

An obese young man with uncontrolled diabetes and insatiable hunger: Prader-Willi Syndrome

Abilash Nair, Shyam Kishore, Ranjan Gupta¹, A. Sharma¹, Jyotsna V. P.

Departments of Endocrinology and Metabolism, and ¹Genetics, All India Institute of Medical Sciences, New Delhi, India

ABSTRACT

Prader-Willi syndrome (PWS) is a rare cause of obesity. With the rising incidence of obesity, clinicians need to be aware of genetic causes of obesity and when to suspect them. A case of PWS, which was diagnosed in adulthood, has been discussed. This case is special because of lack of history of floppiness in infancy and predominance behavioral problems.

Key words: Genetic, obesity, Prader-Willi syndrome

INTRODUCTION

Prader-Willi syndrome (PWS) is a rare cause of obesity. It occurs in 1/15,000-1/25,000 live births.^[1] PWS was first described in 1956 by three Swiss doctors, Prader *et al.*^[2] PWS is caused by the lack of expression of paternally inherited imprinted genes on chromosome 15q11-q13. It was the first recognized disorder related to genomic imprinting in humans.^[3]

Here, we discuss a case of PWS, who presented to our out-patient department with uncontrolled diabetes.

DESCRIPTION OF CASE

Patient was born of non-consanguineous marriage, full-term cesarean section delivery and cried normally after birth. Although he did not have a history of poor suck or floppiness in infancy, he had a delay in motor milestones and started to walk by himself at 2½ years of age and speak sentences at 5 years age. Bilateral undescended testis was

identified at 1 year of age. Patient had severe increase in appetite by 6 years of age and progressive weight gain since 8 years of age with no active weight reduction measures.

Patient was put in a special school due to subnormal intelligence.

Patient underwent Lt orchiopexy with Rt orchidectomy at 15 years age.

At 16 years age detected to have diabetes with osmotic symptoms and initial plasma glucose F-140 mg/dl, PP-250 mg/dl with no H/o ketosis at presentation or thereafter.

He was initially started on oral antidiabetic drugs for 1 year with diet advice, which he could not follow due to intense hunger and craving for food and is on insulin for last 3 years.

Parents were troubled by his compulsive lying, craving for food, cigarettes and beedis. There was a history of sudden mood swings, aggressive behavior and exhibitionism. Started smoking heavily by 16 years age. What was striking was that, he used to cry for food during the day as well as night and complain to doctor on duty saying if he felt so hungry and what was his fault that he ate!

There was no history of visual, auditory problems or polydactyly. Both his parents are diabetic.

Access this article online

Quick Response Code:



Website:
www.ijem.in

DOI:
10.4103/2230-8210.123566

Corresponding Author: Dr. Viveka P. Jyotsna, Department of Endocrinology and Metabolism, All India Institute of Medical Sciences, New Delhi, India.
E-mail: vivekapjyotsna@gmail.com

On examination, he had a height of 145 cm (mid parental height was 173 cm), weight of 79 kg, body mass index of 37.57 and abdominal circumference 112.5 cm.

He had an intelligence quotient (IQ) of 65-69. There was difficulty in articulating sentences. Fundus was normal. Muscular tone was decreased and muscle power was normal bilaterally in upper and lower limbs. Bilateral plantars had flexor response. Stretched penile length was 4 cm, testes was absent on the right side (orchietomy) and was 1-2 ml on the left side. Pubic hair status was Tanner P1.

Investigations

Glycated hemoglobin was 9.6%. Lipid, liver function tests and renal function tests were normal. Serum thyroid-stimulating hormone (TSH), serum T4 was normal. He had hypogonadotropic hypogonadism, hyperinsulinemia and normal cortisol and adrenocorticotropic hormone. Bone age corresponded to 18 years.

His obesity associated with hypogonadism, history of delayed milestones, hyperphagia, subnormal IQ, insatiable hunger with difficult to control diabetes, led us to think of genetic cause.

Cytogenetic analysis of patient showed normal karyotype.

The genomic deoxyribonucleic acid (DNA) was processed for studies of the methylation status of the promoter region of the SNRPN gene for confirmation of the diagnosis of PWS. DNA extraction was followed by sodium bisulfite modification using EZ DNA Methylation-Gold™ Kit (Zymo research, USA).^[4] This was followed by methylation specific polymerase chain reaction (PCR) using primer pairs specific for methylated and unmethylated alleles of the SNRPN promoter region.^[5]

RESULTS

No changes were detected on chromosome 15 at 475 band levels on doing Giemsa trypsin banding. Methylation specific PCR revealed a methylated and unmethylated band in the parents, whereas patient showed the presence of only the methylated band of the promoter region of the SNRPN gene proving the diagnosis of PWS in the patient.

Management

Patient was put on multiple subcutaneous insulin injections, regular exercise, metformin and 1400 calorie diabetic advice. He was started on triweekly testosterone injections.

DISCUSSION

In this case, the diagnosis was suspected on the basis of historical points of obesity, uncontrollable hyperphagia, developmental delay, subnormal intelligence, behavioral abnormalities, undescended testes and hypogonadotropic hypogonadism. However, this case was special as the patient did not have a history of hypotonia, low birth-weight or poor feeding in early life.

