# Can Prader–Willi Syndrome Present with Autism?

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**Prader–Willi syndrome (PWS) typically presents during the neonatal period as hypotonia with poor feeding and is confused with neonatal sepsis; however, these patients eventually develop special facial characteristics and gain weight dramatically. Some of these patients can have autistic behaviors that manifest as loss of social interest, poor communication as well as repetitive movements.**

**We present a case of a five-year-old female who developed hypotonia and poor reflexes soon after birth and was noticed to have Intrauterine Growth Restriction (IUGR). Two months later, she was noticed to have dysmorphic features with delayed developmental milestones. At 30 months, she was diagnosed with obesity and obstructive sleep apnea. At three years, she was diagnosed which raised the suspicion of autism.with PWS and at five years of age, she developed autistic behaviors**

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Prader–Willi syndrome is a rare genetic disorder in which the chromosomal region 15q11-13 is not expressed[1]. This disease can affect males and females equally, and it is considered a fetal cause of childhood obesity.

Affected children usually presented with hypotonia, poor sucking, and failure to thrive during infancy, followed by polyphagia, obesity, and intellectual disability during childhood, and hypogonadism, short stature, and behavioral disturbance during adolescence. In addition, characteristic facial features, such as almond eyes, narrow forehead, thin upper lips, and small hands and feet would be seen[2]. The prevalence ranges from 1/25,000 to 1/10,000 live born children[3].

The majority of patients are secondary to deletion (DEL; 65%–75%), and uniparental disomy (UPD; 20%–30%), the rest (1%–3%) are due to rare imprinting center defects[4-6]. The severity of phenotypic features differed between deletion type and UPD type. The facial features are less severe in the UPD group, but they are prone to psychotic and pervasive developmental disorders[1,2].

Autism is pervasive developmental disorder which is characterized by social, communication problems and stereotypical repetitive behaviors and interests[5]. The prevalence of ASD is nearly 1.5% in the general population while in PWS, it was estimated to be at 26.7%[4]. It is usually diagnosed at 18 to 24 months when social interest and verbal and non-verbal communication impairments become prominent. Autistic children do not share interests with others, do not respond to their name or call parents by their names, may exhibit repetitive movements like hand flapping or spinning and interested to look at lines and wheels[5]. Recent studies showed that neurodevelopmental disorders like autism are strongly linked to uniparental disomy rather than deletion.

The aim of this presentation is to report a case of PWS who developed autistic behaviors.

## THE CASE

The patient is a five-year-old girl, product of non-consanguineous marriage; she was born at 39+6 days of pregnancy by normal vaginal delivery. The patient's birthweight was 1.87 kg, the length was 45 cm and head circumference was 31cm. APGAR score was 9, 10 and 10 at 1, 5 and 10 minutes, respectively. The mother is thirty-nine-year-old G6P2+3 with pregnancy-induced hypertension, Sickle cell trait and G6PD deficiency.

Few hours after delivery, hypoactivity developed with weak sucking and crying, and cyanosis during feeding. She had PSO2 of 89% in room air while feeding, cold peripheral with a delayed capillary refill of 4 sec. She had truncal hypoactivity, lower limb tone of 4/5, no Moro or hand grasp reflexes and her plantar reflexes were downgoing. She was transferred to NICU as a case of IUGR with hypotonia to rule out sepsis, and was treated with antibiotics.

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During her 18 days in the NICU, metabolic screening revealed normal limit; she was diagnosed as failure to thrive. Brain MRI was normal, as well as nerve conduction study.

At two months old, dysmorphic features developed: small mouth, small almond shaped eyes, low set ears, upward eye slanting, depressed nasal bridge and frontal bossing. Chromosomal analysis was performed, which revealed female type (46XX). At four months old, the tone returned to normal with minimal head lag.

Social smile developed at two months, laughing and focused eye contact developed at four months, turnover and head control developed at the age of 7 months. The baby was also able to interact with others, transfer objects from hand to hand and babble at the age of 7 months. She could sit without support at the age of 8 months, walk at the age of 15 months, talk at two years (words like juice, mama, baba, cucumber and a sentence of 2 words). After that, she regressed linguistically and is now unable to construct short sentences, only a few single words.

At 30 months, the baby was admitted due to obesity and obstructive sleep apnea. At three years, PWS was suspected due to excessive weight gain, food seeking behaviors, and increased appetite, which was confirmed by a genetic test.

At the age of four years, adenoidectomy, myringotomy with grommet insertion was performed. The parents noticed that she always likes to play on her own, she prefers to sit on the floor in corners and play with pieces of paper that produce sound while rubbing; she had no interest in interacting with other kids.

She joined kindergarten for two years with no improvement. She could not hold pens, unable to scratch papers or copy shapes, does not respond to her mother, cannot reach for objects; however, she holds her parents' hands when she wants something. She has high pain threshold and still not toilet trained.

