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HYPERPROLACTINAEMIA – A RISPERIDONE SIDE-EFFECT

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SUMMARY

A 47 year old patient has been treated for psychotic depression for the last 5 years. The illness began manifesting through the symptoms of depressive thoughts, intrapsychic tension, projectivity, derealisation phenomena and pre-psychotic fears. She was treated with a combination of antidepressives, anxiolitics and hypnotics in ambulatory conditions. The therapy applied did not obtain the effects expected due to which an atypical antipsychotic was administered subsequently – risperidone, a 2 mg dose in the evening. After commencing the antipsychotic treatment, the symptoms started to weaken and a steady remission was obtained.

Two years after a regular risperidone administration (in combination with fluoxetine, alprazolam and flurazepam) the patient reported some „bleeding" in October 2006. Hormonal blood tests were performed and high prolactin values were registered (2567.0 mIJ/L),due to which a gradual risperidone retractement was indicated. Medicamentous hyperprolactinaemia is a well known side effect of risperidone. A gradual risperidone retractement lead to a lowered and normal prolactin level within a month.

Key words: *psychotic depression – risperidone - hyperprolactinaemia*

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INTRODUCTION

Hyperprolactinaemia is a state which is marked by imbalanced prolactin levels which is exhibited by a rise in serum prolactin in the absence of pregnancy and lactation. This can occure in both sexes yet more frequently in women. The causes of hyperprolactinaemia are various: physiological (pregnancy, lactation), to pathological (hypothalamic lesions, pituitary gland-linked-illnesses) or medicamentous causes. The frontal part of the pituitary gland secretes prolactin, which inhibition is controlled by dopamine released from the tuberoinfundibulary neurons. Main inhibitor of the prolactin secretion is hypothalamic domapmine which is transported via portal bloodstream to the adenohypophysis (anterior lobe of the pituitary gland) actotrophic membranes where it binds on to the receptors and this way ceases the prolactin secretion (Fitzgerald & Dinan 2008).

A significant rise in the serum levels of prolactin can be caused by a large number of medications exhibiting some visible clinical symptoms (galactorrhea, oligomenorrhea, amenorrhea, irregular periods, higher incidences of osteoporosis in women, impotency, oligospermia and infertility in men). The galactorrhea incidence in women with hyperprolactinaemia is between 30-80% (Vrhovac et al. 1997, Harrison 1997).

Being quite frequent in antipsychotic treatments, hyperprolactinaemia is an unwanted side-effect. In these cases, terminology like „prolactin-sparing" and „prolactin-rising" are used rather than „typical" and „atypical" antipsychotic (Haddad & Wieck, 2004).

Risperidone is an atypical antipsychotic which is more often the cause of hyperprolactinaemia than any other antipsychotic from the same group. Risperidone is a selective monoaminergic antagonist with high affinity for serotoninergic $5HT_2$ and dopamine D_2 receptors. It also binds on to the Alpha1-andrenergic receptors and with less affinity on to H1-hystamine and Alpha2-adrenergic receptors. The highest prolactin levels are linked to risperidone (Bushe et al. 2004, Hamner 2002, Kearns et al. 2000).

In high doses, it manifests an increase in prolactin levels which is similar to the prolactin increase in a typical antipsychotic treatment (Chung & Eun, 1998). Women are much more sensitive to the antipsychotic hyperprolactinaemia effect than men (Torre & Falorni 2007).

In treating psychotic depression, besides antidepressives and anxiolitics, atypical risperidone has proven useful. To patients who did not respond well on SSRI treatment, risperidone was added to their therapies which resulted in amelioration in the regulation of sleep biorhythm and sexual dysfunction. This effect was due to the risperidone increase in dopamine activity (Miodownik & Lerner 2000, Ostroff & Nelson 1999, Goto et al. 2006).

CASE REPORT

A 47 year old woman, academically educated, employed, a divorced mother of two children. Early psychomotor development and growing up proceeded normally. She did not suffer from any serious illnesses in her life. Psychiatric anamnesis and heredity were negative.

First mental disturbances occured in the age of 34, following her divorce. She seeked psychiatric help as she began manifesting some depressive symptoms. A depressive episode was diagnosed F32.2 (according to the acknowledged classification systems ICD-10 and DSM IV) and she commenced a treatment with an antidepressive (Sulpirid 200/mg per day). The patient was occasionally examined ambulatorily, she „felt good“ during her therapy so she „felt there wasn't any need for coming more often“ to her check-ups.

