

Two Main Subtypes of Aldosterone-Producing Adrenocortical Adenomas by Morphological and Expression Phenotype

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Background: Aldosteronism is still a considerable diagnostic challenge generally diagnosed in a 3-tiered system (initial screening, a confirmation of the diagnosis, and a determination of the specific subtype). Since the recognition that ¾ of cases are due to bilateral hyperplasia, the spectrum of adenomas needs further characterization to determine the origin of aldosterone secretion.

Design: We selected unilateral aldosterone-producing adrenocortical adenomas (AP-ACA, 33) responsible of primary aldosteronism defined by WHO criteria from a consecutive series of 98 ACA. We analyzed the histological features (growth pattern, nuclear characteristics, cytoplasmic staining qualities) of the tumor and the expression profile by quantitative RT-PCR of key molecular players of glomerulosa differentiation (SFRP2, β -catenin, AT1R, CYP21, CYP11B2, NURR1 and NUR77) in both the tumor and the surrounding parenchyma. RNA was extracted, cleaned from normal and neoplastic tissues (RNeasy columns), first-strand cDNA synthesized using T7-(dT24)-oligomer and used as template for cRNA synthesis.. The peritumoral parenchyma was also evaluated for the cytohistological features of the glomerulosa and its extension into deep cortex/medulla and periadrenal soft tissues. Quantitative results were cross-validated (expression factor >2, significance <0.01). Variables were studied regarding morphological appearances of the tumor and the status of the peritumoral glomerulosa.

Results: Two main groups of AP-ACA were identified morphologically with a corresponding molecular profile. AP-ACA composed predominantly of clear foamy cells (10) that revealed minimal expression of AT1R, CYP21 and CYP11B2 and AP-ACA composed predominantly of eosinophilic cells (23) expressing significantly high AT1R, CYP21 and CYP11B2. The peritumoral parenchyma revealed functional hyperplastic glomerulosa in 31 cases, more prominent and with extra-adrenal extension in clear cell AP-ACA.

Conclusions: The common presence of peritumoral hyperplasia suggests a proliferative response of cells to unidentified paracrine/autocrine factor as main mechanism in AP-ACA, which are not involved in glomerulosa differentiation in the clear cell subtype. Clear cell AP-ACA causes a syndrome of aldosteronism characterized by histologic features intermediate between adrenal adenoma and adrenal hyperplasia.

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