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Visual Vignette

Histopathologic Differences Between Adrenocorticotropic Hormone–Dependent and Adrenocorticotropic Hormone–Independent Adrenal Hyperplasia Causing Cushing Syndrome

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Case Presentation:

Case 1

A 64-year-old man with cushingoid features was found to have bilateral nodular adrenal masses (left > right). Laboratory studies showed elevated 24-hour urinary free cortisol level at 64 μg (reference range, 0-50 μg), abnormal levels for the 1-mg dexamethasone suppression test (cortisol, 4.8 μg/dL; dexamethasone level, 665 ng/dL), and suppressed adrenocorticotropic hormone (ACTH) and dehydroepiandrosterone levels. ACTH-independent Cushing syndrome was diagnosed. He was treated with ketoconazole for 6 years, but owing to worsening symptoms including uncontrolled type 2 diabetes mellitus, bilateral adrenalectomy was performed. The computed tomography (CT) image of the adrenal gland and histopathologic images are shown in Figure 1.

Case 2

A 59-year-old man with a history of well-controlled hypertension presented with progressively worsening hypertension, muscle weakness, weight loss, hyperglycemia, and widespread bruising. His potassium level was as low as 2.4 mmol/L. The 24-hour urinary free cortisol level was 4000 μg (reference range, 0-50 μg), and ACTH levels were significantly elevated at 491 pg/mL (reference range, 6-50 pg/mL), consistent with ACTH-dependent Cushing syndrome. Pituitary magnetic resonance imaging showed no abnormal findings. Positron emission tomography/CT revealed increased radiotracer activity in pelvic nodes and liver nodules. A biopsy of one of the liver lesions demonstrated metastatic neuroendocrine carcinoma with positive staining for ACTH. These findings confirmed the diagnosis of Cushing syndrome secondary to ectopic ACTH secretion. He underwent bilateral adrenalectomy for rapid control of severe hypercortisolemia. The CT image of the adrenal gland and histopathologic images are shown in Figure 2.

What are the differences between the adrenal gland images and histopathology of these 2 cases?

Answer

The CT image of the adrenal gland in Figure 1*A* shows bilateral adrenal nodular disease (left > right).[1] On gross specimen, the right adrenal gland weighed 38.9 g and the left adrenal gland 188.8 g (normal weight, 4-5 g). On histopathology, there were multiple discrete adrenal nodules measuring up to 4.5 cm, findings consistent with macronodular adrenal hyperplasia (Fig. 1*B*, arrows). The low magnification micrograph (×2, Fig. 1*B*) shows a cross section of the adrenal gland distorted by innumerable nodules (black arrows). Each discrete nodule was a molecularly distinct clonal neoplasm (×4, Fig. 1*C*). The nodules were composed of cells resembling normal zona fasciculata with finely vacuolated

Abbreviations: ACTH, adrenocorticotropic hormone; CT, computed tomography.
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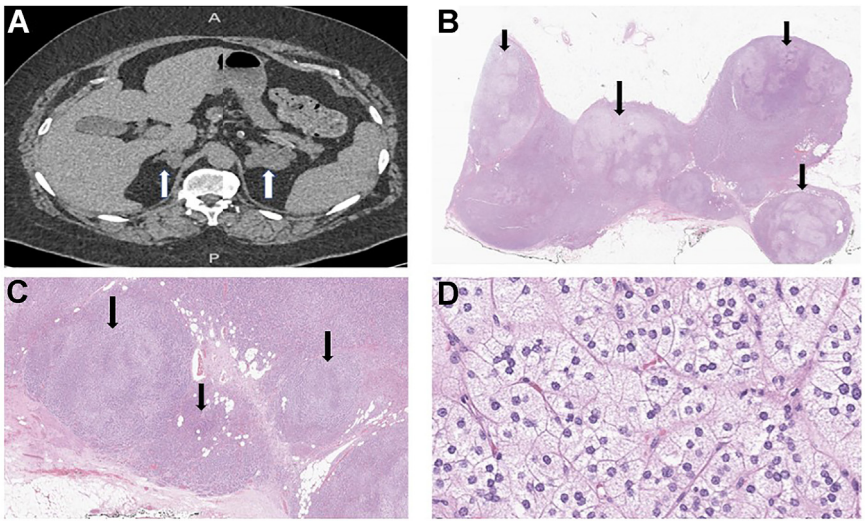

