

Important Consideration in Choosing Antipsychotics in the Treatment of Patients with 22q11.2 Deletion Syndrome: Risk of Convulsion

Seo-Hyun Choi, Sang-Gu Kang, Hee-Yeon Kim, Hye-Young Kim, Jae-Nam Bae, Jung-Sub Lee, Won-Hyoung Kim

Department of Psychiatry, Inha University Hospital, Incheon, Korea

The prevalence of epilepsy and psychosis in 22q11.2 deletion syndrome (22q11.2DS) is higher than in the general population. Recent study on adults with 22q11.2DS reported that the most common trigger for provoked seizures was the use of antipsychotics and antidepressants. In this paper, blonaserin was used because aripiprazole, quetiapine, paliperidone were not effective. The patient had convulsion on the fourth day of taking blonaserin. Neurological and cardiac examination was carried out, and lamotrigine was added at the advice of neurologist. Than the patient didn't have any convulsions and the symptoms gradually improved. When treating patients with 22q11.2DS, the medicine should be chosen carefully, and the patient should be observed closely, paying attention to the possibility of convulsions.

KEY WORDS: DiGeorge syndrome; Psychotic disorder; Seizure; Antipsychotic agents.

INTRODUCTION

A 22q11.2 deletion syndrome (22q11.2DS) is the most common deletion syndrome in humans with an estimated frequency of 1:2,000 to 1:4,000 of live births [1]. More than 180 clinical features have been described, such as cardiovascular malformations, palatal anomalies, immune deficiency, and dysmorphic facial features [2-4]. Neuropsychiatric disorders have frequently been reported [5,6]. Some reports have highlighted the high frequency of schizophrenia among individuals with the 22q11.2 deletion compared to the general population [7,8].

Although psychosis and epilepsy may coexist in adult patients with 22q11.2DS, few reports have discussed the interrelation between schizophrenia and seizure. This paper reports a case of 22q11.2DS in an adult patient, who

had a seizure during the treatment of schizophrenia.

CASE

A 25-year-old woman was admitted to hospital for her first episode of psychosis. The patient was born via a normal vaginal delivery after an uncomplicated full-term pregnancy. The tetralogy of Fallot was diagnosed at 9 months and treated surgically at the age of 1 and 3 years. She had no seizure history until admission and no family history of epilepsy or psychiatric disorders.

At the time of admission, she had swollen eyelids, short palpebral fissures, flat cheeks, a bulbous nose tip, broad nasal root, and low-set ears. Her vital signs were stable and the medical and neurological examination revealed no abnormalities. A mental status examination revealed a psychotic state including paranoid delusions, a delusion of reference, and thought control. In addition, she stated that she heard unfamiliar voices trying to communicate with her continuously. She presented with psychomotor agitation, and a lack of insight. Her Positive and Negative Syndrome Scale (PANSS) score was 96 based on these symptoms.

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Address for correspondence: Won-Hyoung Kim
Department of Psychiatry, Inha University Hospital, 27 Inhang-ro,
Jung-gu, Incheon 22332, Korea
E-mail: ckgodman@hanmail.net
ORCID: <https://orcid.org/0000-0002-6650-3685>

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The neuropsychological assessment revealed a full-scale intelligence quotient of 66 on the Korean Wechsler Adult Intelligence Scale. Her blood count was normal without any signs of infection. The serum calcium level and serum phosphorous level were normal. The thyroid function tests and intact parathyroid hormone were normal. An electrocardiogram revealed a normal sinus rhythm but possible right ventricular hypertrophy. Electroencephalography (EEG) showed generalized fast activities but within the normal limits. The 22q11.2DS deletion was confirmed using a fluorescence *in situ* hybridization probe. Based on these findings, the patient was diagnosed with 22q11.2DS, mild mental retardation, and schizophrenia.

Thirty milligrams of aripiprazole and 800 mg of quetiapine was tried at first and then switched to 30 mg of olanzapine and 400 mg of amisulpride but the symptoms didn't improve. The psychiatrist used olanzapine 30 mg and paliperidone 9 mg for 2 weeks, but the symptoms persisted. Therefore, paliperidone was changed to 8 mg of blonaserin.

