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CASE REPORT

Autistic disorder in Noonan syndrome

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ABSTRACT. Few reports have described the psychiatric co-morbidity of Noonan syndrome. While mental retardation is a common feature of Noonan syndrome, the diagnosis of autism using operational criteria has not been reported. In this paper, the authors describe the association of Noonan syndrome with autism. They propose that the co-morbid diagnosis of autism should be considered during the clinical assessment of persons with Noonan syndrome.

INTRODUCTION

Noonan syndrome is a disorder presenting with short stature, webbing of the neck, congenital heart disease and a characteristic facies. Hypertelorism, epicanthus, palpebral slant, micrognathia and ear abnormalities are common. The cause of the syndrome is not known. Noonan & Ehmke (1963) first described it in a series of male children presenting with Turner-syndrome-like features in the presence of normal chromosomes, although it has since been described in both sexes. It differs from Turner syndrome in that mental retardation is more common, cardiac defect is more often pulmonary valvular stenosis or atrial septal defect, and gonadal defects vary from severe deficiency to apparently normal sexual development (Mendez & Opitz 1985). Other associations include undescended testes, hepatosplenomegaly and evidence of abnormal bleeding (Sharland *et al.* 1992). Some cases show familial tendency and a male-to-male transmission has also been reported, suggesting an autosomal dominant gene with variable expressivity. Prevalence has been estimated at 1:1000 for severely affected individuals, but may be as common as 1:100 in more mildly affected phenotypes. First-degree relatives often show partial expression of the syndrome.

Few reports have described the psychiatric co-morbidity of persons with Noonan syndrome. Krishna *et al.* (1977) described a 32-year-old male with Noonan syndrome and mental retardation who was also diagnosed with schizophrenia on the basis of interpersonal isolation, delusions and auditory hallucinations. Mahendran (1989) reported the case of a 30-year-old oriental woman with mental retardation presenting with hypomania. A number of reports have documented the presence

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of mild mental retardation in this syndrome (e.g. Mendez & Opitz 1985). Although mental retardation is frequently associated with autism, the association of autism and Noonan syndrome using operational diagnostic criteria has not been described. To the present authors' knowledge, only one letter has commented on the presence of 'autistic behaviors' in Noonan syndrome. Paul *et al.* (1983) described a boy with Noonan syndrome who also showed autistic traits. However, details about the diagnosis were not given. In this brief report, the present authors describe a youngster with Noonan syndrome who met the DSM-III-R (APA 1987) criteria for autistic disorder.

CASE REPORT

JW, a 13-year-old white male, was admitted to a child psychiatry in-patient unit for the evaluation of behavioural problems. His mother reported increasingly frequent temper tantrums consisting of screaming, rolling on the floor and growling. In addition, JW had started taking an excessive interest in women. He would accost women in public places and specifically inquire about their marital status, number of children, colour of their husbands' hair and the number of floors in their house.

JW was born after a full-term pregnancy to a 24-year-old woman. The pregnancy was complicated by pre-eclampsia. He was delivered by caesarian section for foetal distress resulting from a prolonged labour. Birth weight was 2·5 kg, and the Apgar scores were 6 and 8 at 1 and 5 min, respectively. Intubation was required in the delivery room. Pathology report of the placenta revealed acute chorioamnionitis with extensive calcification. Cardiac abnormalities (Tetralogy of Fallot) were diagnosed at birth for which he was operated upon at the age of 4 days.

Developmental history revealed a mild delay in motor development. Sensorineural hearing loss was documented at the age of 2 years. This was of a moderate degree and necessitated the wearing of hearing aids in later childhood. JW's mother recalled that he could not tolerate being touched and tried to get away if approached. He cried excessively as an infant and suffered from recurrent abdominal colic. At one year of age, he developed febrile seizures. An EEG at the age of 2 years and 10 months produced central cephalic spike and slow wave activity. JW was placed on phenytoin which was later discontinued after he remained seizure-free for 4 years. He showed a preference for solitary play by 2·5 years of age. At 4 years of age, he showed little desire to engage in reciprocal play with other children and appeared to be more interested in the mechanical details of objects.