Fig. 1. The CT image of the adrenal gland and histopathology of ACTH-independent Cushing syndrome. *A*, Bilateral adrenal nodular disease (left > right). *B*, Low magnification (×2) of cross section of the adrenal gland. *C*, Low magnification (×4) of multiple adrenal nodules in the adrenal gland. *D*, High magnification (×40) of an adrenal nodule. ACTH, adrenocorticotropic hormone; CT, computed tomography.

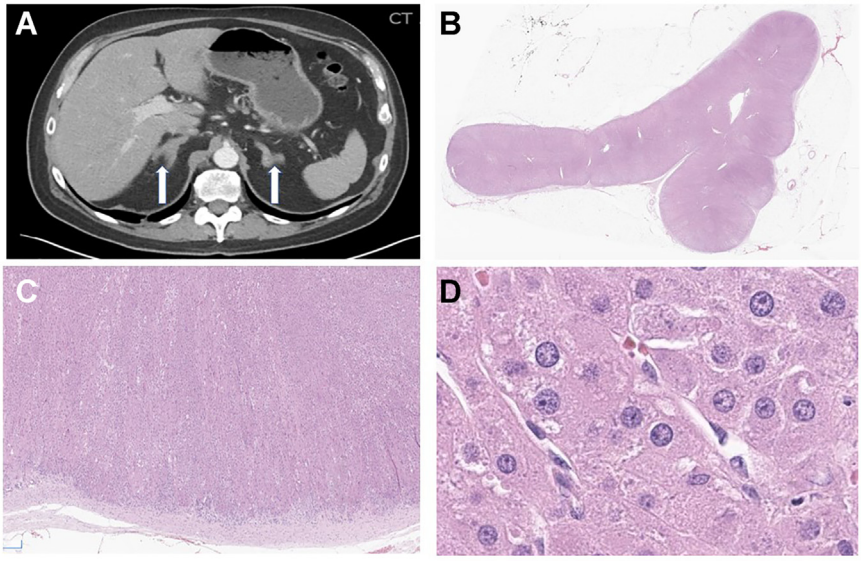

Fig. 2. The CT image of the adrenal gland and histopathology of ACTH-dependent Cushing syndrome. *A*, Bilateral adrenal hyperplasia. *B*, Low magnification (×2) of diffuse adrenal cortical hyperplasia. *C*, Low magnification (×4) of diffusely thickened adrenal cortex. *D*, High magnification (×40) of adrenal cortical hyperplasia. ACTH, adrenocorticotropic hormone; CT, computed tomography.

cytoplasm (×40, Fig. 1*D*). There are no features of malignancy. The patient's fatigue and overall well-being improved postoperatively. His HgbA1C decreased from 9.8% to 6.8% over the following 6 months. The CT image of the adrenal gland in Figure 2*A* reveals bilateral adrenal hyperplasia without any nodularity, which maintains the shape of normal adrenal glands (arrows, Fig. 2*A*).[2] On gross specimen, the right adrenal gland weighed 52.0 g and the left adrenal gland 70.1 g. Histopathology revealed diffuse true adrenal cortical hyperplasia consistent with the elevated plasma ACTH level. At low magnification, the adrenal gland showed a diffusely and markedly thickened cortex (×2, Fig. 2*B*), with a smooth periphery without nodularity (×4, Fig. 2*C*). High magnification showed cords of monotonous adrenal cortical cells with eosinophilic cytoplasm (×40, Fig. 2*D*). After surgery, blood pressure and muscle weakness improved significantly, and the severe hypokalemia resolved.

Disclosure

The authors have no multiplicity of interest to disclose.

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