

CASE REPORT

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Deletion of chromosomal regions 13q21 detected by genetic tests in a boy with special learning disorder: A case report

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Abstract

Specific learning disorder (SLD) is defined as significant and persistent learning difficulties leading to unexpected academic underachievement in terms of the subject's age and cognitive ability, and the level of education provided. SLD has a biological basis determined by genetic and environmental factors. Neurobiological hypotheses have been proposed to account for SLD, and genetic factors have been proved to have a major effect on the etiology. Findings of specific language impairment (SLI), such as speech delay, are frequently seen in early childhood in SLD cases. Recent studies of the etiology of SLI have also focused on genetic causes and have suggested a genetic inheritance. We report the case of a nine-year-old SLD patient with 13q21 deletion, who was a prior diagnosed with language impairment in early childhood. The case is discussed in the light of the current literature.

Keywords: Specific learning disorder, genetics, specific language impairment

Introduction

Specific learning disorder (SLD) is a neurodevelopmental disorder characterized by persistent difficulties in learning and using academic skills. Impaired academic skills can occur in three domains, reading, written expression and mathematics. In the Diagnostic and Statistical Manual for Mental Disorders—Fifth Edition, (DSM–5) the prevalence of SLD across all these academic domains is cited at 5-15% among school-age children across different cultures and languages [1]. There is now strong evidence from twin and association studies implicating genes in the development of reading disorder [2]. Family studies have long shown that dyslexia and overall reading abilities have significant genetic components, with heritability estimated at 54-84% [3].

Language disorders are frequently seen in SLD patients in clinical practice. Research has shown that dyslexia tends to co-occur with other neurodevelopmental disorders, such as specific language impairment (SLI) [4], speech sound disorder [5], and attention deficit-hyperactivity disorder. Several prospective studies have reported an increased rate of subsequent reading disorder with SLI [6]. Relatives of probands affected by dyslexia also have an increased risk of language impairment, while studies of children with language impairments often report a high incidence of

literacy problems. However, the exact relationship between the two disorders (SLI and SLD) remains unclear. We describe a patient with 13q21 deletion, who had been previously diagnosed with SLI in early childhood, and with SLD later during formal education, and discuss the case in the light of the current literature. The parents gave written consent for the publication of this report.

Case Report

A nine-year-old boy living in Istanbul with his family presented to our clinic with low academic achievement and learning difficulties. Despite being in the third year of school, he had failed to fully acquire reading and writing skills. His reading speed was below the expected level, and significant problems were present in reading accuracy. He was confusing letters and numbers. His writing was illegible, with entire words missing. He also had difficulty with arithmetical calculations and time-related concepts. The Wechsler Intelligence Scale for Children-Revised (WISC-R) was applied, eliciting Verbal IQ: 60 and Performance IQ: 85. Following tests and clinical evaluation, the patient's mental level was evaluated as dull normal / low average. He was the youngest child of the family, and had been delivered via the physiological route following a normal pregnancy. Growth retardation was noted in the first few months of life. He was able to sit unsupported at nine months, and to stand while holding onto objects at one year, and started walking at approximately 15 months. He started producing consonant sounds at 10 months, babbled ("baba" or "dada") at 15 months, and spoke his first words at 24 months. He began to form simple sentences at 3-3.5 years. He had no history of hospitalization, seizures, surgical

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procedures, or systemic disease. At approximately four years of age he had been referred to a child psychiatry clinic due to the complaints of poor vocabulary and limited sentence structure and had been diagnosed with expressive language disorder. Following two years of supportive rehabilitation education, he had caught up with his peers in terms of language skills. His family history was negative for any psychiatric or systemic disease.

Specific learning disorder was diagnosed at psychiatric evaluation on the basis of DSM-V diagnostic criteria. No comorbid psychiatric diagnosis was determined. The current learning disability was prevalent in all areas of reading, writing and mathematics. Psychoeducation and special training were started following diagnosis. His appearance indicated physical development below the expected level for his age. Despite being nine years old, he was 121 cm tall and weighed 21 kg. His parents reported that he had always lagged behind his peers in terms of developmental percentiles. Since his recent values were below the third percentile for both weight and height for Turkish boys, the patient was consulted with pediatric medicine clinic. Laboratory examination revealed no pathological findings. Genetic evaluation revealed 16.6 Mb deletion in the band q21.32 q31.1 (66613570-83232587) in the q arm of chromosome 13.

