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Case Study

Dyslipidemia, weight gain, and decreased growth velocity in a 14-year-old male

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Abstract: A 14-year-old male was referred for dyslipidemia. His findings were consistent with metabolic syndrome. Although he lacked the typical physical appearance, his accelerated weight gain combined with a decreased linear growth velocity suggested Cushing syndrome. He was subsequently found to have adrenocorticotropic hormone–independent Cushing syndrome secondary to primary pigmented nodular adrenal disease without Carney Complex. After bilateral adrenalectomy, his lipid profile returned to normal. In this article, we discuss the role of glucocorticoids on lipid and lipoprotein metabolism.

Case study

A 14-year-old Caucasian male was referred to the pediatric lipid clinic for dyslipidemia. Accelerated weight gain started at 8 years of age. In the 2 years before referral, he gained approximately 50 pounds, during which time he reported intermittent fatigue, vague abdominal pain, and pain in his lower back after activities. There was no history of muscle weakness, hypertension, or diabetes. Pubertal onset occurred at approximately 13 years of age.

On physical examination, his height was 146 cm (sixth centile), weight 71.6 kg (97th centile), blood pressure 133/77 mm Hg (systolic 99th centile and diastolic 92nd centile), and body mass index 33.6 (99th centile). Prominent abdominal obesity and acanthosis nigricans were present, along with only minimal increase in the supraclavicular and dorsal adipose tissue. There was no increase in the preauricular adipose tissue, and there were no cutaneous striae, lentigines, or myxomas. Pubertal development was Tanner stage II.

His initial laboratory test results were fasting glucose 101 mg/dL (ref range <100 mg/dL), HbA1c 5.4% (ref range <5.7%), aspartate aminotransferase 95 IU/L (ref range 0–40 IU/L), alanine aminotransferase 208 IU/L (ref range 0–24 IU/L), alkaline phosphatase 128 IU/L (ref range 45–101 IU/L), and total bilirubin 0.8 mg/dL (ref range <1.2 mg/dL). Results of the fasting lipid profile are shown in Table 1 and growth chart in Figure 1.

The mother is obese, but otherwise healthy. The father is hypertensive, but no other information is available regarding his health. Neither were taking lipid-lowering

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Table 1 Advanced lipid profile before and after bilateral adrenalectomy

Test	Units	Preoperative	Postoperative	Reference values
Total cholesterol	mg/dL	245	153	≥200
Triglycerides	mg/dL	75	64	≥130
HDL-cholesterol	mg/dL	73	47	<40
LDL-cholesterol	mg/dL	157	93	≥130
Non-HDL-cholesterol	mg/dL	172	106	≥145
LDL particle number	nmol/L	1894	1157	<1600
LDL size	nm	21.1	21.0	>20.5
Small LDL-P	nmol/L	641	524	≤527
HDL-P	μmol/L	37.3	30.5	≥30.5
LP-IR score	–	43	43	<63

HDL, high-density lipoprotein; LDL, low-density lipoprotein; LP-IR score, lipoprotein-insulin resistant score. Values represent approximately the. Q5

Reference: Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents, National Heart, Lung, and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: Summary report. *Pediatrics*. 2011; 128 Suppl 5:S213-56.

medications nor had undergone lipid testing in the past. The maternal grandmother has hypertension; the maternal great-grandmother has type II diabetes.

Accelerated weight gain during adolescence, accompanied by abdominal obesity, dyslipidemia, dysglycemia, and elevated liver transaminases is commonly encountered in many teens, especially in Hispanics. Therefore, having met 3 of 5 criteria, our patient was assumed to have metabolic syndrome (MetS).[1] However, his dramatic increase in weight, associated with a simultaneous decrease in linear growth (see Fig. 1), suggested the possibility of Cushing syndrome (CS). Furthermore, his dyslipidemia was atypical for MetS, the latter characterized by elevated triglycerides, low high-density lipoprotein (HDL), and increased small dense low-density lipoprotein (LDL). Therefore, additional laboratory studies were requested. Results are shown in Table 2.

The elevated midnight cortisol level, increased excretion of urinary free cortisol, and lack of cortisol suppression after dexamethasone were all consistent with hypercortisolism. To localize the source of excess glucocorticoid production, a computerized tomographic scan of the adrenals was performed. Although not enlarged, the adrenals were noted to have a slight nodular contour with bilateral micronodules. Liver imaging demonstrated steatosis.

A bilateral adrenalectomy was performed. Histologic examination and gross appearance of the tumor demonstrated small, pigmented micronodules of the adrenal cortex. No Carney Complex–associated abnormalities of the testicles, thyroid, skin, liver, or heart were found; PRKAR1A gene mutation analysis was negative. The child's clinical, laboratory, and histologic findings were consistent with primary pigmented nodular adrenal disease (PPNAD) without Carney Complex. Changes in the lipid profile after adrenalectomy are shown in Table 1.

Discussion

Hypercortisolism is uncommon in children, and when present is generally due to exogenous administration of glucocorticoids. Excessive endogenous production of cortisol may be either adrenocorticotropic hormone dependent or independent. The hypercortisolism in our patient was found to be secondary to PPNAD, a rare, autosomal dominant disorder responsible for <1% of CS. PPNAD is more frequent in females, especially after puberty. Bilateral adrenalectomy is the preferred treatment. The condition occurs sporadically, or more commonly, as a familial syndrome known as Carney Complex. The latter is a multiple neoplasia syndrome, which manifests as cutaneous lentigines, myxoma, schwannomas, and endocrinopathy. Carney Complex is most frequently caused by inactivating heterozygous mutations of the PRKAR1A gene encoding for the regulatory subunit type 1α of the cyclic adenosine monophosphate–dependent protein kinase A. Q6

The metabolic consequences of CS are highly atherogenic. Excess corticosteroid has been reported to exert marked effects on lipid and lipoprotein metabolism and to increase cardiovascular disease (CVD) risk. In addition to dyslipidemia, individuals with CS share many features of MetS, a known CVD risk condition. Approximately, 67% have 3 or more components of MetS, including weight gain–obesity (95%), impaired glucose tolerance (21%–60%)–diabetes (20%–47%), hypertension (75%), and hypertriglyceridemia (20%).[2] The most common dyslipidemia of CS (increase in circulating very LDL and LDL, but not HDL, with consequent elevation of triglyceride [TG] and total cholesterol levels),[3] contrasts with that seen in MetS, in which TG is increased, HDL-C is low, and small dense LDL-C is increased. After successful treatment of CS, the lipid abnormalities typically improve or normalize.