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Case Report

Psychotic Symptoms Subsequent to Chronic Untreated Prolactinoma: A Case Report

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Abstract

Prolactinomas are prolactin-secreting pituitary tumors originating from the lactotroph cells of the anterior pituitary gland. With hyperprolactinemia, prolactinoma patients may present symptoms of galactorrhea, amenorrhea, sexual dysfunction, and infertility, as well as symptoms due to tumor expansion. Moreover, high level of prolactin effects on mood and behavior thus may lead to depression, anxiety, and hostility through unknown mechanisms. A couple of previous case reports described psychotic disorders in patients with prolactinoma, but none of them came from Chinese population.

The case presented here is a 24-year-old unmarried woman presenting psychotic symptoms and amenorrhea following menstrual irregularity. Her psychotic symptoms were intermittent and distressed her for 10 months. Her amenorrhea persisted for several years without a standardized therapy. A suspected prolactinoma was confirmed by a high level of serum prolactin and a brain MRI scanning showing a pituitary macroadenoma. Her psychotic symptoms were treated with olanzapine and psychotherapy during hospitalization. She has been maintained on aripiprazole, bromocriptine, and benzhexol after discharge.

Olanzapine is effective and safe in treating psychotic symptoms resulting from hyperprolactinemia. Combination of aripiprazole and bromocriptine are a good option for the maintenance of patients with comorbid psychotic symptoms and prolactinoma.

Keywords: Amenorrhea; Antipsychotics; Bromocriptine; Prolactinoma; Psychotic symptoms

Introduction

Pituitary Adenomas (PAs) are benign neoplasms that account for 10% to 15% of all intracranial masses [1]. Of the subtypes of PAs, prolactinomas account for 57%, nonfunctioning PAs 28%, growth hormone-secreting adenomas 11%, corticotroph adenoma 2%, and unknown functional status 2% [2]. PAs are also categorized based on size, i.e., macroadenoma (≥10 mm) and microadenoma (<10 mm) [3]. Microadenomas are more commonly diagnosed in women, whereas macroadenomas are equally prevalent in men and women. In general, tumor size correlates with serum prolactin levels. A serum prolactin level >250 ng/ml is usually due to a macroadenoma, rather than a microadenoma [4].

Prolactinomas are prolactin-secreting pituitary tumors originating from the lactotroph cells of the anterior pituitary gland [5]. The lactotroph cells secrete prolactin and result in hyperprolactinemia with serum prolactin above the normal range (20-25 ng/ml in pre-menopausal women, 15 ng/ml in men and postmenopausal women) [4]. In addition, prolactinoma causes symptoms of galactorrhea, amenorrhea, sexual dysfunction, and infertility, as well as symptoms due to tumor expansion, such as headache and visual changes [6]. Moreover, high level of prolactin effects on mood and behavior thus may lead to depression, anxiety, and hostility [7,8]. For example, previous case reports described psychotic disorders in patients with prolactinoma, including paranoid schizophrenia in a 25-year-old man with a pituitary macroadenoma [9] and a 29-year-old Singaporean female with a long-standing pituitary macroadenoma [10], acute psychosis in a 52-year-old married woman with a microadenoma [11], a 19-year-old, single, African American woman with a PA (10-11 mm in diameter) [12], and a 29-year-old male patient with chronic, untreated prolactinoma [13].

Although the mechanisms underlying the prolactinoma-induced psychotic disorders remain to be unclear, it is known that the release of prolactin from pituitary is inhibited by dopamine whereas a deficiency of this neurotransmitter increases prolactin secretion. Therefore, the standard treatments for prolactinoma and schizophrenia theoretically appear to conflict with one another. On the one side, standard treatment for a functional prolactinoma may exacerbate psychotic symptoms as it involves use of a dopamine agonist which increases dopaminergic activity. On the other side, antipsychotics, especially the first generation of antipsychotics, are known to induce hyperprolactinaemia in humans and animal studies [14,15].

The case presented here is a 24-year-old unmarried woman, who had been suffering from psychotic symptoms for 10 months until her first admission to the Mental Health Center of Shantou University. In addition, she was distressed by menstrual irregularity and amenorrhea for a couple of years before the presentation of psychotic symptoms. The suspected prolactinoma of the patient was confirmed by high levels of serum prolactin and pituitary macroadenoma shown in a brain MRI. Her psychotic symptoms were treated with

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olanzapine and psychotherapy as well as entertainment therapy during hospitalization. And she has been maintained on aripiprazole, bromocriptine and benzhexol after discharge.

Case Presentation

A 24-year-old, unmarried woman was admitted to the Mental Health Center of Shantou University, China, on September 30, 2018 for psychotic symptoms.

During the workup, the patient was passive eye-contact and irritability along with decreased volitional activity, garrulousness and self-talking, although she was conscious. She complained of verbal auditory hallucinations, delusion of persecution, inappetence, and insomnia. Her body shape was slim (BMI=20.57 kg/m^2) with breast dysplasia.

