Asperger's disorder and Williams syndrome: a case report

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Williams syndrome (WS) is a genetic disorder caused by the hemizygous microdeletion in chromosome 7q11.23. It is characterized by dysmorphic face, cardiovascular disease, idiopathic hypercalcemia, mental retardation, and an uneven profile of cognitive-linguistic abilities and deficits. The presence of autistic features in individuals with WS is a controversial issue. While there are reports that describe them as overly friendly with excessive sociability and good empathic skills, some recent studies focus more on the qualitative impairment of their social abilities. Here, we report the clinical presentation and follow-up of an eight-year-old boy with WS and clear problems in his social interaction, non-verbal communication and circumscribed interests. To our knowledge, this is the first case report on the coexistence of WS and Asperger's disorder. It also differs from previous papers on the comorbidity of WS and autism spectrum disorders, by depicting a highly verbal, non-retarded child followed for seven years through adolescence.

Key words: Williams syndrome, Asperger's disorder, autism spectrum disorders.

Williams syndrome (WS) is a genetic disorder caused by hemizygous deletion of a segment in chromosome 7q11.23, characterized by dysmorphic facies, cardiovascular disease, idiopathic hypercalcemia, intellectual disability, and an uneven profile of cognitive-linguistic abilities and deficits[1].

Some studies overemphasize that subjects with WS have overly friendly, engaging personalities, and excessive sociability with strangers[2,3], and define WS as the opposite phenotype of autism[4]. However, there is also evidence that children with WS experience difficulties with social interaction and communication and display unusual and restricted interests[5-7]. Besides case reports describing individuals with WS and concomitant autism[8-11], some recent studies report that 20-50% of children with WS were classified as "autistic spectrum" using different assessment tools[12-14].

Here, we report a boy with WS, diagnosed as Asperger's disorder (AD) at 8 years of age. We aim to discuss the psychiatric characteristics and the seven-year follow-up of the case in terms of comorbidity between WS and AD.

Case Report

Patient MK was referred for disruptive behavior, problems with peer interaction and learning difficulties at the age of 8. He was unable to sit still, constantly spoke in the class and sometimes showed physical aggression toward his friends. His teacher could no longer manage him in the class and punished him several times by removing him from the room for disrupting the lesson. In addition to his hyperactive and impulsive behavior, his mother was concerned about his interpersonal relationships. Although he liked being with his friends, and tried everything to keep them nearby (e.g. spending all his pocket money on them), he always seemed a loner. He talked continuously about his "favorite" topics even when his friends no longer wanted to listen. He once beat one of his friends for having long and curly hair, which he did not like. He often took his shoes off and bit his toenails in the classroom, ignoring his friends' protests.

His early developmental history was unremarkable. He received the diagnosis of supravalvular aortic stenosis at 3 months of

age and was followed with yearly visits. He started walking and using two-word sentences by 18 months. Due to his dysmorphic features comprised of wide mouth with thick lips, epicanthal folds, flat nasal bridge, dysplastic ears, narrow and high palate, short stature, bilateral position abnormality in the 2nd and 3rd toes, Sydney line in the left hand, and clinodactyly, he was referred for genetic investigation with a probable diagnosis of WS. Genetic analysis by fluorescence in situ hybridization using a biotin-labelled probe revealed hemizygosity at the elastin locus with a karyotype of 46,XY,del(7)(q11.23q11.23). He was diagnosed as WS because of his characteristic physical features, cardiac defect and microdeletion in the 7th chromosome at the age of 6 years. His family history was unremarkable and the parents were non-consanguineous.

He was described as a fidgety, verbally and physically impulsive, inattentive boy, and displayed difficulties in play and social relationships from early ages. He tended to not show interest in toys, but sometimes played with their parts. He was unable to interact in scenario play, understand others' feelings from their facial expressions, or maintain age-appropriate activities with his friends. He was clumsy, especially at sports, and very sensitive to smells, often feeling nauseous due to the smell of places other than his house.

During the interview, he was physically very active, wanted to talk incessantly and interrupted his mother many times. He seemed to stare at the interviewer's mouth, avoided eye contact and his mimes were restricted. He was able to answer the interviewer's questions; however, he repetitively interrupted the conversation by asking the interviewer questions, such as what kind of music the interviewer listened to and what kind of dessert made with tropical fruits she liked, and he shared a lot of information about these topics. He was unable to sustain the interaction appropriately and spoke constantly in his own areas of interest in a monotonous voice. He had special interest in tropical fruits, ties and the music of the 1970's. He could spend a whole day in record stores and approached strangers indiscriminately and talked about their ties.

