ACTS INDEPENDENT MACRONODULAR ADRENAL HYPERPLASIA-AIMAH

ACTH independent macronodular adrenal hyperplasia (AIMAH) is a rare cause of Cushing's syndrome (CS), accounting for less than 2% of all endogenous CS cases; however it is more frequently identified incidentally with subclinical cortisol secretion. AIMAH was thought to be sporadic but recent data has shown that there is likely a genetic component in the majority of cases. Over the last two decades, different studies support that multiple molecular mechanisms may be involved in pathogenesis of AIMAH, suggesting that it may be a heterogeneous group of diseases that have a common presentation. Recently, germline mutation in armadillo repeat containing 5 (ARMC5) gene, have been found in many apparently sporadic and familial cases of AIMAH and are thought to be responsible for the disorder. Somatic second hit mutations of ARMC5 were present in adrenal tumors, suggesting ARMC5 functions as a tumor suppressor gene. As these nodules inefficiently produce cortisol, large nodules are required to produce a clinical syndrome. We present the case of young women with incidentally discovered unilateral adrenal hyperplasia, subclinical CS and germline mutation of ARMC5.

ACTH NEZAVISNA MAKRONODULARNA ADRENALNA HIPERPLAZIJA – AIMAH

Sazetak

Bilateralna ACTH nezavisna makronodularna adrenalna hiperplazija je izuzetno retka, i čini manje od 2% svih slučajeva endogenog Cushing-ovog sindroma (CS). AIMAH se često prezentuje incidentalomima i subkliničkim hiperkorticizmom. Bolest je inicijalno smatrana sporadičnom, ali nedavna ispitivanja ukazuju na genetsku osnovu u većini slučajeva. Rezultati istrazivanja sprovedenih u poslednje dve decenije ukazuju na različite molekularne mehanizme uključene u patofiziologiju AIMAH, upućujući da heterogene grupe bolesti mogu imati zajedničku prezentaciju. U nedavnoj studiji identifikovana je germinativna mutacija *armadillo repeat containing* 5 (*ARMC5*) gena kod velikog broja ispitivanih osoba sa sporadičnom i familijarnom formom AIMAH. Somatska *second hit* mutacija ARMC5 je identifikovana u adrenalnom makronodulu, ukazujući da ARMC5 gen ima funkciju tumor supresororskog gena. S obzirom da su ćelije relativno insuficijentne u steroidogenezi, neophodna je značajna progresija u veličini nodusa da bi nastao klinički manifestan hiperkorticizam. Prikazali smo slučaj mlade pacijentkinje sa incidentalno otkrivenom unilateralnom adrenalnom hiperplazijom, subkliničkim CS i germinalnom ARMC5 mutacijom.