About ten months before the admission, patient became unsociable and eccentric, unwilling to communicate with the others, followed by delusion of persecution and auditory hallucination. Her psychotic symptoms were intermittently, and she worked well when felt fine. Two days before she was sent to the Mental Health Center, the patient felt irritable and unsafe thus came home after a couple of hours by car from her employer. However, she insisted on returning to the employer as soon as she returned home because of the same unsafe feeling.

Past history of the patient revealed that she had been suffering from menstrual irregularity and amenorrhea for a couple of years though her period first appeared normally at the age of 14 and lasted for 5-6 days during each 28-30 days in the first a few years. However, the patient never actively sought a medical treatment for her amenorrhea until 2016, when she was accompanied by her parents to see a gynecologist. She got a drug (the patient did not remember the drug name) from the gynecologist and took it by oral administration for a couple of days. Seeing no reaction discouraged her from continuing the medication. Moreover, the patient expressed no desire to have a regular menstrual cycle.

During the first hospitalization, the patient was given olanzapine (15 mg/day) for the psychotic symptoms. In the meanwhile, Cognitive Behavioral Therapy (CBT, 30 minutes/session, two sessions/week) and entertainment therapy, in which patients are asked to participate in various entertainments including painting, handicraft, playing chess and card activities, outdoor activities and sports activities, as well as watching movies and enjoying music, were supplemented. In addition, a consultation with an endocrinologist was proffered. A prescribed laboratory test showed a high level of her serum prolactin (676 ng/ml; reference values are less than 29 ng/ml in pre-menopausal women and less than 20 ng/ml in postmenopausal women). Then a brain MRI scanning was done showing a pituitary macroadenoma (15 mm×12 mm×11 mm) without invasion to adjacent structures. The patient did not complain of headache and visual loss and/or visual field defect. After her psychotic symptoms were remitted, the patient was discharged from the Mental Health Center and maintained on olanzapine (15 mg/day) and bromocriptine (7.5 mg/day) after discharge.

The patient was followed up six months after discharge. She felt well except for amenorrhea. The second MRI scanning was prescribed at the follow up and turned out a decreased tumor size (9×9×10 mm). Later, fearing the side effects of the drug, the patient stopped the medicine herself. A couple of days later, she felt auditory hallucination and delusion of persecution again. And the symptoms became worse in the following days and interfered with her daily life and work. Consequently, the patient was admitted to the Mental Health Center for the second time. During her second hospitalization, the patient was prescribed bromocriptine (7.5 mg/day), olanzapine (15 mg/day) and quetiapine (300 mg/day). However, quetiapine was discontinued for the adverse effect of dizzy. As did during the first hospitalization, psychotherapy and entertainment therapy were supplemented, along with the medications. Patient was discharged two weeks later when the psychotic symptoms disappeared. She was maintained on aripiprazole (10 mg/day), bromocriptine (7.5 mg/day), and benzhexol (2 mg/day) after discharge.

The second post-discharge follow-up reported a prolactin level of 321 ng/ml and slight defects in peripheral visual field of her two eyes although the eyesight was normal (1.0). However, amenorrhea did not respond to the treatment.

Discussion

This is the first reported case in Chinese population to date presenting psychotic symptoms subsequent to an untreated prolactinoma. A few features of this case deserves to be emphasized. First, a diagnosis of schizophrenia is questionable as the psychotic symptoms of the patient were intermittent, and she worked well when she felt well. Moreover, she responded well to olanzapine, psychotherapy and entertainment therapy. And olanzapine treatment did not increase her serum level of prolactin. Second, there is no doubt that she had a prolactinoma as evidenced by the brain MRI and high level of serum prolactin. It is the high level of prolactin that led to the menstrual irregularity and amenorrhea in the patient. Unfortunately, the patient did not seek a diagnosis thus got no standard treatment for her hypogonadism during a long period of a couple of years. However, it is the symptoms of hypogonadism that did induce the psychotic symptoms of the patient, who became unsociable and eccentric, and was unwilling to communicate with the others, followed by delusion of persecution and auditory hallucination. Third, bromocriptine administration significantly lowered her serum prolactin level and decreased the size of pituitary macroadenoma but did not exacerbate her psychotic symptoms.

Unfortunately, the patient remains to be afflicted by amenorrhea as the prolactin level are still at a high level (321 ng/ml). Now she is maintained on aripiprazole and bromocriptine. Hopefully, this combination will reach the desired purpose of restoring the patient's normal menstrual cycle while protecting her from psychotic symptoms. In support of this treatment plan and anticipation, aripiprazole did not influence the serum prolactin level of patients with schizophrenia in a recent study [16]. Indeed, adjunct aripiprazole with prolactin-elevating antipsychotics reduced prolactin and prolactin-related adverse effects in premenopausual women with psychosis [17]. Moreover, two previous studies on Chinese female patients reported that the vast majority of infertile women with prolactinomas became pregnant after bromocriptine treatment [18,19].

Conclusion

Olanzapine is effective and safe in treating psychotic symptoms

resulting from hyperprolactinemia. Combination of aripiprazole and bromocriptine are a good option for the maintenance of patients with comorbid psychotic symptoms and prolactinoma.

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