

# Clinical Report: A Female with Down Syndrome and Autism

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## Abstract

**Objective:** The association of autism and Down syndrome (DS) is comparatively uncommon, especially in females. We report a female patient with both DS and autism with detailed clinical information. **Methods:** The diagnosis of DS based on a particular set of facial characteristics, delayed growth and chromosomal analysis. Autism Behavior Checklist and the DSM-IV criteria of autism were used for the diagnosis of autism. **Case presentation:** A five-year-old girl was sent to our department due to unusual social development, language delay and restricted behaviour. At 8 months, she was diagnosed to have DS with the karyotype of 47, XX, +21. Autism was diagnosed based on the behaviour and the DSM-IV criteria. On the modified ABC, the score given by her mother was 90, which further supported the diagnosis. **Conclusion:** With low index of suspicion, autism/autism spectrum disorders can easily be missed in patients with DS. Increase in awareness that the 2 conditions can coexist in the same patient is important to paediatricians.

**Key words** Autism; Comorbidity; Down syndrome

## Introduction

Down syndrome (DS) is the most common chromosomal disorder in human with an incidence of 4.7 in 10000 live births in China.<sup>1</sup> Features of DS include intellectual disability, characteristic facial features, increased risk for heart and gastrointestinal malformations, hearing loss, hypothyroidism, and other medical problems. Autism is a disorder of neural development characterised by impaired social interaction and communication, and by restricted and repetitive behaviour with a prevalence of one in 1000 according to epidemiological investigation from several regions,<sup>2</sup> yet currently no epidemiological data of the whole

China has been reported. It has been claimed that the association of autism and DS is comparatively uncommon, with rates of autistic disorder in DS from 1% to 11% depending on the sample size and the criteria used to identify cases of autism spectrum disorders.<sup>3</sup> However, no female with DS and autism has been reported in China before. We described the first case of a female with DS and autism in China.

## Case Report

The patient is a 5-year-old girl. She was born at 40th week weighing 3.0 kg to a 29-year-old G2P1 mother and 36-year-old father via an uncomplicated vaginal delivery. There was no oxygen deficit or asphyxia after birth. The parents were not told the baby suffered from DS at birth. She was taken to the department of developmental pediatrics, Shengjing Hospital of China Medical University at 8 months because of developmental retardation. She was diagnosed DS based on her particular set of facial characteristics, followed by the chromosomal analysis (karyotype: 47, XX, +21).

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When this girl was 4 years old, she was sent to kindergarten. However, several days later, her mother had to take her home because she could not adapt to the life in kindergarten. At age 5, she came to the hospital again because of unusual social development, language delay and restricted behaviour. Although the mother was very dedicated to the patient's training and often encouraged her to interact/play with other children, she exhibited more severe language delay compared to other patients with DS of the same age, and was noted to have poor social adaptability and stereotypic behaviour. Review of early milestones showed global developmental delays with sitting at 18 months, walking independently at 3 years, and delayed speech with only intermittent use of single words such as "Dad" and "Mom" at 5 years old. She showed less attention to social stimuli and diminished responsiveness to her own name, smiled and looked at others less often and always soliloquised. In addition, she had severely restricted behaviour such as walking round and round, walking on a same route and persisting on sleeping with her own pillow even at others' home. Autism was diagnosed based on the behaviour and the DSM-IV criteria of autism. On the modified Autism Behavior Checklist (ABC), the score given by her mother under a professional doctor's guidance was 90. ABC is one of the most commonly used screening and diagnosing devices in mainland which was introduced and modified by Xiaoling Yang from Beijing Medical University in 1989, and it has 57 items grouped into the following five subscales: sensory, relating, body and object use, language, and social and self-help skills. The five subscale scores are derived by adding the weights (from 1 to 4) of all items endorsed for each of the scales. Total scores are the sum of the five subscale scores. It is recommended that individuals with total scores of 67 or above have a high probability of being autistic, the score of 90 prompted obvious autism and supported the diagnosis. Standardised IQ measures were not attempted as the likelihood of completion appeared minimal, and the stress to both the child and her family did not appear warranted at this time.

The girl had no history of convulsions and there was no history of autism or other developmental disorders or mental retardation in the family. The main goals for her are to lessen associated deficits and family distress, and to increase quality of life and functional independence. Family and the educational system are the main resources for treatment. Conducive family environment, intensive and sustained special education programs and behaviour therapy should be given to improve the quality of life.

## Discussion

Autism or autistic disorder in children with DS is not common. The first case was reported by Wakabayashi in 1979, which was a 7-year-old Japanese boy with both DS and autism.<sup>4</sup> But females with both DS and autism were seldom reported. Carter et al reported a predominance of males with DS diagnosed with an ASD in a male to female ratio of approximately 4:1.<sup>5</sup> Although the etiology of the co-occurrence of autism and DS remains unclear, genetic factors appear to play a significant role. Recently, it is reported that there is a protein called Neural cell adhesion molecules2 (NCAM2/OCAM/RNCAM) which exists in a transmembrane and a lipid-anchored isoform, and has an ectodomain consisting of five immunoglobulin modules and two fibronectin type 3 homology modules. It is primarily expressed in the brain, like the granular retrosplenial cortex, where it is believed to stimulate neurite outgrowth and to facilitate dendritic and axonal compartmentalisation.<sup>6</sup> Human NCAM2 is considered a dosage-balanced ohnolog, suggesting that increased expression of NCAM2 as a result of trisomy 21 may cause dosage-related detrimental effects on development. Thus, although NCAM2 is positioned outside the DS critical region of chromosome 21 (gene location: 21q21.1) it has been proposed as one among several candidate genes implicated in the development of DS.<sup>7</sup> Based on genome-wide association studies NCAM2 has also been proposed as a candidate gene for the development of autism.<sup>8</sup> It implies that DS and autism have the common candidate gene which makes them correlated. Unfortunately, we didn't obtain the blood sample of her. This is also the main limitation of this article.

In this study, we described a girl with both DS and autism, which was the first case report in China. It can be seen from the ABC that the patient in our report behaved more severely in sensory, relating and language ability deletion. The diagnosis of autism in DS is difficult, but children with DS are often considered to be social, to gaze longer at people than at objects, to use verbal and nonverbal means to communicate intent, and demonstrate semantic and pragmatic language and play skills generally consistent with measured intelligence. Though recent research suggests that preschool children with DS can exhibit behaviours such as poor social relatedness, delays or absence of speech, and repetitive behaviours, they don't have stereotypy behaviours. Besides, delays in adaptive skills and inability to

communicate in such patient are far more severe than what is typically seen in DS alone. Individuals with both autism and DS experience greater impairments in social interactions and communication and delays in adaptive and cognitive development.

This clinical case emphasizes the clinical features of autism in children with DS and provides further proof that autism can co-exist with DS in females, which is likely to be missed. It implies that we should think more thoroughly of whether a child has autism when he or she was diagnosed DS because of developmental retardation. Early recognition of this association is so significant that these persons may benefit from gaining access to the appropriate services, for the two disease has different training measures. Hopefully, genetics and mechanisms between DS and autism will be investigated further, and early and meaningful pharmacological interventions can be available soon.

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## Conflict of Interest

The authors declare that they have no conflict of interest.

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