Rare adrenocortical carcinoma presenting with cushing’s syndrome: Case report

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Abstract

Background: Adrenocortical carcinoma (ACC) is a rare endocrine cancer with poor prognosis. Classically, ACC is a non-functioning mass. The patient often presents with abdominal discomfort or flank pain due to the mass effect. However, some can produce hormones such as corticosteroid or sex steroid but less likely presenting with the excess hormone manifestations.

Clinical case: A 65-year-old Thai female presented with round face, incidental bruising, muscle weakness and weight gain for 6 months. Physical examination findings showed dorsocervical and supraclavicular fat pad, abdominal obesity, multiple echymoses at extremities and proximal muscle weakness, grading 4/5. Additionally, compared with previous stature, she has lost about 7 cm. of her height. The laboratory evaluation for hypercortisolism demonstrated a high level of 24-hour urinary free cortisol in contrast to a low normal ACTH level. Abdominal computed tomography (CT) revealed a large left heterogenous and hyper vascular adrenal mass with a diameter of 5.9 x 6.2 x 6.6 cm. Left adrenalectomy was performed and histopathology illustrated adrenocortical carcinoma with lymphatic emboli. Then, radiation was prescribed as adjuvant treatment in this patient. After that, the features of fat redistribution gradually resolved within several months and subsequent abdominal CT scan revealed a complete resolution.

Conclusion: Clinical representation of cushing syndrome in adrenocortical carcinoma was infrequently found. Awareness the signs and symptoms of hypercortisolism particularly in elderly may influence on the treatment outcome. Tumor resection and treating the complications of hypercortisolism are gold standard management of cortisol-secreting ACC.

Introduction

Adrenocortical carcinoma (ACC) is a rare endocrine cancer with poor prognosis. The patient often presents with abdominal discomfort or flank pain due to the mass effect, however ACC may produce hormones such as corticosteroid and the patient presents with signs and symptoms of cushing syndrome.

Case

A 65-year-old Thai female presented with round face, abdominal obesity, weight gain and incidental bruising for 6 months. She also complained of difficulty in walking upstairs around a month. Associated complaints included height reduction and low back pain. She had no underlying medical disease and denied symptoms of abdominal discomfort, flushing, sweating or headache. Pertinent physical examinations showed blood pressure of 100/60 mmHg, pulse rate of 72 beats/min, round face, supraclavicular and dorsocervical fat pad, abdominal obesity, multiple ecchymoses at extremities and proximal muscle weakness, grading 4/5. No lymphadenopathy, facial plethora, acne, hirsutism or abdominal purplish striae was observed. Findings of other systems were all within normal limits.

The complete blood count, blood chemistries, plasma glucose, renal and liver function test were within normal limit. The results of 24-hour urine free cortisol were 477.02 mg/day (normal 80-120 mg/day); 24-hr urine metanephrine was 118.96 mg/day (normal <400 mg/day); 24-hr urine normetanephrine was 274.72 mg/day (normal <900 mg/day); plasma morning cortisol was 21 mg/dL; plasma dehydroepiandrosterone-sulphate (DHEA-S) level was 52.2 mg/dL (normal 35-430 mg/dL).

Abdominal computed tomography revealed a large heterogeneously left adrenal mass with a diameter of 5.9 x 6.2 x 6.6 cm. After contrast administration, the mass revealed slight hyper density at the peripheral part with central hypodensity (Figure 1). The mass had an unenhanced attenuation of 40HU, enhanced attenuation of 79HU and delayed phase 10 minutes at 64 HU (absolute 38.5% washout). Left adrenal mass was completely resected and the histopathology finding showed an encapsulated, circumscribed, lobulated and brown mass with foci of hemorrhage and necrosis, measuring 7 x 6 x 5 cm, arising from the cortex of adrenal gland. The definite diagnosis was adrenocortical carcinoma with lymphatic emboli (Figure 2).

Regarding osteoporosis in hypercortisolism patient, the following blood chemistries were explored: calcium level=8.5 mg/dL (normal 8.5-10.5 mg/dL), albumin 3.1 g/dL, phosphate=3.6 mg/dL, intact parathyroid hormone 59.5 pg/mL (normal <65 pg/mL) and 25-hydroxy vitamin D level 12.59 ng/mL (normal > 30 ng/mL). Plain film of spine showed compression fractures at the T11 and L1 levels (Figure 3). Bone Mass Density (BMD) T-score of the L-spine and total hip revealed -2SD and -3SD, respectively.

