Key Words: Risperidone, Fluvoxamine, Galactorrhea, Gynecomastia

Euprolactinemic Gynecomastia and Galactorrhea with Risperidone-Fluvoxamine Combination

By Pratheesh P.J., Samir Kumar Praharaj, Ashish Srivastava

ABSTRACT *~ Risperidone is associated with hyperprolactinemia and its consequent symptoms such as gynnecomastia, galactorrhea and sexual dysfunction in adults, and less so in adolescents. Rarely, serotonin reuptake inhibitors are also associated with such adverse effects. We report a case of gynecomastia and galactorrhea in an adolescent male while on a combination of risperidone and fluvoxamine, although the serum prolactin was within normal range.* Psychopharmacology Bulletin. *2011;44(1):70–73.*

INTRODUCTION

Serotonin reuptake inhibitors and atypical antipsychotics are commonly prescribed medications in the treatment of obsessive-compulsive disorder (OCD). In adults, risperidonehas been reported to cause a marked and sustainedincrease in serum prolactin levels in a sizeable proportion of patients,[1] where as in children and adolescents it has a lesser effect on prolactin concentrationsduring short-term treatment and a negligible effect during long-term treatment.[2] Prolactin-related adverse effects such asgynecomastia in boys and amenorrhea, menorrhagia, breast enlargement, and galactorrhea in girls were reported in 2.2% of children,[2] in contrast with adults where prevalence varies from 9% to 12% in women and from 8% to 19% in men.[3] The lower rates in children and adolescents have been attributed to lower doses of risperidone used in these population, and with higher doses, 5 out of 10 adolescents developed symptomatic hyper prolactinemia.[4] Rarely, SRIs may also lead to increase in prolactin levels with resultant symptoms. Cases of hyperprolactinemia and galactorrhea induced by SSRIs including sertraline,[5] fluoxetine,[6]

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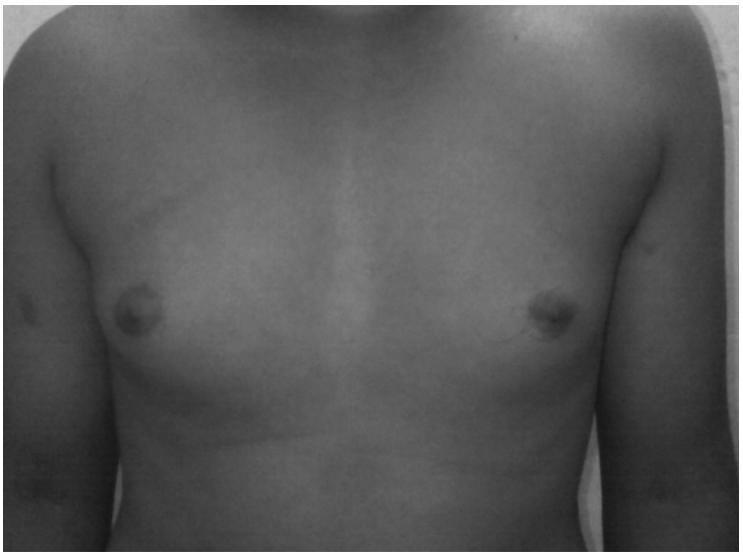
escitalopram[7,8] and fluvoxamine[9] treatment have been reported. We report a case of adolescent male having OCD, who developed gynaecomastia with galactorrhea with normal prolactin levels on a combination of fluvoxamine and risperidone.

CASE REPORT

Mr. S, a 19-year-old single male diagnosed with obsessive-compulsive disorder (OCD) of 3 years duration, presented with history of obsessional doubt that there is something in his mouth and had compulsions to spit repeatedly. He also had doubts that he hasuttered something wrong and would frequently seek reassurance. His birth, developmental and family history was unremarkable. There was no past history major medical or psychiatric illness. He was prescribed sustained-release paroxetine 12.5 mg per day along with risperidone 3 mg per day by a psychiatrist. Because of excessive sedation with paroxetine, it was changed to fluvoxamine 50 mg per day that was gradually increased to 150 mg per day. After 6 to 8 months of therapy, patient reported having bilateral breast enlargement and whitish discharge, but continued to take the medications for two years. Later fluvoxamine was changed to clomipramine, the reason for which is not known. At presentation, his obsessive symptoms were controlled on a combination of clomipramine 75 mg and risperidone 3 mg per day.

FIGURE 1

BILATERAL GYNECOMASTIA



On physical examination, he had bilateral gynecomastia (fig. 1) with galactorrhea. He did not have history of visual disturbances. His libido was normal and there was no history of any sexual dysfunction. Investigations including complete blood counts, renal and hepatic function tests were normal. Also, thyroid profile and serum prolactin levels were within normal range. MRI scan of the brain did not reveal any abnormality. Risperidone was discontinued and he was started on aripiprazole 15 mg per day, and clomipramine was continued on the previous dose of 75 mg per day. Within 10 days of this regimen, there was significant reduction in galactorrhea and it completely stopped in next 10 days. He was referred to plastic surgeon for persistent gynecomastia who advised bilateral mastectomy. Aripiprazole was tapered gradually over the next six weeks and he continues to remain asymptomatic on clomipramine 75 mg per day.

DISCUSSION

In our case, risperidone is the likely culprit, though a rarer possibility of fluvoxamine-induced galactorrhea and gynecomastia cannot be ruled out. Also, the drug interaction between the two might have contributed to such adverse effect. It has been reported that higher doses of fluvoxamine (more than 100 mg per day) may elevate plasma risperidone levels, presumably as a result of a dose-dependent inhibitory effect of fluvoxamine on CYP2D6 and 3A4 mediated 9-hydroxylation of risperidone.[10] In OCD, even risperidone 0.5 mg per day has been shown to be helpful in fluvoxamine non-responders.[11] Therefore, such low dose strategy should be tried first to reduce adverse effects of such combination treatment.

Risperidone, a serotonin-dopamine antagonist, presumably reverses the tonic dopaminergic inhibition of prolactin production in the anterior pituitary resulting in hyperprolactinemia through D_2-receptor antagonism in the tuberoinfundibular tract.[1,2,4] SRIs may cause hyperprolactinemia by a serotoninergic-mediated inhibition of dopamineneurons at the hypothalamus, which exert a tonic inhibitory control over prolactin release.[5–9] In most reported cases, drug-induced galactorrhea and gynecomastia have been associated with increased prolactin levels. Rarely, galactorrhea is described with normal prolactin levels,[12] as seen in our case study.

Aripirazole, a dopamine-system stabilizer, has been reported to reverse risperidone-induced hyperprolactinemia,[13] as noted in our case. Our patient continued medications for two years after onset of such symptoms, which is quite unusual. One possible explanation could be shame associated with disclosure of these adverse effects that prevented

from seeking help earlier. Therefore, it is prudent to actively enquire for such adverse effects of risperidone in adolescents, even with lower prescribed doses. ✤

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