

Isolated ACTH deficiency as a cause of impaired well-being in patients with primary hypothyroidism

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Objective: Isolated ACTH-deficiency (IAD) is considered a rare autoimmune endocrinopathy most frequently associated with autoimmune thyroid diseases (ATD). We have previously diagnosed IAD in four patients with primary hypothyroidism and negative TPO antibodies. The aim of this study was to determine the prevalence of undiagnosed IAD in patients with ATD.

Methods: We studied 45 patients with ATD on stable L-thyroxine replacement (dose range 50–350 µg) and 17 healthy subjects (Group A). Fourteen of 45 ATD patients were negative for TPO antibodies; self-reported well-being was impaired in 31 (Group B) and normal in 14 (Group C). All patients underwent adrenal function assessment by a low dose 1 µg short synacthen test; a peak <18 µg/dl was considered as evidence of impaired corticotrophic function and followed up by further investigations. In addition, all patients completed the SF-36 questionnaire.

Results: Peak serum cortisol did not differ significantly between groups (group A: 22.8±3.2 µg/dl, group B: 25.2±4.8 µg/dl, group C 23.0±3.9 µg/dl). Subjective health status according to SF-36 correlated well with self-reported well-being (Group B versus C). The analysis of individual SST responses revealed that one patient with a peak cortisol of 14.5 µg/dl had failed the short synacthen test; she was TPO positive and had complained about impaired well-being. Further work-up with a 250 µg short synacthen test and an ITT confirmed IAD and she was started on hydrocortisone replacement. Intriguingly, in group C baseline ACTH and cortisol levels were significantly lower than in controls (all $P<0.01$) albeit within the normal range, potentially indicating subtle impairment of corticotrophic function.

Conclusions: Isolated ACTH deficiency may be more common than previously recognized in patients with autoimmune hypothyroidism and impaired well-being, warranting larger studies to define the actual prevalence of IAD in ATD.

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