone balance including anti-androgenic medications such as spironolactone, estrogenic drugs (which are used in treatment of prostate cancer),

[1]Department of Family Medicine, Mayo Clinic Health System – Northwest Wisconsin, Menomonie, WI, USA
[2]University of Minnesota Medical School, Minneapolis, MN, USA
[3]Department of Orthopedic Surgery, Mayo Clinic Health System – Northwest Wisconsin, Eau Claire, WI, USA

Corresponding Author:
Steven L. Rosas, Department of Family Medicine, Mayo Clinic Health System – Northwest Wisconsin, 200 First St. SW, Rochester, MN 55905, USA.
Email: rosas.steven@mayo.edu

finasteride and metoclopramide. Class B medications including ketoconazole, ranitidine, alcohol, antiretroviral medications, and human chorionic gonadotropin are considered to have a highly probable role in causing gynecomastia. Class C drugs, including angiotensin-converting enzyme inhibitors, have minimal supporting evidence to establish a significant association with gynecomastia.[2,8] Non-steroidal anti-inflammatory drugs (NSAIDs) were not included in any category from this review.

We present a case of unilateral gynecomastia in a 55-year-old man which occurred while taking the NSAID, meloxicam and spontaneously resolved after it was discontinued.

Case Description

A 55-year-old male presented with 4 months of left chest wall pain. He noted left nipple discomfort with tenderness to touch. He did not appreciate any enlargement of either breast.

Nine days prior to presentation, he had completed an 8-month course of daily meloxicam 15 mg for knee pain. He was not taking any other prescription, over-the-counter medication, herbal medications or supplements, or tetrahydrocannabinol (THC) containing compounds.

On exam, the patient had exquisite tenderness in the subareolar region of the left breast and palpable breast tissue 4 cm in diameter. The right breast tissue was neither enlarged nor tender.

The differential diagnosis of unilateral gynecomastia and options for further evaluation were discussed with the patient. The patient declined further evaluation but agreed to avoid use of meloxicam and other NSAID medications.

He returned 2 months later and reported that breast tissue tenderness resolved 4 weeks after meloxicam cessation. Clinical examination by the same clinician that had originally seen him revealed no tenderness or palpable breast tissue of either sub-areolar region.

Discussion

Gynecomastia is a common condition encountered in primary care. The diagnosis is determined by clinical exam.[1] Gynecomastia is not always associated with discomfort,[1] but subareolar tenderness helped define the onset and the resolution of the condition in this case.

A step wise algorithm for the evaluation of gynecomastia in the adult male has been developed.[6] A summary of this algorithm is as follows:

The initial physical exam is used to determine whether concerning features for carcinoma are present, such as a hard mass, eccentric location (not directly below the nipple), lack of mobility, skin changes, lymphadenopathy or bleeding from the nipple. Mammography is indicated in these situations. In addition to breast examination, scrotal exam is recommended for detection of testicular tumors. If exam is negative for concerning features and there is a likely causative agent with temporal association with the gynecomastia, further work up may not be needed. If there is not a likely causative agent, laboratory studies to evaluate hepatic, renal, and thyroid function are indicated. If these initial studies are normal, work up proceeds with evaluation of human chorionic gonadotropin (HCG), Prolactin, Luteinizing hormone (LH), and testosterone levels with further studies dependent on results of these tests.

Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) with COX (cyclooxygenase)-2 inhibition,[9] resulting in reduced production of prostaglandins.

We found no previous reports of gynecomastia associated with meloxicam use. However, gynecomastia has been reported with other NSAIDs, both the COX 1 inhibitor sulindac[10] and the COX 2 inhibitor rofecoxib.[11,12] These references present a total of 3 case reports, all of which were published as letters to the editor. There is evidence that the COX-1 inhibitor ibuprofen produces a state of hypogonadism,[13] which is a known etiology of gynecomastia.[1]

Evaluation of gynecomastia can be extensive and lead to significant cost, anxiety, and discomfort to patients. Medication use constitutes a large proportion of reversible causes of gynecomastia.[14,15] This case report presents meloxicam as a potential reversible cause of gynecomastia. If further studies support this etiology, a short period of careful monitoring following discontinuation of the potential offending agent would be appropriate. However, this information is presented as a call for further observation and careful review of medications in patients with gynecomastia. We suggest further evaluation for a possible association between NSAID's and gynecomastia such as database analysis or prospective studies. Clinicians should not use this case report to make clinical decisions in evaluation of a patient with gynecomastia.

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ORCID iDs

Steven L. Rosas https://orcid.org/0000-0001-8324-3144

Mark E. Deyo-Svendsen https://orcid.org/0000-0001-6446-630X

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