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Case Report

Ranitidine-Induced Gynecomastia

M.S. Bhatia[1], Priyanka Gautam[2], Rashmita Saha[2]

[1]Professor & Head, [2]Senior Resident,
Department of Psychiatry, University College of Medical Sciences, Delhi, India.

Corresponding Author: M.S. Bhatia

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ABSTRACT

Gynecomastia is usually physiological in nature but about 20% cases can be iatrogenic. Drug-induced gynecomastia is more common in adults than in children and adolescents. Several other drugs were reported to be associated with gynecomastia. These drugs include antimicrobials, antiulcer drugs, calcium channel blockers, CNS drugs, growth hormones, cytotoxic agents, statins, antiemetics and others. Ranitidine had been rarely reported to cause gynecomastia. We report a rare case of ranitidine- induced gynecomastia.

Key Words: Gynecomastia, iatrogenic, anti-ulcer drugs, ranitidine.

INTRODUCTION

Male mammal glandular tissue proliferates and increases in volume and this benign and generally reversible phenomenon is called gynecomastia. [1] It often causes psychological distress due to physical-appearance alterations. [2]

It is usually physiological in nature (neonatal, pubertal and senile gynecomastia), but sometimes it can be idiopathic (about 25% of cases). [1] Rarely, it is secondary to conditions affecting the levels of circulating sexual hormones (i.e. testicular or adrenal neoplasias, hepatic cirrhosis, hyperthyroidism, hypogonadism, obesity, refeeding syndrome). [2] About 20% cases are iatrogenic. [1] Drug-induced gynecomastia is more common in adults than in children and adolescents. [3]

The exact mechanism inducing gynecomastia is not always clear. An imbalance between estrogenic and androgenic effects on the breast is believed to be the main phenomenon. Excessive local production of estrogen due to increased aromatase activity, decreased estrogen degradation, or changes in androgen or estrogen receptors are all important. [4]

Several other drugs were reported to be associated with gynecomastia. [5-9] These drugs include antimicrobials (e.g. ketoconazole, metronidazole, isoniazid); antiulcer drugs (cimetidine, ranitidine, omeprazole); calcium channel blockers (e.g. diltiazem, verapamil, nifedipine), CNS drugs (e.g. amphetamines, diazepam, methyldopa, phenytoin, reserpine, tricyclic antidepressants, phenothiazines, olanzapine, risperidone), growth hormones, cytotoxic

agents (alkylating agents, vincristine, nitrosoureas, methotrexate), statins and antiemetics (e.g. metoclopramide, domperidone). Certain miscellaneous drugs (e.g. amiodarone, flutamide, furosemide, spironolactone, D-penicillamine, theophylline, marijuana, alcohol) have also been reported to cause the phenomenon.

CASE REPORT

A 17 year old boy presented to psychiatry outpatient unit with complaints of talking big, singing without provocation, excitability, irritable if interrupted, wandering away, spending spree, and decreased need for sleep and food for last 4 weeks. The symptoms had exacerbated for last one week that he became argumentative, had fight with neighbors and wanted to run away from home. There was no history suggestive of suspiciousness, head injury, seizure disorder, drug abuse or medical disorder. There was no past or family of any psychiatric illness.

His mental status examination revealed increased psychomotor activity, increased amount and pressure of speech. His flow of thought was increased and there were delusion of grandiosity. Cognitive function tests revealed poor concentration.

Routine investigations including hemoglobin, complete blood count, renal function tests, liver function tests, lipid profile, blood sugar, urine routine microscopy were all normal. His weight was 55 kg. Provisional diagnosis of mania was made and he was started on aripiprazole 15 mg daily, divalproex sodium 500 mg twice daily and tablet clonazepam 0.5 mg, if required. After 2 weeks he reported slight improvement in manic features and he complained of burning in epigastrium. The dose of aripiprazole was increased to 30 mg and tablet ranitidine was started 150 mg twice daily. There was marked improvement in manic features after 8 weeks. His mother complained that he is having enlargement of breast. Physical examination revealed enlarged breast suggestive of gynecomastia (Figure). He was referred to endocrinologist for opinion, who confirmed it to be a case of gynecomastia. The secondary sexual characteristics were normal. He was investigated and his thyroid functions, lipid profile, serum prolactin, testosterone, FSH/LH, ultrasonography of abdomen, EEG and CT scan (head) were normal. The literature search showed that antiulcer medication, commonly cimetidine and rarely omeprazole and ranitidine have been reported to cause gynecomastia. His anti-manic drugs continued but ranitidine was stopped. Within 8 weeks, the gynecomastia regressed and then disappeared. On following up after 3 months, he again developed gynecomastia. On scrutiny of prescription, it was noticed that a family physician had again prescribed him ranitidine for his complaint of belching. Ranitidine was again stopped and he was advised to take antacids, whenever required. The gynecomastia disappeared after 8 weeks.

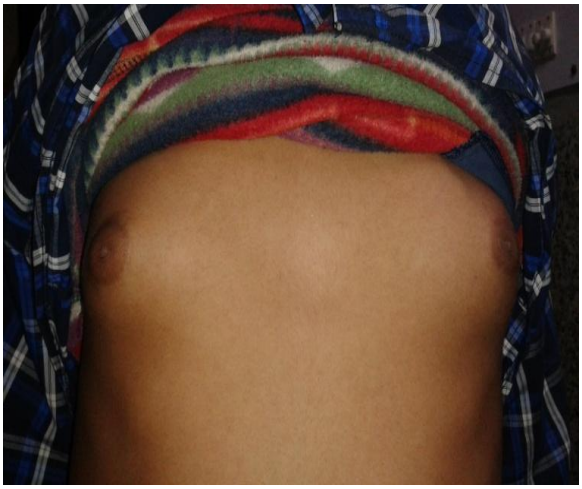

Figure 1: Showing gynecomastia.

DISCUSSION

Gynecomastia has been frequently associated as a side effect of cimetidine, and

has been less commonly associated with omeprazole. Ranitidine had been reported to cause gynecomastia in a single case report. [10] The present case is also a ranitidine-induced gynecomastia. The exact mechanism how anti-ulcer drugs induce gynecomastia is not known. [1,4,5,11] If the gynecomastia is drug-induced, discontinuance of the agent may be all that is needed as was found to be effective in the present case.

CONCLUSION

Drug-induced gynecomastia though common in clinical practice, often goes unrecognized. Many drugs including anti-ulcer ones have been implicated in its causation. Gynecomastia had been commonly reported with cimetidine and less commonly with omeprazole. The present case developed gynecomastia with ranitidine, which disappeared on discontinuation but reappeared on rechallenge. Since anti-ulcer drugs are commonly used in practice and that on chronic basis, the clinicians must be aware about this side-effect because mere discontinuation of drugs results in remission.

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