His language development was also delayed. JW did not speak single words until 2 years of age. He showed marked echolalia around 4 years, which was later replaced by a tendency to ask the same questions over and over again, paying little regard to the social context or to the answers. JW often stared into space for prolonged periods. At times, he laughed without any reason and sometimes made groaning noises. He seldom came to his parents when hurt; instead, any injury that he sustained was only discovered by chance. JW did not follow his mother around the house when he was

a toddler; and when he started imitating others, the act was usually performed mechanically and out of context. At the age of 7 years, a diagnosis of Tourette syndrome was considered but was ruled out. JW was also found to be hyperactive and was placed on methyphenidate (Ritalin) to which he responded with some benefit. Around this age, he started showing preoccupations with time, schedules and routines. By the age of 10 years, extreme reluctance to tolerate changes was noted. JW showed some interest in making friends, but did not know how to initiate conversation and make social approaches. In the past medical history, apart from the cardiac repair mentioned above, he had had myringotomy for hearing problems and an orchidopexy to correct undescended testes.

JW's parents were divorced. His father worked as a musician and lived in a different state. According to the mother, he resembled JW in his physical features. A paternal uncle also looked like JW. Another paternal uncle was mentally retarded and institutionalized; he too resembled JW in his physical appearance. In addition, two of JW's great-uncles on his father's side were also mentally retarded and lived in supervised group homes; apparently, they did not bear any physical resemblance to JW. The mother reported that most males on paternal side presented with facial features similar to those of the patient. Congenital heart disease was also reported in one of JW's first cousins on his father's side. His maternal side was, apparently, free of known psychopathology. The patient had a 4-year-old step-sister by another father. She had no congenital medical problems and did not display any of JW's social problems.

At the time of referral, JW was in a programme for the hearing impaired in the sixth grade. The school reported that he was isolated by peers due to peculiarities in his social interaction. JW had no close friends and was interpersonally inappropriate. Though he tried to participate in organized group activities such as baseball and the boy scouts, he was unable to understand rules of social interaction which often resulted in frustration and despair. His interaction with women was particularly inappropriate. For example, JW would walk up to younger women, usually in the shops, and attempt to start a conversation. Women waiting at bus-stops or elevators were also often approached. The questions he asked were stereotyped and delivered in a monotonous voice. The topic almost always related to the woman's age, her husband, and details about her own and her husband's hair. JW had little idea of the other person's privacy and often did not seem to notice the listener's responses. His eye contact was also not consistent.

On physical examination, JW was found to be mildly obese. His height was in the thirtieth percentile for age and his weight was greater than the ninety-fifth percentile. JW displayed hypertelorism, bilaterally low-set ears and a webbed neck. A grade IV/VI holosystolic murmur was heart both posteriorly and anteriorly and was consistent with the described cardiovascular abnormalities. His nipples were wide-set and the genitalia showed small bilaterally descended testes.

On mental status examination, the patient appeared large for his stated age. JW was casually dressed and had fair hygiene. He sat with his mother, repeatedly interrupting the conversation with irrelevant questions. Eye contact was minimal. His speech showed mild difficulty with articulation but it was generally intelligible;

volume was loud with a monotonous voice and the rate was slightly increased. JW frequently responded to questions with a counter-question relating to the interviewer's family and other personal details. In addition, he was preoccupied with the layout of the building and repeatedly asked questions about the different floors and offices. JW occasionally displayed loosening of associations, but there were no abnormal beliefs of ideas. He seemed to be preoccupied with hair, especially female hair, but this did not appear to be part of an obsessive- compulsive disorder. His mood was stable. He did not show any gross cognitive deficit although his fund of general information was poor.

