Abstract

This paper assesses the case study of Prader-Willi Syndrome and its genetic factors. Prader-Willi Syndrome is a complex, rare genetic disorder that results in either a deletion of the paternal’s chromosome or two non-deleted maternal chromosomes. Signs and symptoms of the disorder are obesity, short height, small hands, feet and genitalia, mentally and physically disability and aggressive behavior. Several studies found that a deletion in chromosome 15, particularly the locus at 15q11q13 plays a role in Prader-Willi. Furthermore, there are several suspected genes that contribute to certain behavioral and physical aspects of the disorder such as the UBE3A gene that’s associated with two non-deleted, methylated maternal chromosomes and silencing the paternal chromosome.

Objective

The goal of this paper was to learn how to write a genetic case study that involves researching and gathering information from peer-reviewed literature papers. Following ethical and classroom guidelines were also incorporated in this case study.

Disclaimer

The purpose of writing this paper is to fulfill course requirements for BBH 411W and to stand as a personal writing sample, but the findings should not be treated as generalizable research.
The genetic case study of Prader-Willi syndrome
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i. Case Description
Patrick Star is a Caucasian male who was diagnosed with Prader-Willi Syndrome (PWS) at the age of 5. As a young child, his parents, teachers and doctor reported intellectual, physical, speech and mental delays in his growth development. As he grew into his teenage years, he also displayed hormonal problems that delayed puberty and had a constant hunger that led to his obesity. Currently at the age of 40, Patrick has mild mental retardation, behavioral problems, and abnormal walking. Furthermore, he is also obese and has small genitalia, hands and feet.

After being diagnosed with PWS, Patrick’s doctor incorporated dietary and behavioral modification. In his teens, doctors also suggested exercise to help fight off obesity and health-related complications, speech therapy, and SSRIs to help decrease Patrick’s skin picking, compulsivity and aggressive behavior. As an adult, he is still receiving treatment as part of his daily life. The purpose of this report is to identify potential genes that contribute to PWS in order to gain insight on the heritability and risk factors of the condition.

ii. Medical Description
PWS is classified as a complex disorder that affects multiple systems relating to hypothalamic insufficiency\(^1\). Although there is no set age criterion for diagnosis, it is important to note that the earlier the diagnosis is made, the more effective the long-term management will be. It affects the individual intellectually, physically, mentally and linguistically. Hypotonia begins prenatally, causing poor feeding and development during the infancy period. If untreated, this leads to obesity after the first two years of age and

\(^1\) Cassidy S. (1997). Prader-Willi syndrome. *Journal of Medical Genetics, 34*: 917-923. doi: 10.1136/jmg.34.11917
abnormally increases hunger in the child. Behavioral issues and short stature may also be prevalent as the child becomes older, hence, behavioral modification and growth hormone treatment can help improve behavior and physical growth of the individual\(^2\).

Clinical diagnostic criteria for PWS are confirmed through genetic testing by DNA methylation analysis\(^2\).

iii. Genetic Description of Potential Genes

A study conducted by Knoll et al. (1989) found a deletion in chromosome 15, particularly the locus at 15q11q13 that plays a role in PWS\(^3\). As a rare genetic disease, there are about 70% of all cases of PWS that relate to paternal chromosomal deletion; about 25% of cases related to 2 non-deleted maternal chromosomes and less than 5% of cases related to imprinting defect\(^4,5\). To detect for PWS, southern blotting is used to detect methylation differences by HpaII\(^6,7\). Although candidate genes at 15q11-13 have been identified, the exact gene (or genes) that gives rise to PWS phenotype is unknown\(^7\).

Suspected genes known to be associated with PWS fall under three categories: paternal alleles (genes MKRN3, MAGEL2 and NDN), maternal alleles (UBE3A and ATP10C) and imprinting (MKRN3, MAGEL2, NDN, UBE3A and ATP10C)\(^8\).

iv. Case Study on Specific Gene


Because the deletion of the paternal allele represents 70% of cases in PWS patients, the gene to be focused on is the Ubiquitin-Protein Ligase E3A, otherwise known as the UBE3A gene. This gene functions as a proteasome pathway and as a transcriptional coactivator\(^9\), increasing gene expression by binding to an activator that will lead to the expression of PWS. Because the gene is highly associated with PWS, it is susceptible to genomic imprinting with preferential maternal-specific expression and a silent paternal allele\(^{10}\). Three exons are visible on the UBE3A gene, where all three exons are conserved only in mammals (Homo sapiens) (see Figure 1).

![Map of UBE3A gene](image)

**Figure 1. Map of UBE3A gene**

**v. Conclusion**

Prader-Willi Syndrome is a rare genetic, complex disorder that affects all aspects of normal development in humans. Although there isn’t a specific age criteria to diagnose the disorder, it’s likely that the earlier the diagnosis takes place, the more effective the long-term treatment and management will be. From a molecular genetics aspect, PWS

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was identified to be in locus 15q11-13 in chromosome 15. Furthermore, it was found that although there aren’t genes within the locus that specifically expresses PWS in individuals, it is suspected that the UBE3A gene plays a role in the methylation of maternal chromosome and a silent paternal chromosome.

vi. References


Cassidy S. B. (1997). Prader-Willi syndrome. Journal of Medical Genetics, 34: 917-923. doi: 10.1136/jmg.34.11.917


