Williams, J Speech Pathol Ther 2023, 8:3

Journal of Speech Pathology & Therapy

Case Report Open Access

Exploring the Association between Potocki-Lupski Syndrome and Autism Spectrum Disorder: A Case Report

Keywords: Speech and language disorders; Potocki-Lupski syndrome; Spectral density; Language impairments; Autism spectrum disorder; Nucleotide variants

Introduction

Potocki-Lupski syndrome is a genetic disorder that has been relatively recently identified. It is characterized by a duplication of chromosome 17 band p11.2. The length of this duplication is typically around 3.7 Mb, and it is estimated to occur in approximately 1 in 25,000 live births [1]. PTLS is associated with a broad spectrum of congenital abnormalities, including mild dysmorphic features, feeding difficulties, sleep apnea, seizures, microcephaly, and various ophthalmic, orthopedic, cardiovascular, oropharyngeal, and renal anomalies [2]. The behavioral and neurodevelopmental manifestations of PTLS are also diverse. The most common symptoms include developmental delay, intellectual disability (ranging from borderline to severe), speech and language disorders, executive function deficits, aggressiveness, anxiety, withdrawal, attention-deficit/hyperactivity disorder (ADHD), and autism spectrum disorder (ASD) features [2-4]. Initial studies suggested that ASD is a relatively common feature of PTLS, indicating a potential involvement of the 17p11.2 region in the genetics of ASD [1]. However, subsequent research has raised questions about the role of autistic features in the PTLS phenotype [5-12]. The most recent review reports a lower prevalence of ASD among PTLS patients, approximately 37.9% [2], compared to an earlier study by Treadwell-Deering et al. where the prevalence was approximately 80% based on a sample of 15 PTLS patients [1]. To contribute to the understanding of ASD in the context of PTLS, we present a case study of a 13-year-old Russian female with a confirmed de novo duplication of 17p11.2 [6]. Our investigation to 2000 seconds (mean duration: 1803 ± 79 seconds). Independent component analysis (ICA) was employed, when necessary, to remove prominent artifacts [20]. Three experienced neurologists, including GP, who were certified experts, independently reviewed and interpreted the EEG data, arriving at a consensus on their findings.

To ensure comprehensive analysis, the EEG process was recorded on video to identify any typical clinical events or seizures.

The following phenomena were examined:

The presence and extent of diffuse rhythmic activity or generalized background slowing.

Epileptiform EEG abnormalities: a. Sporadic wave discharges, spikes, and multi-spikes were categorized as benign focal epileptiform discharges of childhood without clinical manifestations. b. Episodic peak-wave or slow spike-wave complexes, which lacked repetitive structure, generalization, or secondary generalization, and were not accompanied by clinical events. The topography of this activity was also taken into consideration. c. Typical or atypical epileptiform discharges displaying secondary generalized spike-slow wave discharges or spike-wave discharges that either correlated or did not correlate with clinical events.

To explore the prevalence of ASD in individuals with Potocki–Lupski syndrome (PTLS) and analyze existing literature on the topic, we conducted a systematic search in the PubMed database. Relevant articles were identified using the search terms "(Potocki-Lupski) AND (autis OR ASD)" applied to titles and abstracts, limited to studies published in English. Additionally, articles from a previous literature review [2] were included if they were not already identified in the PubMed search. Several exclusion criteria were applied, including: (1) articles that were not in full text format (such as letters and conference theses); (2) studies without original data, including various types of reviews and meta-analyses; (3) animal studies; (4) studies based on group comparisons; and (5) studies involving participants below 18 months of age, as a reliable diagnosis of ASD is not feasible at such early ages [21-23].

