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Case Report / Olgu Sunumu

Paliperidone-Related Gynecomastia and Treatment: a Case Report

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ABSTRACT

Paliperidone-related gynecomastia and treatment: a case report

Hyperprolactinemia is a frequent adverse effect of typical antipsychotics and atypical antipsychotics such as risperidone, amisulpride, and paliperidone. Side effects due to hyperprolactinemia are less frequent in males and sometimes these symptoms are overlooked. The management of a patient with antipsychotic-induced hyperprolactinemia must be patient specific. The recommended treatments include reducing dose of the offending antipsychotic, switching to another antipsychotic, using dopamine receptor agonist, adding sex steroids or aripiprazole to the treatment. In this report, a case that developed gynecomastia in the second month of the paliperidone treatment is presented, and its treatment is discussed.

Keywords: Aripiprazole, gynecomastia, paliperidone, psychosis

ÖZET

Paliperidon ile ilişkili jinekomasti ve tedavisi: Bir olgu sunumu

Tipik antipsikotikler ve atipik antipsikotiklerden risperidon, amisülpirid ve paliperidonun sık görülen yan etkilerinden biri hiperprolaktinemidir. Hiperprolaktinemi ile ilişkili belirtiler erkek hastalarda kadınlara göre daha seyrek gelişmekte ve zaman zaman gözden kaçmaktadır. Antipsikotiklerin yol açtığı hiperprolaktineminin tedavisi hastaya özgü olmalıdır. Önerilen başlıca tedaviler; antipsikotik dozunun azaltılması, antipsikotiğin değiştirilmesi, tedaviye dopaminerjik agonist, seks steroidleri ya da aripiprazolün eklenmesidir. Bu yazıda paliperidon tedavisinin ikinci ayında jinekomasti ile başvuran bir olgu ve tedavisi tartışılmıştır.

Anahtar kelimeler: Aripiprazol, jinekomasti, paliperidon, psikoz

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INTRODUCTION

In general, antipsychotic drugs used in the treatment of psychotic disorders are classified as typical antipsychotics, acting by dopamine receptor antagonist, and atypical antipsychotics acting by serotonin-dopamine antagonism and/or interacting with dopamine receptors in various forms (mesolimbic selectivity, weaker D2 receptor blockade, rapid cleavage of D2 receptors and partial dopamine agonism) (1). When the function of the neurons in the Tubo-infundibular dopaminergic pathway extending from hypothalamus to hypophysis are inhibited by antipsychotic drugs, prolactin release increases. This situation, hyperprolactinemia, can be asymptomatic or can lead galactorrhea, amenorrhea, gynecomastia and sexual dysfunction in short term, and tumorigenesis and osteoporosis in long term (1-4). These side effects can disrupt treatment compliance and lead to serious health problems in the long term (4).

Atypical antipsychotics, which have weaker D2 receptor blockade compared to the strong serotonin receptor blockade and have greater effects on the mesolimbic system than the effects on the nigrostriatal system and the tuberoinfundibular system, raise the prolactin levels less than the typical antipsychotics (1,2,5). Antipsychotic related hyperprolactionemia incidences have been reported to range from 42 to 93% for women and 18 to 72% for men (6). The paliperidone, active metabolites of risperidon and amisulpride, and risperidon's itself are known to cause hyperprolactinemia (7). Studies on paliperidone have been limited (8). On the other hand, it is considered that aripiprazole does not increase prolactin levels with the partial agonist action on D2 and D3 receptors, and even restores hyperprolactinemia

induced by other antipsychotics (9,10). In this paper, a case of gynecomastia after paliperidone use, and its treatment is presented.

CASE

A 23-year-old male patient referred to our outpatient clinic with complaints of enlargement in one breast. His medical history revealed that his first admission to the psychiatry was at the age of 15 due to reluctance and malaise. He used sertraline 50mg/day for a short time due to similar complaints 2 years ago. Approximately 7 months ago he was referred to psychiatrist by his family because of self-talk, increase in the number of religious devotions, visual hallucinations, hearing sounds, nervousness and aggression. He was warning his friends about what they should do to prevent harm from demons. He was admitted to the hospital twice in short intervals with the diagnosis of "acute psychosis". His HBsAg was positive. He was prescribed paliperidone 9 mg/day and quetiapine 25mg/day and the complaints have been decreased with the treatment. Quetiapine was discontinued at follow up examinations. He used bornaprin for a short time for extrapyramidal system (EPS) findings. In the second month of paliperidon treatment he referred to internal medicine clinic upon noticing a mammary growth. Hormon analyses (thyroid function tests, total testosterone, estradiol levels) were normal. The ultrasonography of the breast was reported as "a hypoechoic tissue of 8x14mm without a distinct border in the left mammary retroareolar area (primarily interpreted in favor of gynecomastia). Then the patient
was referred to our clinic.

