EDITORIAL

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How to approach and follow adrenal incidentaloma?

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Adrenal incidentaloma is defined as a previously unsuspected mass ≥ 1 cm in diameter, discovered incidentally during an imaging investigation for a nonadrenal disorder. It is frequently diagnosed, and its prevalence is 1% to 5% in different studies [1]. Advanced imaging techniques and the increased quality of medical services have resulted in more examinations using computed tomography (CT) or magnetic resonance imaging (MRI). Common causes of adrenal incidentaloma may be different according to the ethnicity of the study population. Most studies have shown that a nonfunctioning adenoma is the most frequent cause (60% to 85%) followed by subclinical Cushing syndrome, pheochromocytoma, and adrenal carcinoma; then there are other benign tumors, such as myelolipoma and metastasis, which are rare [2-4].

No consensus exists on the optimal diagnostic approach to adrenal incidentaloma. A report from the National Institutes of Health at a science conference and a review from an experienced clinician both recommended a hormonal evaluation. The diagnostic approach in patients with adrenal incidentalomas should focus on two main questions: 1) whether the lesion is malignant; and 2) whether it is hormonally active [5,6]. A low dose (1 mg) dexamethasone suppression test, providing sensitivity of 98.1% and specificity of 80.5% to 98.9%, is the mainstay biochemical screening test for detecting subclinical Cushing syndrome. A normal result is defined as a cortisol value < 5 μg/dL, even though there is controversy about the optimal cutoff point. Screening for pheochromocytoma is mandatory in all patients with adrenal incidentaloma because of the high rates of morbidity and mortality. Assessment of plasma free metanephrines seems to display better sensitivity than 24-hour urinary total metanephrines and catecholamines. Urinary total metanephrines of at least 1.8 mg/24 hours and vanillyl-mandelic acid of at least 11 mg/24 hours make the diagnosis of pheochromocytoma highly probable. Screening for primary aldosteronism is routinely recommended for patients with hypertension who have an adrenal incidentaloma. A ratio of ambulatory morning plasma aldosterone concentration (ng/dL) to plasma renin activity (ng/mL/hr) > 20 needs to be further evaluated for aldosterone hypersecretion. A radiological evaluation including noncontrast CT attenuation values expressed in Hounsfield units (HU) is the best tool for distinguishing between benign and malignant adrenal masses. All adrenal tumors with suspicious radiological features, most functional tumors, and all tumors > 4 cm in size that lack

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characteristic benign imaging features should be removed. All patients should undergo a hormonal evaluation for subclinical Cushing syndrome and pheochromocytoma, and those with hypertension should also be evaluated for primary hyperaldosteronism.

One report demonstrated that the cumulative risk of developing endocrine abnormalities is 17% at 1 year, 29% at 2 years, and 47% at 5 years. The risk was high in the first 2 years of follow-up for an initial tumor diameter > 3 cm. The cumulative risk of mass enlargement was 6% at 1 year, 14% at 2 years, and 29% at 5 years, and it was greater in patients with normal adrenal function than in those with subtle hormonal abnormalities [1].

Limited data are available on the possible increase in adrenal mass size and hormonal pattern changes over time according to race or ethnicity. Only one prospective study has been reported in Korean patients with adrenal incidentaloma. Kim et al. [4] observed 24 patients with nonfunctioning adrenal incidentaloma for 3 to 72 months. Among them, two patients had increased tumor size of > 1 cm, and one patient developed Cushing syndrome at 10 to 26 months after the initial diagnosis. In this issue of *The Korean Journal of Internal Medicine*, Cho et al. [7] observed the clinical characteristics and the 2-year follow-up findings of patients with adrenal incidentaloma. In that study, 282 patients with adrenal incidentaloma were observed. Among them, 86.2% had a nonfunctioning mass, and 13.8% had a functioning mass; 9.9% were subclinical Cushing syndrome; 2.1% pheochromocytoma; and 1.8% primary aldosteronism. During the 22.5 months of follow-up of patients with nonfunctioning tumors, 4.2% developed functioning masses, pheochromocytoma, or subclinical Cushing syndrome.

According to the recent experts' opinion, in most patients with an adrenal incidentaloma, particularly if the tumor is > 3 cm in size, annual biochemical follow-up for up to 5 years may be reasonable. Patients with adrenal masses < 4 cm in size and a noncontrast attenuation value > 10 HU should have a repeat CT study in 3 to 6 months and then yearly for 2 years. Adrenal tumors with indeterminate radiological features that grow at least 0.8 cm over 3 to 12 months should be considered for surgical resection [3,8].

In summary, adrenal incidentaloma is a common clinical problem, and the diagnostic challenge is to distinguish the majority of benign lesions from other masses, as either malignant or hormone secreting, which require further treatment. An imaging evaluation (CT and MRI) is the key tool to distinguish malignant from benign lesions. All patients should be tested for hypercortisolism and pheochromocytoma, whereas hypertensive patients should only be tested for aldosteronism. Adrenalectomy should be considered for patients with adenoma with or without subclinical hypercortisolism during follow-up with clinical signs of hormone excess or clinical worsening despite optimal medical treatment. Even though there is no standardized international guidelines for the follow-up of endocrine and imaging tests, most experts recommend that hormonal observations should be performed annually for up to 4 to 5 years, an imaging evaluation at 3 to 6 months, and then annually for 1 to 2 years [9,10].

Conflict of interest

No potential conflict of interest relevant to this article is reported.

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