Treatment of Paroxysmal Perceptual Alteration in Catatonic Schizophrenia by Switching to Aripiprazole from Risperidone: A Case Report

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Abstract

Paroxysmal perceptual alteration (PPA) is the occurrence of brief and recurrent episodes of perceptual changes. It is mainly caused by the treatment of schizophrenia patients with antipsychotics. However, diagnosis of PPA is not very prevalent among psychiatrists, partly due to underrecognition or misunderstanding that it is a worsening of psychiatric symptoms. If psychiatrists do not understand PPA, they cannot treat it appropriately, and the patient's quality of life is impaired. We present a case of PPA in catatonic schizophrenia that was successfully treated by switching to aripiprazole from risperidone. We suggest that the disappearance of PPA in our case was due to both discontinuing risperidone, which completely blocks D2 receptors, and replacing it with aripiprazole, which is characterized as a partial agonist of D2 receptors. Treatment of PPA will improve medication adherence and quality of life. It is important to recognize PPA as a possible side effect of treatment with antipsychotics.

Key Words: Paroxysmal Perceptual Alteration, PPA, Schizophrenia, Aripiprazole, Partial Agonist, Risperidone, Antipsychotics

Introduction

Brief and recurrent episodes of changes in perception—called paroxysmal perceptual alteration (PPA)—have been reported to occur occasionally with the use of antipsychotics (1-5). This unusual phenomenon was first described by Yamaguchi and Nakai (1). PPA is characterized by hypersensitivity of perception, psychedelic experiences (such as brightening of colors, sharpening of contrast, visual distortion), and somatic schema disorder (including a feeling of floating, and that one's extremities are being pulled and elongated) (1).

PPA in patients with chronic schizophrenia occurs abruptly, mainly in the evening, often precipitated by fatigue. During the attack, patients also suffer from mood and thought alterations (anxiety, agitation, depressive mood, and inability to distract their thoughts from one thing), but they are aware that the symptoms of PPA are not real and are not apprehensive about them. The patients have a sense of discomfort with themselves and feel anxiety and a disturbance of thinking due to PPA. PPA normally presents as an hour-to-hour phenomenon. The attack ceases gradually and spontaneously while the patient rests or sleeps. These clinical features are clearly different from those of schizophrenic hallucinations (1). These symptoms continue for a long time if PPA is not treated. Although there is no clear definition of the number of symptoms required for a diagnosis of PPA,

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Table 1 Changes in PANSS Scores

	Before Treatment	Treatment by Risperidone	Treatment by Aripiprazole	1-Year Later
PANSS-P	35	18	16	11
PANSS-N	42	40	19	12
PANSS-G	95	80	34	22

PPA is diagnosed comprehensively by a symptom expression pattern and clinical symptoms (e.g., perceptual alteration, psychiatric symptoms, autonomic symptoms, motor symptoms). The severity of PPA has been reported to increase with escalating doses of antipsychotics and to lessen with the use of anticholinergic agents (5, 6). Oculogyric crisis has been reported to occur frequently (36.4%) during episodes of PPA (4).

In a study of 338 patients treated with antipsychotics, the prevalence of PPA was reported to be 3.25%; in addition, a higher rate was reported among patients treated with high-potency antipsychotic agents (3.91%) than in those treated with medium- or low-potency agents (1.16%) (4). Moreover, reports of cases of PPA occurring with the use of second-generation antipsychotics, especially risperidone (7), have recently been published (7-13).

We report a case of PPA that occurred with exposure to risperidone and decreased after substitution of the antipsychotic with aripiprazole. A study reporting that PPA is more prevalent in specific subtypes of schizophrenia has not yet been published, and it is unknown if PPA is more prevalent in schizophrenia with prominent positive symptoms or with more negative symptoms. However, in our case, our patient said that PPA was also present when he had any symptom, but he did not mention it when he was having prominent positive symptoms. We think that further study of PPA is necessary.

Case Presentation

The patient was a 30-year-old male with a twelve-year history of periodic psychotic episodes resulting in two psychiatric hospitalizations. A diagnosis of catatonic schizophrenia was made by a psychiatrist according to *ICD-10* because he was in a motionless, apathetic state and did not react to external stimuli. Antipsychotic therapy with haloperidol 3 mg/day or risperidone 6 mg/day was started. When he was made nervous by events, such as some tests or a Buddhist memorial service, he could not eat or take medication. He was then admitted to our hospital in a catatonic state. On admission, he gazed into space intently and could not speak. His muscle tone was increased, and catalepsy was present. His vital signs, such as body temperature and blood pressure, were normal, and no autonomic lability was present.

All the laboratory data were within normal range; for example, creatinine phosphokinase (CPK) level was 77 IU/l, C-reactive protein (CRP) was 0.2 mg/dL, sexually transmitted disease tests were negative, and neuroleptic malignant syndrome was ruled out. He did not have any history of drug or alcohol use. An electroencephalogram was normal, and α-blocking was positive. Magnetic resonance imaging (MRI) also showed no abnormality. Single photon emission computed tomography (SPECT) showed hypoperfusion in the bilateral frontal lobes, which is common in schizophrenia. His Positive and Negative Syndrome Scale (PANSS) scores were positive scale (PANSS-P) 35, negative scale (PANSS-N) 42, and general psychopathology scale (PANSS-G) 95. Although we treated him with haloperidol at 10 mg/day by intravenous injection and risperidone at 6 mg/day by oral administration, his catatonic state was not improved.

