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Case Report

APPROACH TO BIPOLAR DEPRESSION IN AN ADOLESCENT CASE WITH THE 1Q21.1 MICRODELETION SYNDROME

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ABSTRACT

Aim: This case report will discuss the approach to bipolar depression in an adolescent female patient with the 1q21.1 microdeletion.

Case: A 17-year-old female patient was referred to our clinic in the year 2023 due to a suicide attempt by drug intake and treatment refusal. She had been operated on at the age of 5 due to a diagnosis of pilocytic astrocytoma. At the age of 10, she was diagnosed with epilepsy and mild mental retardation. Her phenotypical anomalies included long philtrum, deeply set eyes, and macrocephaly. Genetic examination and chromosomal analyses resulted in a diagnosis of 1q21.1 microdeletion in the same year. At the age of 14, she experienced a manic episode lasting approximately 3 weeks, followed by recurrent depressive episodes and suicide attempts, for which she was hospitalized in psychiatric services twice. For the last 1 month, she had been experiencing complaints of anhedonia, irritability, and self-harm thoughts, and she had attempted suicide by ingesting medication 2 weeks before her hospitalization. The patient was diagnosed with "Bipolar Disorder Type 1, Current Episode Depression". Valproic acid was preferred as the mood stabilizer due to the nephrogenic effects of lithium, and the dose was adjusted to 1250 mg/day. The treatment was adjusted to risperidone 3 mg/day, quetiapine 900 mg/day, and depot risperidone 25 mg/2 weeks. Cognitive Behavioral Therapy-based patient and family sessions were conducted to address depressive cognitions and suicidal behaviors.

Conclusions: Our adolescent case with identified 1q21.1 microdeletion is presented as noteworthy, as the patient was also diagnosed with bipolar disorder. In the approach to mood disorders comorbid with epilepsy, the mood-stabilizing antiepileptic drug valproic acid, as in our case, may be preferred.

Keywords: 1q21.1 microdeletion, bipolar disorder, epilepsy, pilocytic astrocytoma, suicide, valproic acid

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INTRODUCTION

The 1q21.1 microdeletion is a chromosomal abnormality where a small segment of chromosome 1 in the long (q) arm, specifically the region called "q21.1", is deleted in each cell [1]. This chromosomal change can cause various phenotypical anomalies like long philtrum, prominent forehead, and deeply set eyes. It can also increase the risk of neuropsychiatric problems such as developmental delay, microcephaly, mental retardation, epilepsy, and psychotic disorders [2, 3]. This case report will discuss the approach to bipolar depression in an adolescent female patient with the 1q21.1 microdeletion. Informed consent has been taken from her and her parents.

Case

A 17-year-old female patient was referred to our clinic in the year 2023 due to a suicide attempt by drug intake and treatment refusal. She had been operated on at the age of 5 due to a diagnosis of pilocytic astrocytoma. After the operation, she developed right-sided hemiplegia, right facial paralysis, permanent vision loss in the right eye, and hearing loss in the right ear. She received chemotherapy for 3 years. In addition, she received physical rehabilitation until the age of 6.

At the age of 10, she was diagnosed with epilepsy and mild mental retardation. Her phenotypical anomalies included long philtrum, deeply set eyes, and macrocephaly. Genetic examination and chromosomal analyses resulted in a diagnosis of 1q21.1 microdeletion in the same year. During this period, she was subjected to peer bullying and was diagnosed with major depressive disorder, followed by 2 years of non-pharmacological psychotherapy.

At the age of 14, she experienced a manic episode lasting approximately 3 weeks, followed by recurrent depressive episodes and suicide attempts, for which she was hospitalized in psychiatric services twice. During these periods, she used a large number and variety of antipsychotic and mood-regulating pharmacological agents like olanzapine up to 20 mg/day, lamotrigine up to 50 mg/day, duloxetine up to 90 mg/day, fluoxetine up to 40 mg/day, topiramate up to 200 mg/day, and amisulpride up to 100 mg/day, but no significant clinical benefit was achieved.

For the last 1 month, she had been experiencing complaints of anhedonia, irritability, and self-harm thoughts, and she had attempted suicide by ingesting medication 2 weeks before her hospitalization. Due to the risk of suicide, the patient was admitted to our child psychiatry inpatient unit. No additional pathology was found in the neurological and laboratory examinations. It was learned that her twin siblings and her father also had the 1q21.1 microdeletion. In the mental status examination, the patient was alert, oriented, and cooperative. Her mood was depressed, and her affect was blunted. Her speech rate and amount were reduced, and psychomotor activity was decreased. She had passive death thoughts. There were no active psychotic findings, homicidal, or suicidal thoughts. She had insight. The patient was diagnosed with "Bipolar Disorder

Type 1, Current Episode Depression". The initial treatment was quetiapine 600 mg/day, zuclopenthixol intramuscular injection 200 mg/week, lithium 1200 mg/day, and biperiden4 mg/day. Recently, the patient had complaints of excessive thirst and urinary incontinence. Valproic acid was preferred as the mood stabilizer due to the nephrogenic effects of lithium, and the dose was adjusted to 1250 mg/day. Zuclopenthixol treatment was discontinued as it was thought to be ineffective. Additionally, the treatment was adjusted to risperidone 3 mg/day, quetiapine 900 mg/day, and depot risperidone 25 mg/2 weeks. Cognitive Behavioral Therapy-based patient and family sessions were conducted to address depressive cognitions and suicidal behaviors. The patient, with reduced suicidal thoughts, was discharged in clinical remission in 25 days.

Discussion

The 1q21.1 deletions exhibit a diverse clinical phenotype, typically characterized by intellectual disabilities, seizures, psychosis, language disorder, autism, and microcephaly. Developmental delay and/or learning disabilities have been commonly reported. Behavioral issues such as attention deficit hyperactivity disorder, autism, anxiety/depression, antisocial behavior, aggression, and even hallucinations have been frequently observed [3]. However, manifestations may vary due to interindividual clinical variability, incomplete penetrance, and absence of specific facial features [4]. The 1q21.1 recurrent microdeletion follows an autosomal dominant inheritance pattern, with 18–50% occurring as de novo mutations and 50–82% being inherited [5]. A study has associated three schizophrenia-related copy number variants with bipolar disorder: duplications at 1q21.1, deletions at 3q29, and duplications at 16p11.2 [6]. Additionally, a case report has documented a 17-year-old female with moderate intellectual disability, spastic paraparesis, movement disorder, and bipolar disorder, harboring a 1.802 Mb de novo 1q21.3q22 duplication [7].

Alterations in the 1q21.1 gene, such as deletions and duplications, have been associated with various neurodevelopmental disorders and psychiatric illnesses. In recent years, some studies on the genetic basis of bipolar disorder have found significant changes in this gene. Our adolescent case with identified 1q21.1 microdeletion is presented as noteworthy, as the patient was also diagnosed with bipolar disorder. In the approach to mood disorders comorbid with epilepsy, the mood-stabilizing antiepileptic drug valproic acid, as in our case, may be preferred.

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