Case presentation

The child does not have any siblings, and the pregnancy was free from complications. There were no reported instances of infections, medication usage, smoking, alcohol consumption, or drug intake during pregnancy. At the time of the child's birth, the mother and father were 34 and 30 years old, respectively. There have been no known genetic syndromes in the family. The child was delivered in the 42nd week of gestation due to artificially induced labor caused by an abnormally slow heartbeat and excessive fluid in the lungs. Consequently, she was admitted to a neonatal intensive care unit. The birth weight was 2920 g, which falls within the 25th percentile. From the early months of life, the child encountered multiple difficulties, including failure to thrive, feeding problems characterized by poor sucking and vomiting after meals, and sleep disturbances. During early childhood, she experienced episodes of breath-holding spells with loss of consciousness and febrile seizures associated with high fevers exceeding 40ºC. Gross motor milestones were achieved towards the later end of the normal range, with walking attained at 14 months, although initially, it was unsteady. Fine motor skills remained challenging for some time. Bowel and bladder control were delayed and achieved at 40 months. In terms of language development, there was no history of babbling, and her initial vocalizations were described as "whistling" sounds. She began saying her first words at approximately 18 months, but they were sporadic, and she did not consistently use stable words until she was three years old. It wasn't until four years of age that she started forming simple three to five-word phrases. Additionally, she experienced significant delays in receptive language skills. At four to five years old, she understood approximately 50 words but struggled to follow complex instructions. Her parents found it necessary to break down instructions into smaller parts. Notably, her understanding of language appeared to rely more on context than the meaning of phrases. Furthermore, her own speech was challenging for others to understand due to international issues and a limited vocabulary. By the age of five, she received diagnoses of developmental delay, sensory-motor, ADHD, speech and language impairments, and several learning disorders such as dyslexia, dysgraphia, and dyscalculia. The child's mother also mentioned that clinicians who assessed her noted traits of ASD. The child was initially referred to the research team at the age of 11 for a comprehensive evaluation, which revealed delays in speech and cognitive development, difficulties in adaptive functioning, and concerns about the genetic basis of her conditions. Later, at the age of 13, genetic testing was recommended, and the family trio underwent whole-exome sequencing (WES) to analyze their genomes. The analysis identified multiple de novo single nucleotide variants (SNVs) and copy-number variations (CNVs), two of which were clinically significant: a deletion in the 15q11.2 region and duplication in the 17p11.2 region. Molecular cytogenetic testing using fluorescence in situ hybridization (FISH) did not confirm the presence of the 15q11.2 deletion. However, the 17p11.2 duplication was confirmed, leading to the diagnosis of Potocki–Lupski syndrome. The patient's clinical presentation aligns closely with the main features of the syndrome, including multiple developmental delays, muscle hypotonia, feeding difficulties, and behavioral disorders.

At the age of 13, the patient was enrolled in a regular public school and received education through an individualized plan in inclusive settings, primarily designed for children with ASD. However, her parents observed persistent difficulties in comprehending spoken language and experienced challenges with pronunciation, intonation, and fluency. Academically, she was described as falling behind, as she had recently started developing writing skills and faced difficulties in arithmetic and memorization. The patient's mother characterized her as highly sociable, friendly, and trusting. She exhibited a strong attraction to people, displayed high levels of empathy, and thoroughly enjoyed engaging in play with peers, particularly in storytelling and role-playing activities.

Language improvement

The patient's performance on the RPLS-5 assessment revealed significantly lower scores compared to her peers. She achieved raw scores of 56 out of 65 for Auditory Comprehension and 54 out of 67 for the Expressive Communication subscales. Her overall language ability in Russian was equivalent to that of a five-year-old and two-month-old child, although caution is warranted since the norms used were based on English-speaking populations only.

Discussion

In this case report, we present a detailed evaluation of a female patient with PTLS, focusing on clinical, behavioral, and electrophysiological aspects, particularly regarding the features and associations of ASD, which is commonly observed in this syndrome. The reported prevalence of ASD among individuals with PTLS varies from 37.9% to 80% [24]. This range appears to be wider compared to other common genetic syndromes, where the prevalence of ASD ranges from 11% to 61%, as shown in a systematic review and meta-analysis conducted in 2015 [25].