She has an elder brother and a sister. There is no family history of any syndromes or any psychiatric illnesses. Currently, her weight is 50 kg above 99.6 centile and her height is 86.5 cm; she is morbidly obese with a BMI of 37.8.

Genetic test revealed abnormal methylation pattern in the SNRPN gene region that confirm the diagnosis of PWS, with no deletion and this confirm that the diagnosis is uniparental disomy. The psychological review revealed IQ level of severe mental impairment.

Autism DSM5 score was: 45.5. She had verbal and non-verbal communication deficit, with poor eye contact and difficulty making friends; this fulfills the DSM-5 criteria for autism.

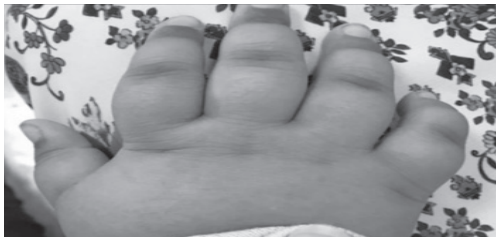

**Figure 1: Small Hand**

**Figure 2: Small Foot**

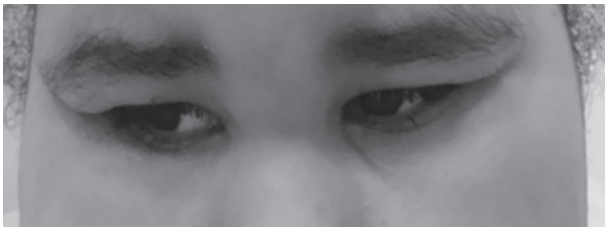

**Figure 3: Small Almond-Shaped Eyes**

## DISCUSSION

Prader–Willi syndrome was described in 1956 by Andrea Prader, Alexis Labhart, and Heinrich Willi[7]. The characteristic features are neonatal hypotonia, small hands and feet, early-onset childhood obesity and excessive hunger.

Early in neonatal life, they are hypotonic, weak muscle and poor sucking and feeding difficulty. During early childhood, they tend to overeat and their weight increase dramatically. In addition, they have an intellectual disability and low to moderate IQ level and prone to behavioral problems.

The main cause of this syndrome is a defect in chromosome 15 that can be detected by genetic testing. There are many different mechanisms of this defect it could be due to deletion on chromosome 15 or maternal uniparental disomy or imprinting deletion. Unfortunately, there is no cure for this syndrome, only to limit the complications .

We found only a few articles about PWS associated with autism[8]. The association increased with maternal uniparental disomy 38% comparing to deletion 18%[8]. Screening for autism is different across countries, but all have difficulty to establish the diagnosis due to intellectual disability.

Patients with autism have special manifestations characterized by repetitive, restrictive behaviors while patients with PWS exhibit repetitive, compulsive behaviors[8].

## CONCLUSION

**The association between Prader–Willi syndrome and autism is rare. Further studies are advised to promote management in the early stages for better outcome.**

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**REFRENCES**

1. Ogata H, Ihara H, Murakami N, et al. Autism Spectrum Disorders and Hyperactive/Impulsive Behaviors in Japanese Patients with Prader-Willi Syndrome: A Comparison Between Maternal Uniparental Disomy and Deletion Cases. Am J Med Genet A 2014; 164A (9):2180-6.
2. Veltman MW, Craig EE, Bolton PF. Autism Spectrum Disorders in Prader-Willi and Angelman Syndromes: A Systematic Review. Psychiatr Genet 2005; 15(4):243-54.
3. Whittington JE, Holland AJ, Webb T, et al. Population Prevalence and Estimated Birth Incidence and Mortality Rate for People with Prader-Willi Syndrome in One UK Health Region. J Med Genet 2001; 38(11):792-8.
4. Bennett JA, Hodgetts S, Mackenzie LM, et al. Investigating Autism-Related Symptoms in Children with Prader-Willi Syndrome: A Case Study. Int J Mol Sci 2017; 18(3): 517.
5. Lord C, Cook EH, Leventhal BL, et al. Autism Spectrum Disorders. Neuron 2000; 28(2):355-63.
6. Dimitropoulos A, Schultz RT. Autistic-Like Symptomatology in Prader-Willi Syndrome: A Review of Recent Findings. Curr Psychiatry Rep 2007; 9(2):159-64.
7. What is Prader Willi Syndrome? Foundation for Prader-Willi Research. https://www.fpwr.org/about-prader-willi-syndrome/ Accessed in May 2017.
8. O'Neil A, Quirk SE, Housden S, et al. Relationship Between Diet and Mental Health in Children and Adolescents: A Systematic Review. Am J Public Health 2014; 104(10): e31–e42.