Discussion

Dyslexia, the most commonly investigated form of SLD, is a complex neurodevelopmental disorder with a multifactorial etiology which probably involves small effects of numerous genes and gene-gene interactions [7], as well as gene-environment interactions [8]. Growing interest in genetic studies has led to an increase in the numbers of reports concerning associations between SLD with specific genes and chromosomes. Reviews discussing the genetics of dyslexia and learning disorders have identified several loci and chromosomes related to dyslexia, including 15q21.3, 6p22, 2p16-p15, 6q13-16.2, 3p12-q13, 18p11.2, 11p15.5, 1p36-p34, and Xq27.3 [9-11].

In SLD cases, language problems are often seen not only during the diagnosis of SLD but also in the developmental story. SLI is clinically defined as failure to develop language normally, despite the presence of a suitable environment for language development and the absence of hearing deficits, mental retardation, oral motor/structural abnormalities, or of neurological or psychiatric impairments affecting language acquisition [12]. The etiology of SLI, like that of many complex neurological disorders, is not well defined, although research over the last decade suggests that the condition is highly heritable. Several genes and loci have already been implicated in SLI through linkage and targeted association methods [13]. Chr13q21 has been identified as a major susceptibility locus for SLI [12]. Reviews summarizing the chromosomal etiology of reading disorder and SLI have identified 13q21 (SLI3) as a chromosome region linked to SLI, and 1p34-36, 2p15-16, 3p12-q13, 6p22, 15q21, 18p11 and Xq27.3 as chromosome regions linked to reading disorder [5].

Many children diagnosed with SLI early in their life subsequently develop characteristics of dyslexia after starting school [14, 15]. Children with SLI often have other language disorders, or learning disorders, such as reading disorder, speech sound disorder, attention deficit hyperactivity disorder or autism. This suggest the possibility of an overlap of genetic risk factors [16]. The strong links between both dyslexia and SLI and phonological impairments

have encouraged speculation that language impairments and reading disabilities may represent different manifestations of similar neurological deficits [14].

The biological cause of reading disorder and SLI remains poorly understood. However, the manifestations of the conditions are clearly the result of multiple interacting factors, many of which are genetic in origin. It is very probable that SLI and reading disorder arise due to various shared genetic/neurobiological mechanisms, as well as non-shared causal factors [17]. In their recent review of the literature, Snowling and Melby-Lervåg suggested that a phonological processing deficit can be conceptualized as an endophenotype of dyslexia that increases the continuous risk of reading difficulties [18].

Conclusion

Similarly in our case, the patient had been diagnosed with expressive language disorder in early childhood and had received speech therapy for this. SLD was diagnosed after beginning formal school education. Physical examination indicated findings of growth retardation. In the literature, common clinical features of 13q21 deletion include moderate to severe mental retardation and growth retardation. Our subject exhibited growth retardation, but no mental retardation [19]. In one case with deletion in similar coordinates, bilateral sensorineural hearing impairment, cataract, corneal opacity, retinal detachment, weight loss, absent speech, generalized seizures, and severe global developmental delay were reported on a genetic database [20]. We think that the genetic coordinates detected at analysis probably represent the common genetic constituent of SLD and SLI. To the best of our knowledge, this is the first case in which SLI and SLD were both present in the context of 13q21 deletion. The only physical finding in the examination of our patient was poor physical development which let us to consider pediatric consultation. Considering the prevalence of SLD, clinicians should pay particular attention to minor phenotypic findings in patients with the condition, which may indicate the type of further examination required. This approach will also be helpful in identifying the etiology of SLD. We also think, in the light of the present case, that particular studies on the association between SLD and 13q21 are now needed.

Competing interests

The authors declare that they have no competing interest.

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