Management of a Patient with Schizophrenia and Underlying Pituitary Macroadenoma

Dear Editor,

Hyperprolactinemia was found to be prevalent in a multi-centred study of 402 patients with schizophrenia, schizoaffective disorder and schizophreniform disorder treated with conventional antipsychotics and Risperidone.[1] Antipsychotics inhibit the dopamine receptors and induce hyperprolactinemia via the tubulo-infundibular pathway, with subsequent downstream effects on multiple systems. Hyperprolactinemia brings about reduction in oestrogen and testosterone, causing bone resorption and reduced bone mineral density. Hyperprolactinemia in women causes lowered oestrogen and nitric oxide levels, with a consequent elevation of blood pressure. Hyperprolactinemia causes diminished sexual drive and menstrual irregularities, and may increase a person's risk of developing breast cancer. The following case report will focus on the management of a patient with schizophrenia and underlying pituitary macroadenoma with hyperprolactinemia.

Case Report

Ms P is a 29-year-old Singaporean female, with a family history of schizophrenia. She presented to the psychiatric hospital after hearing voices for a month, and believed that people could read her thoughts and that they wanted to kill her. Mental state examination revealed presence of auditory hallucinations in 3rd person, delusions of thought broadcast and persecution. Laboratory investigations of full blood count, liver and thyroid functions were normal and her urine drug screen was negative for illicit substances. She was diagnosed with paranoid schizophrenia and started on Trifluoperazine. However, because of non-compliance, Ms P required 2 hospitalisations for worsening psychotic symptoms. Due to Ms P's poor response during the course of her illness, her medications were switched several times, alternating between Risperidone and Olanzapine which are atypical antipsychotics. During her second admission when she was still on Risperidone, Ms P complained of poor memory and concentration. She reported visions of ghosts. Mental state examination revealed new onset visual hallucinations and persistent persecutory delusions.

In view of her poor response to antipsychotics, and newly developed visual hallucinations, a computed tomography (CT) scan of the brain was ordered and showed a homogenous pituitary mass. Subsequent magnetic resonance imaging (MRI) scan of the brain showed a 28 x 24 x 16 mm mass that occupied the whole pituitary fossa, with expansions inferiorly within the sphenoid sinus, laterally into the left cavernous sinus and superiorly on to the optic chiasma, which was compressed and displaced. Findings were suggestive of a long-standing pituitary macroadenoma.

Ms P was transferred to a general hospital for further management. She was managed by a multidisciplinary team which included a neurologist, neurosurgeon, endocrinologist, ophthalmologist and psychiatrist. Subsequent investigations revealed serum prolactin level of 13,588 mIU/L (Premenopausal: 64 - 575; Postmenopausal: 64 - 426). Polyethylene glycol (PEG) prolactin level was 84% (<40% Predictive of tetrameric macroprolactin; 40% to 60% Equivocal; >60% Predictive of monomeric prolactin). Other investigations included Adrenocorticotropic hormone (ACTH): 3.9 pmol/L (range, 1.6 to 13.9); Insulin Growth Factor 1: 293 μg/L (range, 117 to 329); Growth Hormone (GH): 2.98 mIU/L (range, 0.16 to 13); Cortisol at 1500hrs: 289 nmol/L (8 am: 171 to 536; 12 mn: 64 to 340); Luteinising Hormone: 2.5I U/L (indicative of Follicular Phase); Follicular Stimulating Hormone: 3.9 IU/L (indicative of Follicular Phase); Oestradiol: 40.3 pmol/L (indicative of Ovulatory Phase).

Ms P's antipsychotic was switched from Risperidone 6 mg to Aripiprazole 15 mg at night; Bromocriptine was started at 0.625 mg with titration to 2.5 mg at night for 5 weeks. The ophthalmologist monitored her visual disturbances. Upon stabilisation, she was discharged and managed as an outpatient. Over a period of 10 months, Ms P's psychotic illness remitted and is currently maintained on Aripiprazole 15 mg at night.

Discussion

The points for discussion are: 1) screening patients with schizophrenia for symptoms of hyperprolactinemia before starting antipsychotics; 2) monitoring the patients on antipsychotics for development of hyperprolactinemia and 3) subsequent management of hyperprolactinemia.

Visual field disturbances and headache will be important symptoms to screen for pituitary tumours and

hyperprolactinemia prior to starting antipsychotics. In females, history regarding regularity of menstrual cycles and presence of galactorrhea should be obtained. In males, it will be important to ask about sexual drives and erectile dysfunctions.

Investigations like serum prolactin can be done to screen and monitor patients who arouse clinical suspicions of hyperprolactinemia. Levels greater than 2000 mU/L are likely to be secondary to pituitary tumours, for example a micro-prolactinoma; levels greater than 4000 mU/L are more likely to be secondary to a prolactinoma.[2] Depending on the hormones secreted by the pituitary adenoma, other conditions such as Acromegaly (GH secreting), Cushing's Syndrome (ACTH secreting), and Hyperthyroidism (Thyroid Stimulating Hormone secreting) may surface.

Should there be symptoms and signs of hyperprolactinemia described above or raised prolactin levels, CT or MRI scan of the brain should be performed to investigate and monitor the size of the tumour. Subsequent monitoring will include regular surveillance for symptoms of hyperprolactinemia; serum prolactin levels may need to be repeated periodically.

Treatment for antipsychotic induced hyperprolactinemia includes decreasing the dose of antipsychotic. In patients who need to remain on antipsychotic because of active symptoms, treatment with dopamine-agonist such as Bromocriptine can be considered.[3] However, Bromocriptine may exacerbate psychotic symptoms and its use will need to be weighed against normalising prolactin levels.

Switching to a prolactin-sparing antipsychotic can lower prolactin levels. Quetiapine, Olanzapine and Aripiprazole are some examples. Kapur and Seeman[4] suggested that drugs rapidly dissociating from dopamine receptors provide an antipsychotic action without extrapyramidal side-effects, hyperprolactinemia and secondary negative symptoms. Aripiprazole, an atypical antipsychotic, induces a transient and mild prolactin elevation due to its lower affinity to dopamine receptors and faster dissociation. A study reported that in patients with hyperprolactinemia taking Haloperidol, adjunctive treatment with Aripiprazole reversed hyperprolactinemia in 88.5% of patients at 8th week of treatment and reinstated menstruation in 7 females.[5] With a return of normal prolactin levels, both male and female patients should be warned of the return of fertility and appropriate contraception should be advised.

A multidisciplinary team approach will be paramount. The neurosurgeon may offer excision of prolactinoma should the tumour be threatening to eye sight; the ophthalmologist can monitor visual disturbances; the endocrinologist can help manage hormonal disturbances in a patient with pituitary tumour.

Conclusion

This case report exemplified how screening and monitoring should be done for patients with schizophrenia to detect hyperprolactinemia and its subsequent management. Continued liaison between the members of the multidisciplinary team of psychiatrist, endocrinologist, neurosurgeon and ophthalmologist is essential.

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