Prader-Willi syndrome: most common genetic cause of life-threatening obesity

Prader-Willi syndrome (PWS) is a rare complex multisystem genetic disorder. It is recognized as the most common known genetic cause of obesity in humans which can be life-threatening, if not controlled. PWS affects about 1 in 15,000 births occurring in both genders, all races and geographies. The cause of this rare genetic condition is generally due to loss of genetic information that is active on the father's chromosome number 15.The typical deletion involves the long arm of chromosomes 15 which is inherited from the father while about one-fourth of PWS individuals have both chromosome 15s inherited from the mother and no chromosome 15 from the father which is referred to as maternal disomy 15. This observation of parent specific gene activity led to the discovery of genomic imprinting where the activity of the genetic information on genes on chromosome 15 depends on the parent of origin.

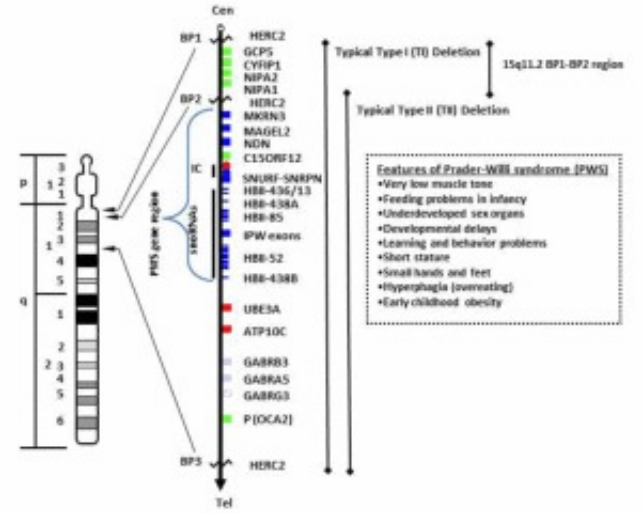

Fig. 1. Pradet-Willi syndrome (PWS) is a complex obesity-related disorder usually caused by a paternal 15q11-q13 chromosome deletion. This review article summarizes genetics, diagnosis and treatment approaches for clinical practitioners using a bulleted format with topics searchable with a table of contents and focuses on individuals affected with this rare genetic condition. Genes on chromosome 15 that cause PWS (shown in blue color) are imprinted and expressed only on the father's chromosome 15. The genes shown in red color are expressed only on the mother's chromosome 15 while the genes in green or lavender color are expressed or active on both the mother's and the father's chromosome 15.

The important features seen in this syndrome include poor muscle tone (hypotonia) and poor suck with feeding problems noted during infancy along with underdeveloped or small sex organs, small size or failure to thrive, small hands and feet due to low growth and other hormone levels and

minor birth defects. Later in early childhood, food seeking is noted leading to hyperphagia (compulsive overeating) and obesity with developmental delays, learning and behavioral problems such as obsessions, compulsions, outbursts, and skin picking (self-injury). The learning and behavioral features correlate with the specific genetic findings seen in PWS and may differ between those with the chromosome 15 deletion from the father and those with two chromosomes from the mother (maternal disomy 15). The collection of findings including learning/behavior problems, hormone deficiencies and complications related to obesity in this syndrome poses difficult management and care issues for the doctors, nurses and health care providers, teachers, patients and their families.

This review article provides a bulleted list of terms that are in a searchable format by using a table of contents approach and relate to the needs of the practicing clinician in the clinical setting when evaluating patients and their family members at any age (infancy, childhood/adolescence, or adulthood) presenting for clinical services including the description of clinical findings and presentation, background information and diagnostic genetic aspects. Other related topics about Prader-Willi syndrome include recommendations for the clinician about diagnosis, management, treatment and care options. This review will guide the clinical practice of affected individuals presenting with a wide range of medical challenges throughout their lifespan. The information provided in this report is supported by evidence-based medical knowledge obtained from experienced clinicians, published reports and syndrome-specific health care guidelines as early diagnosis is important in this disorder. It is vital that the medical team is aware of this information as provided and grouped into sections in this report and arranged in a bulleted format with a table of contents for the clinician to quickly identify pertinent information. Diagnostic tests and approaches to clinical treatment and management are described and include diet recommendations and food security, exercise, medications and hormone use with treatment options for behavioral and psychiatric problems and other health issues that are commonly seen in PWS. The recommendations are intended for health care providers and those assisting in the care and treatment at all ages of individuals with PWS. The clinical practice and laboratory recommendations in this report are based on current medical practice and knowledge learned and supported by medical evidence reported by clinicians and geneticists with expertise in syndromic-specific conditions such as PWS which is essential for smooth and effective provision of care for those affected with this classical but rare genetic disorder with obesity, high morbidity and mortality related to behavior problems and obesity complications.

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