Development of Graves´ hyperthyroidism caused primary symptomatic adrenal insufficiency induced by megestrol acetate

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Introduction

Megestrol acetate (MA) is commonly used to promote weight gain in patients with HIV infection.
Adrenal insufficiency (AI) has been reported as an adverse effect of MA but this association isn´t frequently recognized in clinical practice and only few cases have developed symptoms of AI.
We describe a case of symptomatic AI precipitated by Graves´ hyperthyroidism in a HIV patient on long-term MA treatment.

Case report

A 44-year-old man with HIV-HCV co-infection, followed in Infectious Diseases Unit since 1999, was admitted at hospital by weight loss, tremor and tachycardia. Thyroid function study revealed autoimmune hyperthyroidism (TSH: 0.01 µUI/ml; FT4: 4.88 ng/dL and positive TSH receptor antibody). Therapy with thiamazole was started. He was taking 240 mg of MA daily irregularly, for more than eleven years, with wide medicine-free intervals, but never developed symptoms of AI. One month after discharge, he developed diarrhoea, abdominal pain, hypotension and asthenia. Laboratory analysis found hyponatremia and hyperkalemia and thyroid function still remained uncontrolled (elevated FT4 and undetectable TSH). Serum cortisol was 1.1 µg/dL and after cosyntropin stimulation, were 7.6 µg/dL and 10.7 µg/dL at 30´ and 60´, respectively. The adrenocorticotropic hormone level was <5 pg/mL (normal, 5-50 pg/mL) and adrenal antibodies were negative. MA was discontinued and steroid replacement was initiated. The symptoms disappeared and the patient improved progressively. During follow-up, corticoids dose was progressively decreased to discontinuation, and radioactive iodine was prescribed to control hyperthyroidism. One year later, cortisol and ACTH levels were normal without the need for corticoids.

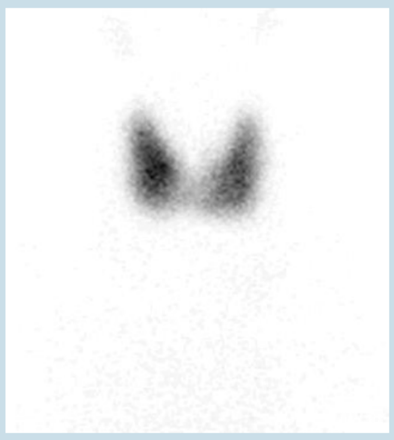

Figure 1: thyroid gammagraphy showing thyroid gammagraphy showing increased global uptake

Table 2: Rapid ACTH-stimulation Test			
	0´	30´	60´
ACTH (pg/mL)	<5	ND	ND
Cortisol (µg/dL)	1	7.6	10.7

ND: not determined

Table 1: Thyroid function and cortisol levels prior to admission, at adrenal crisis and thereafter	2010 (Taking MA)	2011 (Hospital admission)*	2011 (One month after discharge)$	2012 (Follow-up)#
TSH (mIU/L) N: 0.3 - 5	1.14	0.01	0.01	2.20
fT4 (ng/dL) N: 0.9 – 2.1	1.31	4.88	3.74	0.98
fT3 (pg/mL) N: 2.57 – 4.43	3.53	9.93		2.5
TRAb (IU/L)		+++		
Na (mEq/L) N: 135 - 145	139	140	129	141
K (mEq/L) N: 3.5 – 5.5	4.3	4	5.6	4.4
Cortisol (µg/dL) N: 3.7 – 19.4	4.40		1.1	19.8
Anti-21 hydroxylase antibody (U/mL)			<0.5	

N: normal range; MA: megestrol acetate; TRAb: TSH receptor antibody; *Thiamazole started; $ Corticoids replacement started, rapid-ACTH stimulation Test performed (table 2). # After I^{131} therapy and pregressive corticoids dose decrease to discontinuation.

Conclusions

To the best of our knowledge, it hasn´t been reported that Graves´ hyperthyroidism causes a symptomatic AI in patients with unrecognized or subclinical adrenocortical disease associated with MA treatment.
Clinicians should be alert to the possibility of development of AI in patients under MA treatment, particularly if a stress situation is present.

References

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