Mental examination of the subject revealed that; his associations were slow, his affect was monotonous, did not define positive psychotic symptom, the memory and orientation were natural and he had psychomotor retardation. Prolactin level was determined as 136.3ng/ml (normal prolactin level is <25ng/ml in women, <20ng/ml in men). Paliperidone was decreased to 6mg, and aripiprazol 10mg/day was added. Since the patient was an adult, he was diagnosed as psychotic disorder and has switched from another antipsychotic, aripiprazole was started in moderate doses. In addition to hyperprolactinemia EPS developed with paliperidon treatment. Therefore it was planned to switch from paliperidone to aripiprazole and continue with monotherapy. The patient was reevaluated 10 days after the treatment switch. No positive psychotic symptoms were found, the prolactin level was 22ng/ml, and the growth in the breast tissue was resolved. Paliperidone was reduced to 3mg/day on the 14th day of the treatment with aripiprazole and completely terminated at the first month of treatment. Treatment of the patient, who has been in remission for approximately 6 months, is continued with aripiprazole 20mg/day and quetiapine 25mg/day.

DISCUSSION

It has been reported that hyperprolactinemia develops more frequently in females and younger patients, and the risk increases with higher drug doses (2,9). Our young male patient has been treated with paliperidone, an atypical antipsychotic that is commonly known as causing hyperprolactinemia. In addition to galactorrhea, hyperprolactinemia leads to hypogonadism, sexual dysfunction, infertility, and amenorrhea due to hypothalamic-pituitary-gonadal axis suppression. While in female patients the symptoms are immediately noticeable, in male patients these symptoms are less frequent and are sometimes overlooked. Prolactin levels are elevated within a few hours after initiation of treatment, and elevated hormone levels can persist for a long time after cessation of therapy (9). Gynecomastia, that occured in the second month of the treatment in our case, is a rare side effect among male patients. Gynecomastia may be unilateral, or unilateral as seen in our case.

In the treatment of hyperprolactinemia due to the use of antipsychotic drugs, it is recommended to reduce the antipsychotic drug dose, to change the antipsychotic, to add dopaminergic agonist or sex steroids in treatment (11). Treatment with aripiprazole has been reported to be an effective and safe alternative

in the treatment of antipsychotic-associated hyperprolactinemia (12). In our case, due to the EPS and gynecomastia related with paliperidone, a gradual transition from paliperidone to aripiprazole was planned. Paliperidone was reduced from 9mg/day to 6mg/day, and 10mg/day aripiprazole was added to treatment. It was seen in the follow-up visits that the prolactin levels decreased to normal ranges and gynecomastia regressed without exacerbation of psychotic symptoms.

There is controversy regarding whether or not to check prolactin levels before starting the treatment. Some authors recommend routine screening, whereas others do not recommend or recommend screening for just high-risk drugs and patients (11,13,14). There is no consensus on whether the patient's prolactin levels should be monitored at follow up visits, either. While some authors recommend quarterly or annual prolactin levels evaluations, treatment guidelines generally recommend analyzing prolactin levels when the patient develops symptoms (11,13,14). According to the Schizophrenia Treatment Guideline of the Psychiatric Association of Turkey it is recommended: a) to check the baseline prolactin level of all patients, b) to repeat prolactin analysis after 3 months in patients who have no signs of hyperprolactinemia in the follow-ups, but use risperidone, paliperidone, amisulpride or typical antipsychotic drugs, c) in case of moderate elevation in prolactin level, to question symptom progression and effects and to repeat prolactin test every 6 months; and d) in case of a significant elevation in prolactin level, either to change medications or to treat hypogonadism.

In conclusion antipsychotic-induced hyperprolactinemia is a condition that can disrupt treatment compliance and lead to serious health problems in the long range. There is no consensus about screening and follow-up of prolactin levels. Therefore, it is of great importance to question the side effects due to hyperprolactinemia in high-risk drugs and patients, especially in male patients where symptoms can be overlooked. Treatment of hyperprolactinemia should be patient specific.

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