His electroencephalography and neurological examination were normal. Assessment of the intellectual level with Wechsler Intelligence Scale for Children-Revised version (WISC-R) showed a full scale IQ of 78 (Verbal IQ: 95, Performance IQ: 64).

His parents' and the teacher's Conners rating scales revealed hyperactivity, impulsiveness and inattention. MK met the Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV) criteria[15] for attention-deficit/hyperactivity disorder (ADHD), and he was started on methylphenidate, which improved his ADHD symptoms and academic achievement. In addition, he received the diagnosis of Asperger's disorder due to the severe impairment in his reciprocal social interaction, and his absorbing narrow interests, non-verbal communication problems, and motor clumsiness.

MK's hyperactivity decreased with age but problems with attention deficit and impulsivity persisted and necessitated medication. He developed rocking behavior after the age of 8. Although MK was followed for about seven years and received both special education and formal education, problems related to his areas of interest and attitudes towards others did not change significantly. However, other topics that consumed his time were added, and included scientists, perfumes, Islam, and foreign languages. He continuously argued with his parents about buying different encyclopedias and dictionaries and spent most of his time reading and seeking information on the internet on these areas of interest. He often wore his special velvet suit and bow-tie and postured like old scientists at home, and was punished for using the school laboratory for conducting experiments without permission. During the follow-up, he showed some improvement in relating with his peers but was often left alone when the others no longer wanted to listen to his ideas about science or his other areas of interest. He gained some insight into his problems, but his one-sided and rigid thinking continued to be problematic in his interactions.

Discussion

Although ADHD is frequent in WS, occurring in two-thirds of the cases[16,17], to our knowledge,

this is the first case report on the coexistence of WS and AD. It also differs from previous reports on the comorbidity of WS and AD by depicting a highly verbal, non-retarded child followed for seven years through adolescence. Nearly all case reports and research studies diagnosed AD in young children with limited language, including older toddlers and younger preschoolers in general and older children with greater language delays. This age range gives rise to questions about the stability of the socio-communicative impairment in older children, adolescents and adults with WS[12,13]. Our case showed the stability of problems in reciprocal social interaction and restricted repetitive behavior, which impaired daily functioning, despite developmental effects and the treatment of the coexisting ADHD.

Our patient had clear problems with social interaction and nonverbal communication. Despite his strong tendency to be with his friends, he could not maintain his relationship with them and was unable to take part in age-appropriate play and activities. He suffered from lack of empathy and had serious difficulties in understanding others' feelings. Although his tendency to be with others and his indiscriminate approaches to strangers are compatible with characteristics observed among subjects with WS, his lack of empathy, deficits in make-believe play and impairment in eye contact, gestures and mimes are not common in subjects with WS. Interestingly, these subjects are known for their sensitivity to the feelings of others and are repeatedly reported to be fascinated with looking towards the face and eyes[18,19]. Therefore, the social-communicative deficits seen in this subject do not seem to be an inherent part of WS and suggest the coexisting diagnosis of AD.

In addition, the persistent circumscribed interests such as outdated music, tropical fruits, scientists, and languages, etc., show similarities with cases with AD. Although a previous report mentioned that most of their subjects (81.3%) with WS had spontaneous musical interest[16], the existence of the other unusual and persistent areas of interest that had a deep negative influence in the quality of our patient's life seems to be related with AD.

The coexistence of WS and AD is explained by several factors. First, some rate of co-occurrence would be expected by chance alone, particularly given that the presence of mental retardation increases the risk of AD[20]. Second, it is possible that both share risk at the genetic level in that some AD susceptibility genes have been identified on 7q[21]. Lastly, there might be shared anatomic localizations and pathophysiology that contribute to overlap in symptoms. For example, both individuals with WS and those with AD show abnormalities of the cerebellum and parietal and/or frontal lobe areas[22-25].

In conclusion, the present report highlights the importance of the need for consideration of the presence of AD in sufferers of WS. Since early diagnosis and intervention programs for AD significantly improve the patient's long-term outcome[26], comprehensive evaluation of behavior, language and social skills of children with WS and of other medical conditions appears vital. Additionally, further studies on the pathophysiological and etiological mechanisms that underlie AD and WS are required to understand the converging and diverging expressions of these two neurodevelopmental disorders.

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