CASE REPORT

Good clinical history scores over extensive workup in unmasking a case of galactorrhoea

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SUMMARY

The clinical presentation of a young woman with galactorrhoea is described in detail including the history and clinical examination findings. While the patient and her family members feared a serious medical condition which had so far been an obscurity despite a number of investigations, we tried to diagnose the patient starting from the basics, which after a proper history revealed a levosulpiride-induced galactorrhoea. This again lays emphasis on the old adage in medical field that 'a proper history and examination are the key to diagnosis'. There are few reports pertaining to levosulpiride-induced galactorrhoea making it a rare side effect of this drug. We further try to discuss the different causes of galactorrhoea in a young non-pregnant woman which can be encountered in clinical practice.

BACKGROUND

Hyperprolactinaemia that presents as a gynaecological problem may or may not be accompanied by galactorrhoea, and galactorrhoea cannot be a certain proof for hyperprolactinaemia.¹ Although there are many causes of galactorrhoea, drug-induced hyperprolactinaemia with galactorrhoea is a common entity which is often neglected in view of finding a fascinating pathological cause for it. Many drugs are known to cause hyperprolactinaemia (typical antipsychotics, antidepressants, antihypertensives), but many a times this side effect is still missed despite being caused by a known agent due to lack of knowledge regarding mechanism of action of drugs among physicians—levosulpiride in our case.

CASE PRESENTATION

A 21-year-old unmarried woman of Pauri district of the Indian state of Uttarakhand presented to the out-patient department of Internal Medicine, All India Institute of Medical Sciences, Rishikesh with complaints of milky discharge from both nipples since 3 months. Initially, discharge occurred on few occasions but presently its frequency and amount had increased to the extent of staining her clothes. There was no history of recent sexual intercourse, nipple stimulation, visual disturbances, headache, trauma, abnormal uterine bleeding, breast lump, cyclical mastalgia, family history of breast cancer, cough, breathlessness, haemoptysis, haematuria, burning micturition, lethargy, cold intolerance, use of ill-fitting brassiere, trauma, breast or spinal cord surgery and trauma. The patient also complained of

depressed mood, feeling of hopelessness, insomnia and decreased appetite from the past 3 months. She reported a recent weight gain of approximately 3 kg in the last 2 months. She had irregular cycles from past 2 months—cycle length ranging 40–45 days, bled for 5 days, amount seemed to be normal, no dysmenorrhoea and no clot passage. Menarche was reported at 14 years of age.

On probing the patient further, it was brought to notice that she had complaints of dyspeptic symptoms from the last 1 year for which she used to consume levosulpiride over the counter, on and off without prescription which her brother used to bring for her from a local pharmacy.

On general examination, vitals of the patient were stable. No coarse facies, coarse hair, abdominal stria, buffalo hump. Breast examination revealed B/L symmetrical breast with no lump but discharge was present—milky, thick in consistency, not blood tinged. The skin over breast seemed normal with no overlying lesion. All the systemic examinations were within normal limits. On ophthalmological reference, there was no visual field defect, 6/6 visual acuity and no extraocular muscle deficit.

INVESTIGATIONS

Urine pregnancy test of patient was negative. On reviewing the previous reports—serum thyroid-stimulating hormone (STH) 1.32 μ U/mL (normal), serum prolactin 130.55 ng/mL (high value, normal = 2–29 ng/mL for non-pregnant woman), luteinising hormone (LH)—5.3 mIU/mL (normal), follicle-stimulating hormone (FSH)—6.2 mIU/mL (normal). Her random blood glucose, serum cortisol, liver function test, kidney function test, urine routine/microscopy and haemogram were found to be appropriate for her age. An MRI brain done 15 days back showed a normal study. Ultrasonogram (USG) bilateral breast showed prominent ducts measuring 1.8–2 mm in diameter bilaterally. Chest X-ray was also normal. She was further worked up for gastritis which showed urease positive *Helicobacter pylori* gastritis. Upper gastrointestinal (GI) endoscopy was found to be normal.

DIFFERENTIAL DIAGNOSIS

The investigations done before the patient presented to physician had exhausted the patient economically as well as mentally as during the process she was being counselled that we are searching for some tumour somewhere.

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Based on history, examination and investigations, local and central causes of hyperprolactinaemia with galactorrhoea were ruled out. Hence, a diagnosis of levosulpiride-induced galactorrhoea was made based on adverse effect profile of antipsychotic drugs. Basically, drug-induced galactorrhoea is diagnosis of exclusion. One has to rule out all the possible causes to reach this diagnosis. The following are a few causes which were kept in mind while working up the aforementioned case.

The physiological causes of hyperprolactinaemia include stress, sucking, sleep, sexual intercourse, puberty and menopause. The patient was stressed due to galactorrhoea; stress did not induce galactorrhoea in her. There was no history pertaining to recent sexual intercourse, nipple stimulation and so on.

Although galactorrhoea is not associated with breast cancer, it may be associated with pituitary neoplasm—most commonly prolactinoma and non-pituitary malignancies—bronchogenic carcinoma, renal adenocarcinoma and so on. The patient presented to the gynaecologist with the complain of galactorrhoea where pituitary neoplasm was considered, and she was referred to ophthalmologist for ruling out any visual field defects. MRI brain was done subsequently to be sure as patients symptoms persisted, the reports were normal.