On the fourth day that blonaserin was administered, the patient fell to the ground with generalized shaking of her extremities for 20 seconds. At that time, blonaserin was discontinued, and cardiology and neurology consultations were requested. The ECGs performed after the events revealed an incomplete right bundle branch block and prolonged QTc (483 mc). A sleep deprived EEG indicated localized cerebral dysfunction and bilateral temporal areas. The magnetic resonance imaging revealed multiple iso and high signal intense lesions in the bilateral periventricular white matter and subcortical white matter. The neurologist recommended the addition of lamotrigine to reduce the likelihood of seizure activity and the careful prescription of antipsychotics. She had three more absence-like seizures on five days after the first seizure. The neurologist recommended that lamotrigine be increased to 75 mg twice a day. After lamotrigine was increased, there were no more seizures, and the psychotic symptoms improved. The patient was discharged 10 days after remaining seizure-free on olanzapine 30 mg and lamotrigine 150 mg daily.

DISCUSSION

The effectiveness and safety of antipsychotics in the treatment of psychosis associated with 22q11.2DS are not

well established. 22q11.2DS is relatively unresponsive to currently used antipsychotic drugs [9]. Quetiapine and olanzapine appear to be efficacious in 22q11.2DS patients with schizophrenia because they are in idiopathic schizophrenia, whereas risperidone may be less effective [10-12]. Clozapine has been shown to reduce schizophrenia symptoms and hospitalizations as effectively in 22q11.2DS patients as it does in idiopathic schizophrenia, and at a lower average dose. On the other hand, neurological side effects with antipsychotic therapy tend to increase in 22q11.2DS patients and with clozapine in particular. These include generalized tonic-clonic seizures, focal seizures, myoclonus, rigidity, and tremors, with seizure being the most severe and most common [13,14].

The prevalence of epilepsy and acute symptomatic seizures in adults with 22q11.2DS is higher than in the general population [7,15]. A recent study on adults with this condition reported that the most common trigger for provoked seizures was the use of antipsychotics and antidepressants, even though a history of hypocalcemia was also common [16]. The incidence of seizure reported from US Food and Drug Administration approval trials was highest with clozapine, olanzapine, and quetiapine compared to a placebo. Only a slight increase was observed with ziprasidone, aripiprazole and risperidone [17]. In epileptic patients, risperidone has a low risk of inducing seizure activity [18]. In this case, it is presumed the convulsion occurred by adding blonaserin to the high capacity of antipsychotics. Although recent studies have shown that blonaserin prevents convulsion, but in this case blonaserin increases the potency of antipsychotics, and did not prevent convulsion [19]. After the convulsion was stopped, the previously used olanzapine was again used as 30 mg, but seizure did not occur again and the psychotic symptom also improved. Careful observation is always needed because high doses of psychotic drugs are risk factors for convulsion in 22q11.2DS [17].

For the seizure risk, a detailed history, full neurological examination and neurologist consultation to assist in the selection of the most appropriate anticonvulsant or augmentation agent is recommended in 22q11.2DS [18]. After seizure events, antipsychotics should be switched to others or stopped. Previous papers have reported similar cases. Additional monitoring, such as ECG or EEG, should be repeated at consecutive intervals during treatment in the 22q11.2DS [20].

When treating schizophrenia patients with 22q11.2DS, the high dose of antipsychotic drugs should be chosen carefully, and the patients should be observed closely, paying attention to the possibility of convulsions. This is important for preventing potential adverse neurological events.

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■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

■ Author Contributions

Conceptualization: Won-Hyoung Kim, Seo-Hyun Choi. Investigation: Seo-Hyun Choi, Sang-Gu Kang. Resources: Won-Hyoung Kim, Seo-Hyun Choi. Supervision: Hee-Yun Kim, Hye-Young Kim, Jae-Nam Bae, and Jung-Sub Lee. Writing – original draft: Seo-Hyun Choi. Writing – review & editing: Won-Hyoung Kim.

■ ORCID

Seo-Hyun Choi <https://orcid.org/0000-0002-2726-5610>
 Sang-Gu Kang <https://orcid.org/0000-0003-0824-9022>
 Hee-Yeon Kim <https://orcid.org/0000-0002-6766-5969>
 Hye-Young Kim <https://orcid.org/0000-0002-2313-8892>
 Jae-Nam Bae <https://orcid.org/0000-0002-5024-6231>
 Jung-Sub Lee <https://orcid.org/0000-0001-5585-0334>
 Won-Hyoung Kim <https://orcid.org/0000-0002-6650-3685>

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