On neuropsychological testing, JW had a full-scale IQ of 69 on the WISC-R, a performance IQ of 75 and a verbal IQ of 65. His chromosome analysis was normal. The EEG showed nonspecific abnormalities. On the Vineland Adaptive Behaviour Scales, JW scored an age equivalent of about 6 years. On the test of Clinical Evaluation of Language Fundamentals-Revised (CELF; Semel *et al.* 1987) he scored 59 and 72 on the expressive and receptive components, respectively (mean=100; SD=15). On the Test of Problem Solving skills (Zachman *et al.* 1984), which measures the ability to take turns during conversation and other pragmatic kills, JW scored 24 (mean=100; SD=15). His score on the modified Autism Behaviour Checklist (Krug *et al.* 1980), as scored by his mother, was 80 (cut-off for autism is 67). On the Child Autism Rating Scale (Schopler *et al.* 1980), he received a score of 31·5 (cut-off for autism is 30). On the DSM-III-R (1987), JW met 12 of the 16 criteria required for the diagnosis of autistic disorder: marked lack of awareness of the feelings of others (e.g. inability to notice the distress of others; tendency to intrude on others' privacy without realizing it); abnormal seeking of comfort at times of distress (e.g. failure to ask for help and comfort even when severely hurt); markedly impaired imitation and a tendency to imitate others mechanically; and markedly abnormal social play (as indicated by his difficulty in interacting with peers on a reciprocal basis). In addition, JW showed a gross impairment in the ability to form peer friendships despite interest in making friends; abnormal nonverbal communication (as indicated by his inconsistent eye contact and his difficulty in respecting others' personal space); lack of interest in stories or imaginary events; marked abnormalities in the production of speech (characterized by a high-pitched monotonous voice); and a marked impairment in the ability to initiate and sustain a meaningful reciprocal conversation. Stereotyped body movements such as hand-flicking were also present. JW showed an unreasonable insistence on following routines (such as insisting on going to school by the same route every day and getting excessively upset if the route was changed), and had a restricted range of interests (such as playing nintendo on the computer and taking an unusual interest in the texture of people's hair). Based on the developmental history and the above findings, therefore, a diagnosis of DSM-III-R autistic disorder (APA 1987) was made. The scores on the Autism Behaviour Checklist and the CARS also supported the diagnosis.

DISCUSSION

JW had the typical features of Noonan syndrome and also met the required criteria for a DSM-III-R diagnosis of autistic disorder. His father showed some physical resemblance to his son but had not been diagnosed as suffering from Noonan syndrome. One of his father's brothers was mentally retarded and institutionalized and another had a marked facial resemblance to JW. One of JW's paternal cousins also suffered from the same cardiac anomalies. This transmission of the syndrome is consistent with similar reports described in the literature. It was not known if any of them showed autistic traits; attempts to contact them was not successful.

Research over the years has strongly suggested that autism is a developmental disorder caused by an as-yet-undefined brain abnormality. This hypothesis is supported by the association of autism with a variety of abnormalities affecting the brain, such as mental retardation. Up to 75% of autistic persons suffer from mental retardation. Though mental retardation is said to be a common feature of Noonan syndrome, few attempts have been made to categorize it or to comment on the presence of autistic traits in these patients. For example, the case of Noonan syndrome and schizophrenia described by Krishna *et al.* (1977) presented with a full scale IQ of 63; a verbal IQ of 67; and a performance IQ of 59. He was said to have a few friends, and was described as being emotionally distant from his siblings. Wilson & Dyson (1982) reported on the speech and language evaluation of a 7-year-old girl with Noonan syndrome. This girl did not have the ability to utilize language for metalinguistic purposes, such as fantasy and humor. Although some of these features may occur in autism, it is now known if this diagnosis was considered. In another study aimed at focussing on the presence of cognitive deficits in Noonan syndrome, Money & Kalus (1979) compared the IQ scores of eight males. They found that the full-scale IQ scores ranged from 64 to 124 with a mean in the average range. Subtest scores were variable providing evidence of disparities between verbal and performance IQ's. One subject had a verbal score superior to performance score by 32 points; three had higher performance scores, and in the remaining four subjects, the differences between the verbal and performance scores were not significant. Again, details about the developmental history of the patients were not given.

The present case report does not aim to propose an association between Noonan syndrome and autism, as it is likely that the occurrence of these two disorders could have occurred by chance. Rather, its purpose is to suggest that some patients with Noonan syndrome may suffer from autism and that clinical assessment of this disorder should include inquiry with respect to features typical of autism.

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