In October 2004, the patient came for her check-up. At that time, her symptoms comprised of bad feelings, passiveness, loss of interests and energy. She reported a list of physical difficulties – neck and shoulders pain, a pressure in her chest, heart palpitations, tremor, extremities' rigidity. She complained she felt „inner restlessness“. She had difficulties falling asleep, she used to wake up several times during the night, she reported having bad dreams. „I sorted out everything“, but day by day, she became increasingly more depressed and felt worse. She reported of her own experience of failures in all the important spheres of her life. She was socially isolated, which was accompained by the feeling of alienation and non-belonging, fearing the potentially close realtions with people. Self-insecurity was quite pronounced accompained by a negative anticipation of the future.

Despite her neat and tidy appearance, the patient was evidently overnourished. It was necessary to channelise the abundant spontaneous production. She was psychomotorically anxious, intrapsychically tensed, affectivelly pale, emotionally incontinent. In content, she reported depressive thoughts out of a moral and health related sphere with somatisations which were of a pre-psychotic level, followed by reality problems. Her volition and instincts were reduced. She verbalised her suicidal thoughts, without a plan and pulsions while being adequatelly critical towards them.

An expanded psychiatric examination was conducted: psychiatric and psychotherapeutic interview, psychological testing, thyroid gland tests, EEG and SKID I and II. According to the ICD-10 criteria and the DSM-IV classification, depressive episode with psychotic elements (F33.3) was diagnosed. Due to a pronounced intrapsychic tension, the pre-psychotic fears and derealisation phenomena, besides SSRI (fluoxetine), anxiolitic (alprazolam) and hypnotic (flurazepam) it was decided to introduce an atypical antipsychotic (risperidone) into her treatment. This dose was gradually increased during a month and a half untill it reached a dose of 2 mg in the evening.

The administration of the therapy mentioned gradually lead to a better mental state of the patient. The major symptoms of the illness were successfully pruned. Psychomotorics and her thinking processes became more adequate, the mood became more stable, the suicidal thoughts and psychotic symptoms disappeared. The patient became efficient in her everyday activities, with a satisfactory level of functioning. Besides a medicamentous therapy and regular ambulatory check-ups with a psychiatrist, she joined a group psychotherapy (once a week).

At her routine control examination the patient reported „bleeding“ which occured two years after the risperidone therapy commencement (2 mg). No side-effects of the medicament were noticed untill then. She underwent a gynaecological examination and hormonal blood tetsts were done which revealed rised prolactin levels (2567.0 mIJ/L). Due to prolactinaemia, risperidone was retracted. Within a month after risperidone being removed from the patient's therapy, prolactin level reached referential values. Taking into account the recidive of the depressive episode it was necessary to introduce an antipsychotic (ziprasidone) again.

DISCUSSION

Unwanted side-effects often depend of the kind of the medicament but also of individual characteristics of patients (age, sex). Risperidone treatment brings a risk of hyperprolactinaemia which can be reduced by applying lower therapy doses (Bostwick et al. 2009, Haddad & Wieck 2004). In the case described, despite a low risperidone dose, hyperprolactinaemia developed.

The fact that every medicament can induce some side effects does not make antipsychoics an exception. Antipsychotic administration requires knowledge about potential side effects of the medicament. The antipsychotic choice depends on the potential side effects but also of patient's characteristics, which needs to be taken into consideration and taken care of. During the antipsychotic treatment, the prolactin level can be

ten times higher than the initial values. Prior to the antipsychotic commencement, it is advisable to measure the prolactin level just as conducting regular check-ups during the treatment course (Riecher-Rössler et al. 2009).

It would be useful to question the patient aiming at the possible hyperprolactinaemia symptoms. In case of positive anamnestic data and especially if diagnostics reveals hyperprolactinaemia, it is necessary and compulsory to switch the existing antipsychotic with an alternative, if possible with the one of a lower potential risk of causing the development of hyperprolactinaemia (Compton & Miller 2002, Molitch 2008).

Considering hyperprolactinaemia as a well known antipsychotics' side effect on one side and on the other side the fact that it is much frequently present as a side effect of the atypical antipsychotics (Bushe et al. 2008, Torre & Falorni 2007, Brunelleschi et al. 2003) it would be recommendable for an everyday clinical practice to define the intervention algorhytm for hyperprolactinaemia caused by antipsychotic administration.

CONCLUSION

Risperidone is applied, besides its general indications, in psychotic depression treatment. Although hyperprolactinaemia is a known risperidone side effect, which has previously been described in the literature, it is necessary, while monitoring the patient on risperidone, to think about the potential risk of developing hyperprolactinaemia. It is crucial to detect the subclinical manifestations of the medicament's side-effect and rectify the therapy on time.

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