Unilateral adrenalectomy for Cushing syndrome caused by primary pigmented nodular adrenocortical disease

Shinji Higuchi, Rie Kawakita, Yuki Hosokawa, Yuki Yamada, Maki Oyachi, Kana Kitayama, Tohru Yorifuji
Division of Pediatric Endocrinology and Metabolism, Children's Medical Center, Osaka City General Hospital

Introduction
Bilateral primary pigmented nodular adrenocortical disease (PPNAD) is one of the rare causes of Cushing syndrome, which has traditionally been treated by bilateral adrenalectomy. However, bilateral adrenalectomy mandates lifelong adrenal hormone replacement therapy, and the patients remain at risk of adrenal failure for the rest of their lives. In adult patients with PPNAD, there have been a few reports of successful unilateral adrenalectomy. However, to our knowledge, there has been no report of unilateral adrenalectomy for pediatric patients with PPNAD, in whom slight hypersecretion of cortisol could be detrimental for growth. Here, we report successful unilateral adrenalectomy in a 10-year-old boy with PPNAD.

Patient report

【Chief complaints】Retarded growth, truncal obesity
【Past and family history】None
【Current history】The patient was a 10-year-old Japanese boy who presented with growth arrest and excessive weight gain over the past 6 months.
【Physical findings】Height 137.5 cm (-0.2 SD), body weight 42.0 kg (0.7 SD), blood pressure 82/52 mmHg, heart rate 110 bpm, skin pigmentation (+), hypertrichosis (+), moon face (+), truncal obesity (+), skin streaks (+).
【Laboratory data】AST 17 U/L, ALT 18 U/L, LDH 218 U/L, BUN 10.3 mg/dL, Cr 0.51 mg/dL, Na 146 mEq/L, K 3.5 mEq/L, Cl 108 mEq/L, Ca 9.4 mg/dL, IP 3.3 mg/dL, ALP 634 U/L, Glu 129 mg/dL, T-Chol 270 mg/dL, HDL-Chol 105 mg/dL, TG 157 mg/dL, LDL-Chol 133 mg/dL, HbA1c 5.4%

Clinical course after the operation
The levels of urinary free cortisol on day 1 and 2 were above 70 μg/m²/day. The levels of blood cortisol were elevated without diurnal rhythm. Blood cortisol was not suppressed by 1 mg and 8 mg dexamethasone, and adrenal CE-MRI revealed the presence of multinodular adrenals on both sides (the nodules were larger on the right side than on the left). 113I-adosterol scintigraphy showed bilateral uptakes which were stronger in the right adrenal gland. A diagnosis of Cushing syndrome due to multinodular adrenal hyperplasia was made. An endoscopic right adrenalectomy was performed to preserve adrenal function.

Macroscopic cut surface shows brownish nodules up to 14 × 9 mm in size (E)
Histologically, nodular lesions consisting of relatively large cortical cells with eosinophilic and alveolar bodies were observed. The cells show presence of lipofuscin (F, G)
Some cells show a slightly high nucleus-to-cytoplasm ratio; Ki-67-positive cells are also present (H)

【PPNAD】

PPNAD

➢ PPNAD involves an ACTH-independent hyperplastic nodular lesion and most cases are related to Carney Complex (CNC). CNC is a syndrome characterized by tumors with skin pigmentation, myxoma, and abnormal endocrine function.
➢ PRKAR1A (70%) is one of the candidate genes for PPNAD. This gene encodes the regulatory subunit of protein kinase A.
➢ Unilateral adrenalectomy has been performed in some adult patients who showed different levels of cortisol secretion between the right and left adrenal gland. However, there has been no report of unilateral adrenalectomy performed in pediatric patients.

Discussion

➢ The patient developed Cushing syndrome because of PPNAD and adenoma.
➢ Although the follow-up period was 1 year, adrenal function has been preserved. Growth rate had improved, and truncal obesity had disappeared. He has had no recurrence.
➢ Unilateral adrenalectomy could be considered for pediatric patients with Cushing syndrome caused by PPNAD, especially when the uptake of 113I-adosterol and the size of nodules show dominance on one side of the adrenal gland.

Conclusion
Unilateral adrenalectomy could be considered for pediatric patients with Cushing syndrome caused by PPNAD, especially when the uptake of 113I-adosterol and the size of nodules show dominance on one side of the adrenal gland.

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