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Case Report

Drug Induced Expressible Galactorrhea in Patient with Fibromyalgia and Vascular Headache

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Abstract

Drug-induced Galactorrhea associated with Hyperprolactinemia has been rarely reported with agents such as antidopaminergic, antiemetics, antidepressants etc. Galactorrhea related with Hyperprolactinemia is an unwanted consequence of the treatment in which there is an increased serum prolactin levels usually associated with an abnormal whitish fluid like secretion from the breast. We report a case of expressible Galactorrhea at multiple occasions in a 44-year-old female patient with Fibromyalgia and Vascular headache related to Fluoxetine, Amitriptyline, Flunarizine, Domperidone used at different intervals of treatment. This report highlights the mechanism of these drugs which induces galactorrhea and subsequent reduction in the side effect when the active drugs are withdrawn.

Keywords: Hyperprolactinemia, Galactorrhea, Prolactin, Fluoxetine, Amitriptyline, Flunarizine, Domperidone.

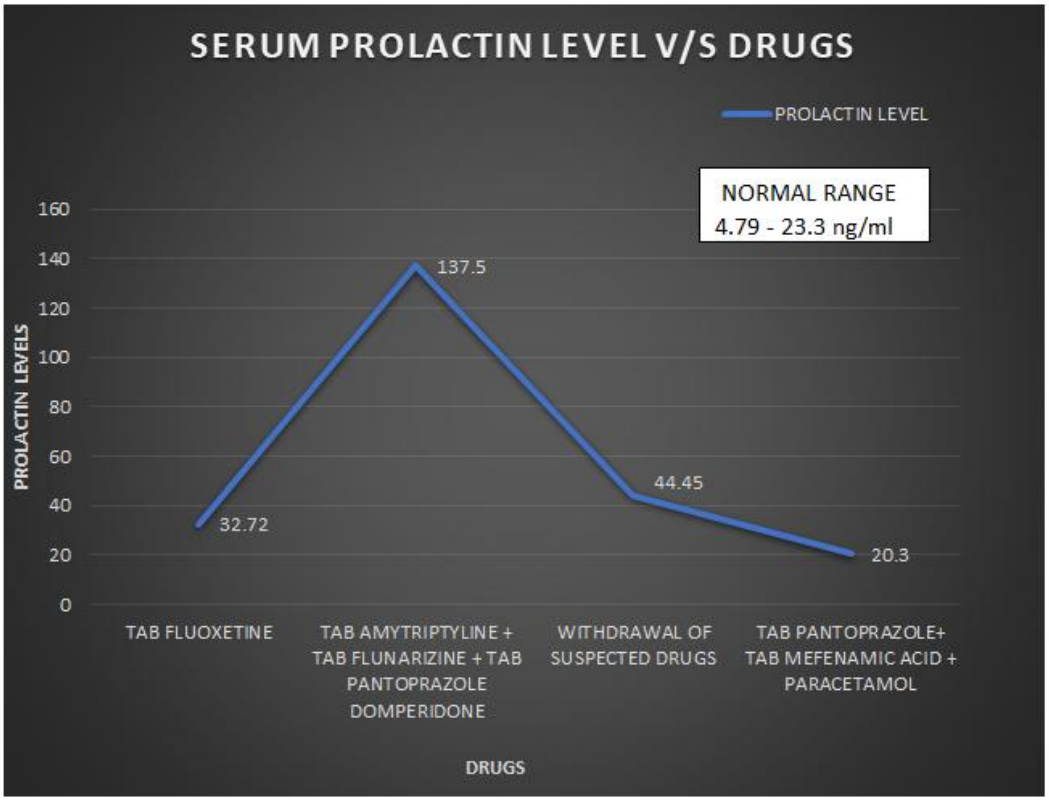
INTRODUCTION

Drug-Induced Hyperprolactinemia associated with Galactorrhea is an undesirable effect that has been rarely reported with agents such as antidopaminergic, antiemetics, antipsychotics, anti-depressants, etc [1]. Selective serotonin reuptake inhibitors (SSRI) and Tricyclic antidepressants are less considered to cause galactorrhea [2, 3]. Fluoxetine and Amitriptyline is a class of selective serotonin reuptake inhibitors and tricyclic antidepressants respectively. Serotonin stimulates prolactin release directly through postsynaptic 5- Hydroxytryptamine receptors in the hypothalamus [4], or indirectly by inhibition of 5-HT mediated tuberoinfundibular dopaminergic neurons [5]. Fluoxetine and Amitriptyline induced Galactorrhea is not often reported among anti-depressant related side effects. Domperidone is a peripherally acting Dopamine receptor antagonist, which has a dominant role in gastric and intestinal smooth muscle motility and is commonly used to relieve the symptoms such as nausea, vomiting and hiccoughs. The drug as an anti-emetic blocks the dopamine receptors in the chemoreceptor trigger zone present in the anterior pituitary which results in the elevation of serum prolactin usually <100ng/ml. Neurological adverse effects and hyperprolactinemia are reported rarely. Abdominal cramps, diarrhoea, constipation, mastalgia are the least observed side effects of the drug treatment. Flunarizine, a calcium antagonist which is widely used for the treatment of migraine and vertigo, hinder central dopaminergic systems which may increase basal and stimulated prolactin levels with a consequent resetting of a hypo-modulated central opioid tonus toward normal values. We are reporting a case of a 44-year-old lady who developed an expressible Galactorrhea associated with Hyperprolactinemia while on treatment with these Drugs on different occasions. Fluoxetine, Amitriptyline, Domperidone, Flunarizine.