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Cushing syndrome such as round face, easy bruising, truncal obesity, proximal muscle weakness, high blood pressure, hyperglycemia and/ or osteoporosis. The diagnosis of glucocorticoid-producing ACC is confirmed by evidence of hypercortisolism in contrast to ACTH suppression, adrenal imaging and histopathology. Complete surgical resection is the treatment of choice [5] for localized ACC. Resection of tumor can ameliorate signs and symptoms of cushing as well as its complications such as cardiovascular disease and osteoporosis. Adjuvant therapy can be consider in high risk patient based on tumor size, positive margin, rupture capsule and high grade tumor. Adjuvant chemotherapy such as etoposide, doxorubicin and cisplatin along with radiotherapy provide benefit but the prognosis is depend on tumor staging and drug adverse effects. Several recent studies [6-8] demonstrates that mitotane, synthetic derivative of the insecticide dichlorodiphenyltrichloroethane (DDT), is an adrenal cytotoxic agent, but its exact mechanism of action is unknown. Mitotane selectively damages the zona reticularis and zona fasciculate of adrenal cortical tissue, so can be used as adjuvant therapy for increase survival in cases of aggressive or non-operable adrenocortical carcinoma (response rate 10-30%). A large retrospective study [9] in 177 patients with ACC who undergo radical surgery in Italy and Germany between 1985 and 2005 found recurrence-free survival was significantly prolonged in the patient who receive adjuvant mitotane, as compared with the patient who was surgical alone.

Based on the available data, adjuvant mitotane therapy is controversial because no randomized prospective trials adjuvant mitotane have been publish. The ADIUVO trial is first prospective, randomized, controlled, open label, multicenter phase III trial on going to assess the efficacy of adjuvant mitotane in low to intermediate risk ACC patients.

Systemic therapy for advance ACC is mitotane single agent or combinations of chemotherapy with mitotane. FIRM-ACT trial [10] comparing first line treatment of metastatic ACC with combined etoposide, doxorubicin, and cisplatin (EDP) with mitotane versus combined streptozocin with mitotane. The result shows the EDP-mitotane group had a significantly higher response rate the streptozocin mitotane group (23.2% vs. 9.2%, P<0.001) and longer median progression-free survival (5.0 months vs. 2.1 months; hazard ratio, 0.55; 95% confidence interval [CI], 0.43 to 0.69; P<0.001). Overall survival and toxicity not difference between both groups.

Apart from chemotherapy and mitotane, the molecular targeted therapy (MTT) [11], for example, imatinib, sunitinib, cixutumumab or everolimus also shows good clinical responses in progressive ACC. Treatment of hormone excess and its complications is also important. Patient with glucocorticoid-producing ACC should be evaluated and treated for hyperglycemia, hypertension, electrolyte imbalance and osteoporosis. Caution should be made for adrenal insufficiency during therapy can be consider in high risk patient base on tumor size, positive margin, rupture capsule and high grade tumor. Adjuvant chemotherapy such as etoposide, doxorubicin and cisplatin along with radiotherapy provide benefit but the prognosis is depend on tumor staging and drug adverse effects. Several recent studies [6-8] demonstrates that mitotane, synthetic derivative of the insecticide dichlorodiphenyltrichloroethane (DDT), is an adrenal cytotoxic agent, but its exact mechanism of action is unknown. Mitotane selectively damages the zona reticularis and zona fasciculate of adrenal cortical tissue, so can be used as adjuvant therapy for increase survival in cases of aggressive or non-operable adrenocortical carcinoma (response rate 10-30%). A large retrospective study [9] in 177 patients with ACC who undergo radical surgery in Italy and Germany between 1985 and 2005 found recurrence-free survival was significantly prolonged in the patient who receive adjuvant mitotane, as compared with the patient who was surgical alone.

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In this case, the patient was received adjuvant radiation after surgery because of capsular invasion and less than 0.1 cm resection margin. Surveillance of non-metastasis ACC with imaging study and biomarkers, detected functioning tumors should be performed every 3-6 month up to 5 years.

Conclusion

Cushing’s syndrome in adrenocortical carcinoma was infrequently found. Awareness the signs and symptoms of hypercorticolism particularly in elderly may influence on the treatment outcome.
Even though, tumor resecting and chemotherapy are gold standard of adrenocortical carcinoma but treating the complications of hypercorticolism is also important.

References