Therefore, we treated him with electroconvulsive therapy (ECT). The ECT was bilateral and a modified method using a muscle relaxant. The seizure duration of each ECT was approximately 40 seconds. After the fifth ECT, his catatonic state was improved. We stopped intravenous administration of haloperidol because he could take medication orally and reduced risperidone to 4 mg/day, although this is below the recommended dosage for schizophrenia because he complained of sleepiness as a side effect of risperidone. His PANSS-P score improved to 18 from 35. However, his negative symptoms, such as decreased motivation, were severe; his PANSS-N score was 40, PANSS-G was 80, and he stayed in bed all day. When we asked him to describe his symptoms carefully, he said, "I sometimes feel and see that everything is bigger and closer to me than normal, then my thoughts are stopped. I feel fear and have palpitations because I'm afraid my body may become hardened. When I have this feeling, I just lay down on the bed, and those symptoms disappear in a few minutes."

We diagnosed the symptoms as PPA and decided to switch to aripiprazole, which causes partial agonism of D2 receptors, because we thought that PPA was caused by ris-

peridone. Therefore, his treatment was changed from risperidone 4 mg/day to aripiprazole 18 mg/day. One week after changing to aripiprazole alone, his PPA had disappeared and his motivation was improved. His PANSS-P score was 16, PANSS-N was 19, PANSS-G was 34. As a result, the patient was discharged on aripiprazole after three weeks of treatment with it.

Based on this hypothesis, it is possible that aripiprazole, which is characterized by partial agonism of D2 receptors, ameliorates PPA and risperidone worsens it.

One year after discharge, the clinical improvement was maintained, and there is no worsening of psychiatric symptoms or PPA. His PANSS-P score is 11, PANSS-N is 12, and PANSS-G is 22. Because he is able to watch soccer on TV and go out alone, his quality of life has improved dramatically. The changes in the PANSS scores are shown in Table 1.

Discussion

PPA is characterized by paroxysmal hypersensitivity of perception, psychedelic experiences, and somatic schema disorder. In patients with chronic schizophrenia, PPA occurs abruptly, mainly in the evening, often precipitated by fatigue. During the attack, patients also suffer from mood and thought alterations, but they are aware that symptoms of PPA are not real and are not apprehensive about them. The attack ceases gradually and spontaneously while the patient rests or sleeps. These clinical features are clearly different from those of schizophrenic hallucinations (1).

One hypothesis of the pathophysiological mechanism of PPA was suggested by Watanabe (7, 14). Treatment of schizophrenia with antipsychotics causes dopaminergic dysfunction of the midbrain cortex, midbrain limbic cortex, and chronic block of D2 receptors (7, 14). When circadian variations of dopaminergic activity are added to these changes, acute dopaminergic activity decreases. As a result, increased noradrenergic activity (compensatory) causes hyperarousal, mood disorder (anxiety, agitation), hyperesthesia, and perceptual alteration. On the other hand, relatively increased acetylcholinergic activity causes thought disorder, mood disorder (depression), and motor symptoms (dystonia) (7, 14). Based on this hypothesis, it is possible that aripiprazole, which is characterized by partial agonism of D2 receptors, ameliorates PPA and risperidone worsens it.

Suggested treatments for PPA include reducing the dosage of antipsychotics (15), adding anticholinergic agents (5, 6), switching to antipsychotics with a transient and loose binding affinity for D2 receptors (10, 12), and administration of a β-blocker or benzodiazepines (14). Thus, aripiprazole might be effective because it maintains the dopaminergic nervous system in a steady state by partial agonism of D2 receptors (16). In our case, although switching medication carried the risk of worsening the patient's positive symptoms, we chose aripiprazole, which is characterized by partial D2 receptor agonism and less sedation, because he complained of sleepiness. We diagnosed his symptoms as PPA caused by risperidone.

We suggest that the disappearance of PPA in our case was due to both completely stopping risperidone, which reduced the blockade of D2 receptors, and switching to aripiprazole, which is characterized as a partial D2 receptor agonist, even considering the 20-hour half-life of risperidone and 75-hour half-life of aripiprazole.

Conclusions

We report a case of PPA in catatonic schizophrenia that was successfully treated by switching to aripiprazole from risperidone. In our case, the patient's positive symptoms may have been improved by ECT and risperidone. However, his negative symptoms did not improve because he was suffering from PPA. After we noticed his PPA and changed his treatment to aripiprazole from risperidone, his symptoms and quality of life improved dramatically because his PPA disappeared. One year after discharge, his condition has been maintained. Thus, in this case, PPA may have been a side effect of risperidone. Moreover, aripiprazole, which is characterized by partial agonism of D2 receptors, was very effective. In our case, we are confident that the PPA was a side effect of risperidone and aripiprazole was effective to treat PPA. Treatment of PPA improves patient medication adherence and quality of life. It is important to pay attention to PPA as a side effect of antipsychotics.

Declaration of Interest

None.

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