Case Study:
Prader-Willi Syndrome

Prader-Willi Syndrome (PWS) is a disorder of chromosome 15 affecting approximately one in every 15,000 births. It affects both sexes equally and is present in every race. Genetic testing is used to confirm a PWS diagnosis, which typically presents during infancy with hypotonia, low birth weight and failure to thrive. Hypogonadism, cognitive impairments, behavioral problems and hyperphagia characterize the condition after infancy, with morbid obesity often leading to a range of other health complications. The severity of cognitive impairment and comorbidities can vary significantly, and most individuals with PWS share distinct facial features including almond-shaped eyes, bitemporal narrowing and a downturned mouth. Other common problems include scoliosis, striae, lack of eye coordination, thick saliva, speech problems, sleep apnea, short stature, small hands and feet, skin picking and hypopigmentation. Primary treatments include dietary management, growth hormone, regular monitoring of comorbidities and behavioral and cognitive therapies.

Here we profile two patients who presented to Nationwide Children’s Hospital and were diagnosed and/or treated in the Prader-Willi Syndrome Clinic, a collaboration among experts in endocrinology, genetics, nursing, dietetics, social work and psychology. These PWS specialists also coordinate with dedicated physicians familiar with PWS in psychiatry, dentistry, dermatology, gastroenterology, general surgery, neurology, ophthalmology, otolaryngology, physical/occupational/speech therapy, pulmonary medicine, sleep medicine, urology and other disciplines as needed. Faculty in the Prader-Willi Syndrome Clinic work to provide continuity of care for PWS patients and their families.
The Genetics of PWS

Approximately 70 percent of PWS cases result from a non-inherited deletion in the paternal chromosome 15; another 25 percent result from two copies of the maternal chromosome 15 and no paternal contribution (UPD); the remaining cases result from chromosomal rearrangement or an error in imprinting of the paternal chromosome 15.

Individuals with the UPD genotype typically display fewer facial characteristics associated with PWS and are less likely to have hypoglycemia than those with deletions. In addition, these patients typically have milder behavioral problems and an increased verbal IQ, but they are also more likely to have an autism spectrum disorder.

PWS is typically diagnosed with DNA-based methylation, which detects 99 percent of cases due to abnormal parent-specific imprinting within the PWS region of chromosome 15. This test differentiates between the diagnosis of PWS and Angelman syndrome. Chromosomal microarray, or FISH, is a test that detects 99 percent of cases due to abnormal parental imprints. Chromosomal microarray is a test that detects 99 percent of cases due to abnormal parental imprints. The test is used to confirm the diagnosis of PWS and to determine the extent of the deletion.

The complex genetic test revealed an atypical large deletion present in a region not previously considered a common distal breakpoint for unbalanced translocations. By clarifying the exact genetic cause of PWS, members of the clinic have been able to target medical surveillance toward their more severe phenotype. Growth hormone treatment has reduced the hypotonia in this patient, but her more severe phenotype will result in more significant lifelong developmental delays than most PWS patients. She continues as a patient of the PWS Clinic.

Patient 2 Case Elements

The patient’s early care deteriorated over time due to parental instability. The mother, who was treated with chemotherapy for multiple sclerosis prior to awareness of her pregnancy, went into long-term inpatient care for her condition. The father struggled with anxiety and homelessness. The patient began growth hormone by 6 months of age and used a gastrostomy tube until 18 months of age, when the patient’s fraternal twin brother pulled it out. A scrotal ultrasound did not identify testes prior to hCG treatment. He had speech delays and the right eye had occasional strabismus. The twins entered foster care at age 5, by which time follow-up care for the patient’s PWS had ceased.

The foster mother re-initiated medical treatment for the patient at 5 years of age. Ophthalmology prescribed glasses and physical medicine provided fitting devices. Small bilateral tests were identified with repeat ultrasound after treatment with hCG, and orchidopexy was scheduled.

The patient’s rapid improvement upon receipt of growth hormone — returning his ability to walk within 2 months of treatment — highlights the dramatic improvement in muscle tone and strength that can be obtained with proper use of growth hormone. The assistance of a social worker and an involved nurse coordinator enabled the patient to secure appropriate developmental therapies. He continues as a patient of the PWS Clinic.