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CASE REPORT

A Mild and Atypical Presentation of 15q11.2 BP1-BP2 Microdeletion: Absence Epilepsy without Neurodevelopmental Impairment

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Abstract

We present a 17.5-year-old female with a de novo 15q11.2 BP1-BP2 microdeletion who developed absence epilepsy despite entirely normal neurodevelopment and excellent academic performance. Her seizures were successfully managed at different times with antiepileptic drugs (AEDs) from three pharmacological classes, with optimal mood stabilization achieved under lamotrigine. Whole exome sequencing identified no additional pathogenic variants associated with epilepsy or neurodevelopmental disorders. Parental testing confirmed de novo occurrence and written informed consent for publication was obtained from the patient and her guardians. This case highlights the phenotypic variability and incomplete penetrance of the 15q11.2 microdeletion and underscores the value of genetic testing even in neurodevelopmentally typical individuals presenting with atypical seizure patterns.

Keywords: Epilepsy, Neurodevelopment, Seizures, 15q11.2 BP1-BP2 microdeletion

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1. Introduction:

Epilepsy is a neurological disorder, typically chronic, characterized by abnormal and repetitive fluctuations in electrical activity within neuronal cells. These fluctuations lead to sudden and uncontrollable contractions, involuntary movement, and loss of consciousness, all of which are manifested as seizures. Epileptic seizures may originate in a specific region of the brain or result from widespread electrical activation throughout the brain. The underlying causes of these abnormal discharges can vary significantly. While epilepsy can arise from numerous factors, this case report aims to emphasize the role of genetic influences in epilepsy, specifically the potential contribution of inherited or spontaneous (de novo) microdeletion.

Within this genetic framework, the 15q11.2 BP1-BP2 microdeletion has typically been reported in association with severe epilepsy, neurodevelopmental delay, and structural brain abnormalities [1,2]. To date, only three cases have been described in association with isolated childhood absence epilepsy, and in these reports, detailed information on neurodevelopmental outcomes is lacking [3]. Therefore, our case is particularly noteworthy, as the patient presented with absence epilepsy without any neurodevelopmental impairment.

15q11.2 BP1-BP2 microdeletion is a recurrent Copy Number Variation (CNV) implicated in a wide spectrum of neurodevelopmental conditions, including developmental delay, autism spectrum disorder, behavioral dysregulation, and epilepsy [4-6]. The penetrance and expressivity of this CNV are highly variable. Absence epilepsy, as a sole manifestation without developmental impairment, is rarely reported in association with this deletion [7,8].

We report a neurodevelopmentally intact adolescent with a de novo 15q11.2 microdeletion and absence epilepsy demonstrating excellent antiepileptic response and no other clinical abnormalities.

2. Case Presentation:

A 17.5-year-old female with no family history of epilepsy first presented at age 9 with brief episodes of staring and unresponsiveness. Early neurodevelopment was normal, with milestones such as sitting, walking, and speech achieved ahead of schedule. The patient exhibited excellent academic performance and no behavioral abnormalities.

Electroencephalography (EEG) confirmed typical absence seizures. Treatment with valproic acid led to complete seizure control, which persisted until the medication was discontinued at age 11. The patient remained seizure-free for approximately one year before experiencing a generalized tonic-clonic seizure at age 12, after which levetiracetam was initiated.

Levetiracetam was discontinued after two years of seizure freedom and normalization of EEG findings. Following a recurrence of generalized seizures, lamotrigine therapy was initiated, resulting in optimal seizure and mood stabilization.

Due to the atypical course and absence of familial epilepsy, genetic testing was pursued. Chromosomal microarray analysis revealed a de novo 15q11.2 BP1-BP2 microdeletion encompassing NIPA1, NIPA2, CYFIP1, and TUBGCP5 1. Parental studies confirmed the deletion was not inherited. Whole exome sequencing identified no additional pathogenic variants associated with epilepsy or neurodevelopmental disorders.

3. Discussion:

The 15q11.2 BP1-BP2 microdeletion has been increasingly recognized as a susceptibility region for a spectrum of neurodevelopmental and neuropsychiatric disorders [1,2]. Most reported cases associate this deletion with developmental delay, cognitive impairment, speech and motor deficits, behavioral abnormalities (e.g., ADHD, OCD, autism), and, in some cases, dysmorphic features or congenital anomalies [4-6]. However, this case documents an adolescent patient with isolated absence epilepsy with the 15q11.2 BP1-BP2 microdeletion, normal neurodevelopment, normal structural brain imaging, and above-average cognitive and social functioning.

The literature reports only three previous cases of isolated childhood absence epilepsy associated with 15q11.2 microdeletion, and detailed neurodevelopmental outcomes were not provided [3].

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Our case is therefore particularly noteworthy because the patient presented with absence epilepsy without any neurodevelopmental impairment.

While microdeletion in the 15q11.2 region has previously been implicated in neurological disorders, speech delay, and behavioral syndromes [4-6] the presentation of epilepsy in isolation without any developmental, behavioral, or structural brain anomalies is extremely rare. This suggests that 15q11.2 BP1-BP2 deletions can manifest solely as epileptic phenotypes and challenges the view that neurodevelopmental impairment is a prerequisite for clinical relevance of this CNV.

Furthermore, unlike previous reports where affected individuals often exhibited significant impairments or dysmorphisms and were diagnosed in early childhood, our patient was diagnosed in adolescence and exhibited none of the core features such as intellectual disability or motor delays. Additionally, the patient's seizures were well managed with lamotrigine monotherapy, and whole exome sequencing revealed no other pathogenic variants that could explain the phenotype. This constellation of findings highlights the potential for highly attenuated expression of this microdeletion and underscores the importance of individualized genetic interpretation in clinical settings.

4. Conclusion:

This case presents a uniquely mild and underreported phenotype of the 15q11.2 BP1-BP2 microdeletion, characterized solely by absence seizures in an adolescent with normal neurodevelopment, normal structural brain imaging, and above-average cognitive and social functioning. Unlike the majority of reported cases involving this microdeletion, which often include intellectual disability, speech delay, or behavioral disturbances [7-9], our patient showed none of these features. This clinical profile expands the known phenotypic spectrum and underscores the highly variable expressivity and incomplete penetrance associated with the deletion. Most notably, it challenges existing assumptions that 15q11.2 BP1-BP2 deletions invariably produce developmental impairments. Given this atypical yet genetically confirmed presentation, our findings support the utility of chromosomal microarray and, when necessary, whole exome sequencing in pediatric epilepsy patients who appear neurotypical but deviate from standard epilepsy classifications. This case contributes to the evolving understanding of 15q11.2 deletion and raises awareness of isolated epilepsy as a possible sole manifestation.

Informed Consent Statement: Informed written consent was obtained from the patient for publication of this report and any accompanying images.

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A	Data Curation
B	Formal Analysis
C	Original Draft
D	Writing Review & Editing
E	Formal Analysis
F	Methodology
G	Investigation

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