According to the consensus diagnostic criteria,^[6] he had 6 major and 6 minor criteria with the total score 9 (8 required for diagnosis).

The syndrome shows great variability, with different features during a patient's life's different stages.^[7] As a new born, the individual might suffer from severe hypotonia with feeding problems and global developmental delay. During infancy, these characteristics impede the acquisition of gross motor and language milestones. As a child, there is a development of hyperphagia that can lead to early onset. This is most probably caused by a hypothalamic dysfunction, which is also responsible for growth-hormone and TSH deficiencies, central adrenal insufficiency and hypogonadism.

During infancy, the child with PWS shows a characteristic problematic behavioral pattern, which has been reported to worsen with age.

The features which are sufficient to prompt a genetic testing for Prader- Willi Syndrome according to age at assessment include the following:^[8]

Birth to 2 years, hypotonia with poor suck.

2-6 years:

1. Hypotonia with history of poor suck
2. Global developmental delay.

6-12 years:

1. History of hypotonia with poor suck (hypotonia often persists)
2. Global developmental delay
3. Excessive eating (hyperphagia; obsession with food) with central obesity if uncontrolled.

13 years through adulthood:

1. Cognitive impairment, usually mild mental retardation
2. Excessive eating (hyperphagia; obsession with food) with central obesity if uncontrolled
3. Hypothalamic hypogonadism and/or typical behavior problems (including temper tantrums and obsessive-compulsive features).

Table 1: Consensus diagnostic criteria for PWS

Major criteria	
Hypotonia in neonatal period	0
Failure to thrive	0
Rapid weight gain after 1 year	1
Characteristic facial features	1
Hypogonadism (1. Small phallus, cryptorchidism, 2. Delayed gonadarche)	1
Developmental delay	1
Hyperphagia	1
Deletion 15q 11	1
Minor criteria	
Decreased in utero activity	0
Behavioral abnormalities: Temper tantrums, violent outbursts, obsessive compulsive, rigid argumentative, oppositional, stubborn, lying (5 or more reqd)	½
Sleep disturbance/apnea	½
Short stature (relative to bone age)	½
Hypopigmentation	0
Small hands and feet	½
Narrow hand with straight ulnar border	½
Esotropia, myopia	0
Viscous saliva	0
Articulation difficulty	½
Skin picking	0
Supportive findings	
High pain threshold	0
Decrease vomiting	0
Temperature instability	0
Scoliosis/kyphosis	0
Early adrenarche	0
Osteopenia	0
Skilled at jigsaw puzzles	0
Normal neuromuscular indices	+

PWS: Prader-Willi syndrome

CONCLUSION

With the rising incidence of obesity, we need to be aware of genetic causes of obesity and when to suspect them. A case

of PWS - one of the genetic causes of obesity, which has been diagnosed in adulthood, has been described. This case was special for the lack of history of floppiness in infancy and for predominance of behavioral problems.

REFERENCES

1. Crinò A, Di Giorgio G, Livieri C, Grugni G, Beccaria L, Bosio L, *et al.* A survey on prader-willi syndrome in the Italian population: Prevalence of historical and clinical signs. *J Pediatr Endocrinol Metab* 2009;22:883-93.
2. Prader A, Labhart A, Willi H: A Syndrome characterized by obesity, small Stature, cryptorchidism and oligophrenia following a myotonia-like Status in infancy. *Schweiz Med Wochenschr; Basel*, 1956;86:1260-1.
3. Driscoll DJ, Waters MF, Williams CA, Zori RT, Glenn CC, Avidano KM, *et al.* A DNA methylation imprint, determined by the sex of the parent, distinguishes the angelman and prader-willi syndromes. *Genomics* 1992;13:917-24.
4. Miller SA, Dykes DD, Polesky HF. A simple salting out procedure for extracting DNA from human nucleated cells. *Nucleic Acids Res* 1998;16:1215.
5. Kosaki K, McGinniss MJ, Veraksa AN, McGinnis WJ, Jones KL. Prader-willi and angelman syndromes: Diagnosis with a bisulfite-treated methylation-specific PCR method. *Am J Med Genet* 1997;73:308-13.
6. Holm VA, Cassidy SB, Butler MG, Hanchett JM, Greenswag LR, Whitman BY, *et al.* Prader-willi syndrome: Consensus diagnostic criteria. *Pediatrics* 1993;91:398-402.
7. Elena G, Bruna C, Benedetta M, Stefania DC, Giuseppe C. Prader-willi syndrome: Clinical aspects. *J Obes* 2012;2012:473941.
8. Gunay-Aygun M, Schwartz S, Heeger S, O'Riordan MA, Cassidy SB. The changing purpose of prader-willi syndrome clinical diagnostic criteria and proposed revised criteria. *Pediatrics* 2001;108:E92.

Cite this article as: Nair A, Kishore S, Gupta R, Sharma A, Jyotsna VP. An obese young man with uncontrolled diabetes and insatiable hunger: Prader-Willi syndrome. *Indian J Endocr Metab* 2013;17:S680-2.

Source of Support: Nil, **Conflict of Interest:** None declared.