CASE HISTORY

44-year-old female patient with a known case of Fibroid Uterus and had s/p TLH+B/L salpingectomy. Clinical diagnosis of the patient was made and presented to the OP with complaints of Fatigue, Generalised aches and pains, Fibromyalgia and Vascular headache. She was then started on Tab Fluoxetine 10mg 0-0-1 which showed a progressive improvement in the patient's complaints. However, the

patient developed Expressible Galactorrhea (whitish discharge from the patient's right nipple/breast) with breast pain. The patient had no previous history of galactorrhea, thyroid disease and polycystic ovarian disease. The Patient hasn't noticed any dark coloured or foul-smelling discharge from her nipple nor did she report any sexual dysfunction. The patient's serum prolactin showed an elevated value of 32.72 ng/ml (ref range 4.79–23.3ng/ml). Because the patient's galactorrhea developed after initiation of prescribed medication i.e., Tab fluoxetine, the medication was discontinued. The patient showed subsequent reduction and cessation of galactorrhea. The patient was then started on Tab Amitriptyline 10mg 0-0-1, Tab Flunarizine 10mg 0-0-1 and Tab Pantoprazole Domperidone 1-0-0 in view of Intermittent giddiness, Nausea, Dyspepsia and unilateral headache. However, the patient has again witnessed spontaneous discharge of whitish fluid from the right breast/nipple (Expressible Galactorrhea), based on which her serum prolactin levels were sent for investigation and the result showed a marked increase in the blood prolactin level of 137.50 ng/ml (hyperprolactinemia). No visual defects, no other significant clinical features suggestive of microadenoma was detected and hence upon discussion with the Endocrinology department, the decision was made to stop the offending drugs which cause the adverse reaction in the patient. Hyperprolactinemia secondary to drugs the patient has been advised to stop Tab. Amitriptyline, Tab Flunarizine and a combination of Tab Pantoprazole Domperidone. After stopping these medications patient's Blood Prolactin levels showed a significant reduction to 44.45 ng/ml (pooled prolactin) and her symptoms subsided. During 6 months of follow up period, the patient remained well on Tab Pantoprazole 40mg 1-0-0, Tab Meftal Forte 1 sos (Mefenamic Acid + Paracetamol) for Vascular headache and dyspepsia and there was no redevelopment of galactorrhea and prolactin levels were pooled and diluted, attained a normal value of 20.3ng/ml with a normal mammogram.



