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Letter to the Editor

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Autism Spectrum Disorder and Phenylketonuria: Dyzygotic Twins with Double Syndrome

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Dear editor,

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by qualitative impairments in communication and social interaction and the presence of repetitive behavior and restricted interests that occurs in approximately 1% of the population (1). Although its main cause is unknown, several factors have been discussed as a reason in its etiology, including inborn errors of metabolism. The risk of autistic features or ASD increases in children with inborn errors of metabolism, particularly in the presence of cognitive and behavioral deficits. The presence of ASD or autistic characteristics has been reported in various metabolic disorders such as phenylketonuria (PKU) (2). Although the exact prevalence rate of autism in PKU is unknown, the relationship between the two disorders is well documented in single case reports and case series. The point common in all cases is that the late diagnosis or untreated forms of PKU could be a reason for ASD or ASD-related phenomenology (3,4,5).

A 2.5-year-old male with normal hearing test results and evaluation performed by the Neurology Department was referred to the Department of Child and Adolescent Psychiatry for an investigation of speech delay. It was learnt that the doctors had recommended a diet 3 weeks after he was born. His mother did not know why they had started her son on a diet, and she had stopped it after 5 months because she thought that her son was not gaining weight because of the diet. The patient showed no difference in development during the first 8 months along with his twin. However, he began to show a decline in interest with his surroundings; he did not make eye contact, and his movements slowed after the 8th month. His dizygotic male co-twin did not show these. The patient was assessed with the Ankara Developmental Screening Inventory (AGTA) and was diagnosed as having developmental retardation. He was diagnosed with ASD after performing a clinical assessment that included the Autism Behavior Checklist (ABC) and Childhood Autism Rating Scale (CARS). In addition, the patient was examined in terms of metabolism and was diagnosed as having PKU.

Eight months after the phenylalanine intake diet was initiated, he began to make eye contact, look when his name was said, and form two-word sentences. His ABC scores fell from 57 to 46, and his CARS scores fell from 48 to 42. His AGTA was still abnormal.

There are several theoretical constructs on the reason for dysfunctional brain development in a child who presents with symptoms of ASD. One of the theories emphasizes the behavioral dysfunction of a final common pathway in the central nervous system and views autistic syndromes as the behavioral equivalent of the cognitive deficit of mental retardation (6). In this theory, Gillberg and Coleman divided an autistic population into two groups. The disease entities of autism was the largest group, and it contained children who usually meet classical Kanner phenotypes and whose medical disease entities were generally found in individuals with autism. The double syndrome was the smaller group of patients who had dual diagnoses of an autistic syndrome and an already described medical condition. To meet the criteria of a double syndrome, children with autistic symptoms should have a second syndrome that is a disease originally described in non-autistic patients and a majority of patients with the second syndrome should not have autism. Gillberg and Coleman suggested that the co-morbidity in children with ASD and PKU is a double syndrome and that if PKU is not treated immediately after birth, irreversible brain damage may occur and can cause ASD or ASD-related phenomenology (6,7).

In conclusion, there is a need for caution in interpreting the significance of similarities or co-morbidities among ASD and the behavioral phenotypes of ASD and PKU. However, the recognition of ASD or ASD-related phenomenology in individuals with metabolic syndromes is crucial in ensuring that individuals receive appropriate behavioral management and educational placement.

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