Hypothalamic pituitary disorders causing galactorrhoea include craniopharyngioma, empty sella syndrome and infiltrative disorders. Certain endocrine disorders have been associated with hyperprolactinaemia—hypothyroidism, Cushing syndrome, acromegaly. The patient had no history suggestive of cold intolerance, lethargy (she had weight loss but no weight gain), examination showed no clinical features suggestive of hypothyroidism, serum TSH along with T3 and T4 were normal. The patient had no clinical features suggestive of Cushing syndrome like striae, buffalo hump, disproportionate limb growth, coarse facies. Morning serum cortisol levels were normal. Additional tests done to rule out acromegaly, pituitary involvement like glucose tolerance tests, serum FSH, serum LH were normal. Galactorrhoea can occur due to chest wall irritation due to ill-fitting brassieres, skin conditions such as herpes simplex, atopic dermatitis and burns. There was no such lesion found on current examination or in the past.

Breast surgeries, including implant placement and reduction mammoplasty can cause postoperative galactorrhoea. Case reports have discussed galactorrhoea associated with spinal cord injury or surgery, as well as cord tumours.^{2,3} Severe oesophagitis and oesophageal reflux may cause galactorrhoea by stimulating the thoracic and spinal nerves.⁴ There was no such history of surgery or trauma. Although the patient had *H. pylori* gastritis, this was not distressing her to the limit so as to irritate the nerves and this did not explain the increased serum prolactin levels. Furthermore, the improvement of galactorrhoea and serum prolactin levels on stopping the drug proved the causative aetiology.

TREATMENT

Patient was advised to defer further consumption of levosulpiride. She was given triple therapy for *H. pylori*—(tablet) omeprazole, clarithromycin and amoxicillin. She was referred to psychiatry for depression where she was given counselling and selective serotonin reuptake inhibitor (SSRI)—fluoxetine was started.

OUTCOME AND FOLLOW-UP

On follow-up visit of patient after 2 months, she had improved symptomatically and her serum prolactin levels were found to be

well within the normal range. Her mood was found to be better and she was doing well in her daily life.

DISCUSSION

Galactorrhoea is the term given to inappropriate lactation from breast. It is a relatively common problem but exact incidence is unknown, it is estimated that about 20%–25% experience this during their lifetime.⁵ Some studies have suggested the prevalence of hyperprolactinaemia is 61% and galactorrhoea 48% in women with abnormal uterine bleeding.¹ Lactation requires intricate web of oestrogen, progesterone and prolactin (the release of which inhibited by dopamine and increased by thyrotropin-releasing hormone).

Drug-induced galactorrhoea with hyperprolactinaemia is a common occurrence, but its generally missed in practice. But certain drugs have known association with hyperprolactinaemia which should always be considered in the list of differentials so that it saves the patient from extensive and economically burdening investigations. The following are few well known and lesser known causes of hyperprolactinaemia:

- Antipsychotics—phenothiazines;
- Antihypertensives—atenolol, methyldopa, verapamil, reserpine;
- Antihistamines (H2)—cimetidine, ranitidine;
- Antidepressants—SSRIs, buspirone, alprazolam;
- Others—octreotide, domperidone, triptans, valproic acid.

Patient's perspective

I was suffering from this illness for a long time. Initially I could not muster the courage to tell about it to any of my family members. I used to feel very shy. When the problem worsened and my clothes started getting stained, I had to tell my mother, who discussed it with my father. We consulted many doctors, but my symptoms did not abate. I consulted with a gynaecologist. She ordered many investigations and started me on treatment but to no avail. I was asked to undergo an MRI of my brain because a brain tumour was suspected. It caused a lot of anxiety and panic for me as well as my family because I was wanting to get married soon, and other relatives also came to know about it. Due to this, my marriage was in jeopardy. I later consulted with the physician in the Medicine department, who checked all my investigations and then told me that the medication I am taking for my gas in the stomach might be the cause of my symptoms. Then they stopped my medication. This led to relief of my symptoms. It was a thing of immense relief to me. That is why I have written this personal statement, so that someone else may also benefit from this.

Learning points

- ▶ In a young non-lactating woman presenting with galactorrhoea, the possibility of a drug-induced cause can be easily ruled out based on a good history alone which is often missed in search for some elusive organic cause.
- ▶ Levosulpiride is a drug which is commonly prescribed not just as an antipsychotic but also for dyspepsia.
- ▶ While prescribing drugs like levosulpiride, especially for longer periods, the patient needs to be educated about the commoner as well as rarer adverse effects because with long-term use, the rare side effects may become more frequent.

But there have not been many reports as far as our knowledge in an Indian context is concerned, exemplifying levosulpiride to be a cause of galactorrhoea. However owing to its close relation with antipsychotics in dopaminergic blockade, it can cause galactorrhoea and amenorrhoea as explained in a few clinical trials.⁶

Levosulpiride is levorotatory enantiomer of sulpiride, a substituted benzamide. Chemically, it is N-(1-ethylpyrrolidin-2-yl) methyl- 2methoxy-5- sulfamoyl-benzamide. The drug is being used as an antipsychotic, an antidepressant, an antiemetic and an antidyspeptic.⁷ It may also find use in treatment of somatoform disorders, premature ejaculation, burning mouth syndrome.^{8 9} The mechanism of action of levosulpiride for antipsychotic and dyspeptic action is blockade of dopaminergic receptors D₂, preferentially located at presynaptic membranes in brain and GI tract.⁷ There has been a postulated role of the drug in 5-HT₄ receptor stimulation for its efficacy as a prokinetic agent.

It is well known to cause movement disorders due to dopamine inhibition as rabbit syndrome, acute dystonias, parkinsonism-like features.¹⁰ As with other antipsychotic (first generation—typical), levosulpiride can also block dopamine release which is inhibitory to prolactin release causing hyperprolactinaemia.

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