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CASE REPORT

Prader–Willi Syndrome: A Case Report

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We report a case of Prader–Willi syndrome (PWS), a congenital disease, in a 10-year-old, obese, male, hyperactive child, which was diagnosed by karyotyping with microdeletion of chromosome 15. He had classical features of increased appetite with hyperphagia, temper tantrums, mild mental retardation, and bilateral undescended testis. Testicular localization could not be done. He had no pubertal growth but height gain over 3 years was normal and developed type 2 diabetes mellitus (T2DM) accompanying with dyslipidemia at the age of 13 due to uncontrollable weight gain despite lifestyle and behavioral therapy. Managing diabetic dyslipidemia in pediatric population is controversial and no clear consensus exists regarding the low-density lipoprotein (LDL) level at which pharmacotherapy should be initiated.

Introduction

Development of obesity in children, in the background of Prader–Willi syndrome (PWS), is common. Intense craving for food is the pillar that leads to uncontrollable weight gain and morbid obesity. PWS is classically presented by mental retardation, muscle hypertonia, obesity, short stature, and hypogonadism.[1] Here we report a case of PWS that presented with symptoms of hyperphagia, obesity, delayed puberty, and mild mental retardation, followed by type 2 diabetes mellitus (T2DM) in association with dyslipidemia but without short stature.

Case Report

Master PS was a hyperactive, mild mentally retarded, obese child, presented with undescended testis in 2008. He was second of two siblings and was born with birth weight 2.1 kg by caesarean section from non-consanguineous parents. His mother was diabetic at 7 months of pregnancy and was treated with insulin. Knock knees was the first difficulty detected during walking when he was 2 years old. From two-and-half years of age, he had an insatiable appetite with subsequent obesity. Temper tantrums and hyperactivity in new situations with unfamiliar surroundings were noted from his early childhood. However, the vision and hearing development were normal.

Physical findings revealed a mentally retarded 10-year-old boy with obesity and bilateral undescended testis. His height was 120 cm (below 3rd centile) and body weight was 49 kg (above 97th centile). Eyes were almond shaped, up slanting with blue iris, with narrowing of temporal region both side of face. There was a markedly obese abdomen with striae over the flank, arm, and thigh. He had generalized lipomastia and small hands and feet. There was obvious evidence of incomplete sexual development as the undescended testis was present bilaterally with small phallus (measuring 4 cm in length) which was buried in the suprapubic fat pad.

Laboratory investigations revealed normal hemoglobin (11.8 g/dL), normal thyroid profile (T4: 8.39 ug/dL, TSH: 2.0 uiu/mL), glycemic status of FPG (79 mg/dL) and PPPG (148 mg/dL), and normal liver function tests. The other biochemical tests were also normal: calcium (10.1 mg/dL), phosphorus (5.2 mg/dL), sodium (143 mmol/L), and potassium (4.9 mmol/L).

In view of obesity and abdominal striae, basal cortisol (8 A.M) was measured and reported high. Overnight dexamethasone suppression test adequately suppressed

cortisol (<1.10) and ruled out the possibility of hypercortisolism.

Ultrasound abdomen failed to detect enlarged adrenal glands and any sonological evidence of testicular tissue in the bilateral inguinal region or abdominal cavity. History and physical examination led to the diagnosis of PWS, which was confirmed by karyotyping (microdeletion of chromosome 15).

Testis remained impalpable and testosterone level failed to rise following 1 month of LH hormone therapy (1000 IU dose thrice weekly). A futile attempt with MRI abdomen to localize testis was made and surgical option for localization and removal of testis was not convincing to the pediatric surgeon.

He was managed with lifestyle therapy and behavioral therapy. Three years after his diagnosis, at the age of 13, he developed T2DM. By this time, he gained in height from 120 cm to 145 cm (at 10th centile), gained in weight from 49 kg to 73 kg (at 97th centile), and BMI remained stable at 34.

At presentation, he was in a poor glycemic state (FPG 277 mg/dL, 2-hour PPPG 396 mg/dL, HbA_{1C} 9.9%), with dyslipidemia (TC 240 mg/dL, high-density lipoprotein [HDL] 54 mg/dL, low-density lipoprotein [LDL] 136 mg/dL, TG 373 mg/dL), and normal thyroid profile (FT4 1.30, TSH 3.25). Glimepiride and metformin were started to control the diabetes, but statin was not started despite high LDL.

Discussion

Langdon Down described the first patient with PWS in an adolescent girl in 1887.[1] In 1956, Prader *et al*. reported a series of patients with similar phenotypes.[2] Deletions located between bands 15q11 and 15q13 is the site for PWS.[3] PWS has been reported worldwide and the prevalence rate is estimated 1 per 45,000 population.[4]

Most children with PWS present with symptoms of hyperphagia with progressive development of obesity. The diagnosis of this syndrome is based entirely on clinical observation, and the patient we have described displays many of the common characteristics of the condition.

Short stature is common in PWS during childhood due to growth hormone deficiency.[5] Our subject was short at presentation but attained normal height later. Obviously, growth hormone testing was not done. Pubic and axillary hair may grow prematurely in children with PWS, but other features of puberty are generally delayed or incomplete.[5] Testicular descent has not occurred in our patient and we failed to locate intra-abdominal testis despite our best effort; he did not show any sign of puberty till 13 years.

Patients with PWS often exhibit behavioral problems, like temper tantrums, stubbornness, and obsessive-compulsive behaviors that often compromise the level of academic performance.[6] Temper tantrums and stubbornness were very predominant behavioral issues of this child at presentation, which improved over time, as well as his academic performance.

Due to progressively increasing obesity, he developed diabetes at the age of 13 with dyslipidemia. Glycemic control was achieved with glimepiride and metformin. Managing dyslipidemia is controversial in pediatric population. American Academy of Pediatrics (AAP) is in favor of pharmacotherapy when LDL is more than 130 mg/dL whereas American Heart Association (AHA) recommends pharmacotherapy only when LDL is more than 160 mg/dL. The recommendations are shown in Table 1. In the mist of confusion, it was decided to postpone statin therapy till a repeat LDL level is available following a rigorous lifestyle intervention for 6 months.

Conclusion

Obese children with behavioral problems should be evaluated for PWS. Not all Prader–Willi children are short and growth-hormone deficient. Behavioral issues often improve over time. T2DM is a common complication, which fairly responds to oral antidiabetic agents. Managing diabetic dyslipidemia in pediatric population is controversial

Table 1 | Pharmacological treatment of dyslipidemia in children >8 years of age with elevated LDL

American Academy of Pediatrics	American Heart Association
No cardiovascular disease (CVD) risk factors Treat when LDL>190 mg/dL despite diet therapy	No CVD risk factors Treat when LDL > 190 mg/dL
Family history of premature heart disease or ≥2 additional CVD risk factors present Treat when LDL >160 mg/dL despite diet therapy	Risk factors present (blood pressure elevation, diabetes, obesity, strong family history of premature CVD) Treat when LDL > 160 mg/dL
Diabetes Consider treatment when LDL > 130 mg/dL	
*Diet therapy recommended for all high-risk groups	*Lifestyle modifications recommended for all patients if LDL > goal

as different LDL targets for pharmacotherapy are set by different guidelines.

References

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"If you don't get what you want, you suffer; if you get what you don't want, you suffer; even when you get exactly what you want, you still suffer because you can't hold on to it forever. Your mind is your predicament. It wants to be free of change. Free of pain, free of the obligations of life and death. But change is law and no amount of pretending will alter that reality."

— Socrates