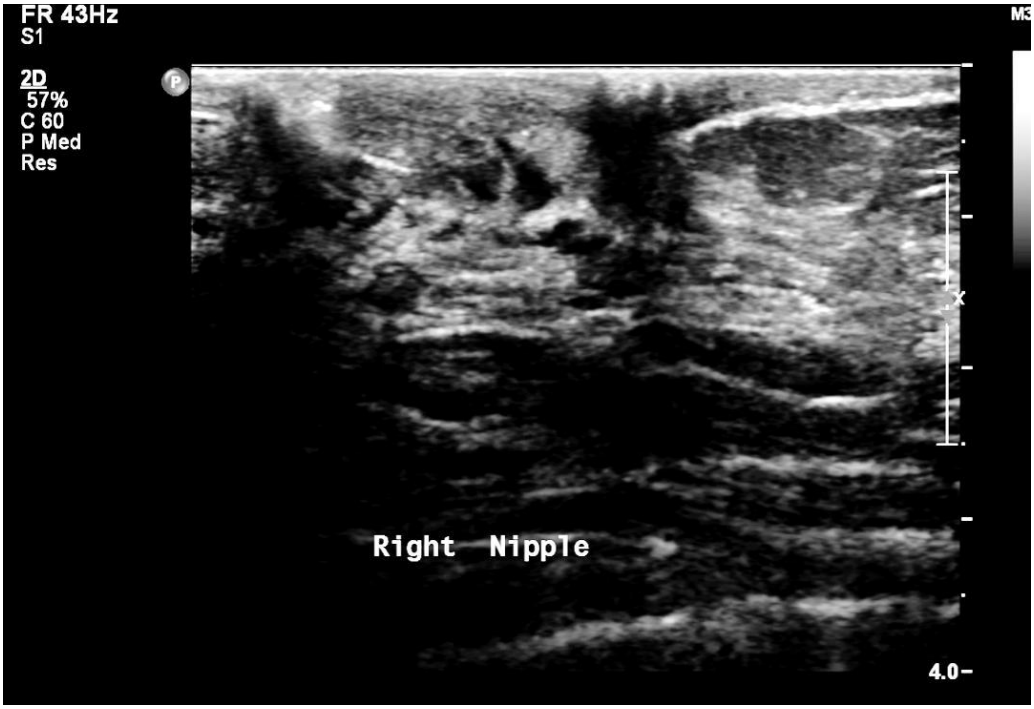


Figure showing mammogram of the right breast

DISCUSSION

The treatment with Fluoxetine showed a dramatic elevation in prolactin levels resulted in inducing other stimuli such as fenfluramine, insulin and 5-hydroxytryptamine [6]. The exact mechanism of galactorrhoea is always unpredictable and unknown. The patient developed galactorrhoea with an elevation of serum prolactin after beginning fluoxetine therapy. The relation between the use of the active drug and the onset of galactorrhoea, as well as the resolution when the drug was discontinued, suggests a link between the two phenomena. In the literature, there are a limited number of case reports on the emergence of hyperprolactinemia during fluoxetine treatment with results resembling those reported. In the case with drug Amitriptyline, which belongs to the class of Tricyclic antidepressants, dopamine strongly inhibits the prolactin release as a result of which serotonin exerts a stimulatory role in the release of prolactin by making the well profound action on postsynaptic 5-hydroxytryptamine receptors located in the hypothalamus or by indirectly inhibiting the tuberoinfundibular dopaminergic pathway. Domperidone is a selective dopaminergic (D2) receptor antagonist which peripherally restricts the activity to the upper GI tract. Moreover, it inhibits the effects associated with motility including lower oesophageal sphincter and intraabdominal pressure. Domperidone does not usually cause extrapyramidal symptoms by crossing the blood-brain barrier but exerts some kind of side effects in some parts of the central nervous system that lack this barrier, such as the chemoreceptor trigger zone. The Extrapyramidal syndromes and hyperprolactinemia are reported rarely. Stomach aches, diarrhoea, constipation, myalgia includes other side effects which have been rarely seen [7]. Flunarizine, Calcium antagonists act by blockade of voltage-gated L-typed Ca2+. Various hypotheses have been considered: blocking of 5-HT release, interfering with neurovascular inflammation or cortical spreading depression, inhibition of CGRP release, enhancing of analgesic effect. Although expressible galactorrhea induced by these medications is rarely seen, the patient developed expressible galactorrhea with a normal mammogram, indicating a causal relationship between medication usage onset and galactorrhea.

CONCLUSION

Physicians should consider these medications (fluoxetine, Amitriptyline, Flunarizine, Domperidone) as an elicit case for galactorrhea even with normal prolactin levels. However, serum prolactin levels are not routinely tested in clinical practice unless clinical symptoms such as galactorrhea occur. Therefore, potential aetiological factors should be investigated in patients presenting with galactorrhea by determining the prolactin level and by cranial MRI. Both physician and caregiver have to be vigilant regarding these rare side effects. Such drug-induced adverse effects would require a change of the drug altogether, as was the case with our patient.

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