Persistent hyperprolactinemia in female patient with partial empty sella, under multiple antipsychotics and finally clozapine: Case-report and review of literature.

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Objectives

Description and Investigation of a very rare case of hyperprolactinemia (HP), persisting after clozapine initiation and cessation of any other previous antipsychotic treatment (AT), in a young patient with resistant schizophrenia, without any previous signs of prolactin level elevation. Literature review for rare cases of unusual effects of clozapine on prolactin levels.

Background

HP is a common consequence of AT, followed by a constellation of organic and psychological symptoms. Cessation of HP-inducing, AT, followed by clozapine administration, leads vastly to restoration of normal prolactin levels (PLs). There is only one published case of non – transient, long – term increased PLs persistence, after clozapine introduction as sole AT. This, has led to the adoption of MRI scans and endocrine function monitoring as further clinical investigation practices for this group of patients, for exclusion of other possible causes of HP (ex. prolactinoma). Thyroid function may be also affected in HP.

Materials and Methods – Clinical Investigation

08.2017. A young female with schizophrenia, was admitted to the psychiatric department, for relapse, with severe behavioral problems, agitation, paranoia and minimal compliance to social norms. She has been treated initially with quetiapine and topiramate. Zuclopenthixol and risperidone were introduced a week later. PLs were found elevated above baseline (1687 mUI/L) on 06.09.2017. Haloperidol and clozapine were introduced. Risperidone, topiramate and quetiapine were discontinued, followed by haloperidol. Amisulpride, a known cause of PRL level increase, was introduced, leading to remission of symptoms and discharge.

01.2018. Second admission followed. The patient complained for dysphoria, menstrual disorders, obesity, hypertension and increased facial hair growth, all compatible with a diagnosis of HP. PLs were 3013mUI/L. Radiological and hormonal examination followed.

MRI showed partial empty sella (PES) and pituitary gland dislocation. Patient was found(+) for Anti- TPO and anti- TG, with normal T3 and T4 levels, compatible with early stage HP.

Materials and Methods – Clinical Decision making

Factors Contributing to PRL level increase

- Partial Empty Sella – non modifiable – without previous clinical manifestations
- Amisulpride – Modifiable
- Anti TPO / Anti- TG were considered as effects
- Time of measurement (transient effect of clozapine)

First Treatment Option :

- Amisulpride discontinuation and Clozapine dosage increase.
- PRL level monitoring - ≥ 2 consecutive measurements

Second Treatment Option (if PRL > normal):

- Exclusion of other causes of hyperprolactinemia
- Bromocriptine initiation

First Treatment Option: Amisulpride was discontinued. Clozapine remained as monotherapy in higher dosage. On 08.02.18 PLs were 1451mUI/L. Psychotic symptoms remitted. The patient was discharged. PLs remained high (1255mUIL) on 07.05.18, when tested again, checking for a delayed answer to regiment change..

Second Treatment Option: All other possible hyperprolactinemia causative factors were thoroughly excluded and treatment with bromocriptine was initiated. PLs resumed to normal and remain stable 18 months after bromocriptine initiation.

Results and Conclusions

Results: Menstrual circle, BP and facial hair have been restored to normal with no dysphoric symptoms. No long- term psychological effects from HP have been recorded after a series of psychological interviews. Patient has responded to clozapine and continues with her studies and a local mental health hospital funded job, for well- functioning patients.

Literature Review

A review of the published scientific literature in Pubmed gave only one case report of persistent HP under clozapine, in patients under clozapine treatment (in red color in References), with or without sella turcica emptiness. There are reports for other HP-resistant patients, under different AT types. HP under clozapine is considered a transient effect, which occurs few hours after administration.

Conclusions: AT-induced HP may be only partially controlled during clozapine monotherapy in certain predisposed subgroups. It has been speculated for long that only 75% of patients with AT induced HP, may respond to a dopamine agonist treatment like bromocriptine. Anatomical abnormalities of the HPA axis, may contribute to HP persistence, as causal factors of dysregulation of the inhibitory hypothalamic control of PRL secretion by the lactotrophs, due to compression of the axis vascular system. This may occur, in combination with the main HP AT-induced causal factor, which is chronic AT and subsequent D2 lactotroph membrane receptor blocking and functional dysregulation, which may also act as the main, independent factor, even in patients with PES, but no previous history of HP before AT. Relevant neural network function instabilities and dysregulation of putative PRL-releasing factors under AT may be another contributing element.

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