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Generalized glucocorticoid resistance in an adolescent girl with severe hyperandrogenia without mutations in *NR3C1* gene.

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Nothing to disclose

Introduction: Generalized glucocorticoid resistance (Chrousos syndrome) is a rare inherited disease characterized by tissue insensitivity to glucocorticoids and associated with defects in human glucocorticoid receptor (hGR) gene (NR3C1, 138040). Despite of elevated serum and urine cortisol the patients do not develop clinical picture of Cushing syndrome but present with hyperandrogenia and/or hypertension.

CLINICAL CASE

Clinical data

A15-year-old girl was presented with **hirsutism, severe acne and secondary amenorrhea**. Blood pressure was normal. No signs of Cushing syndrome (Fisure1.)

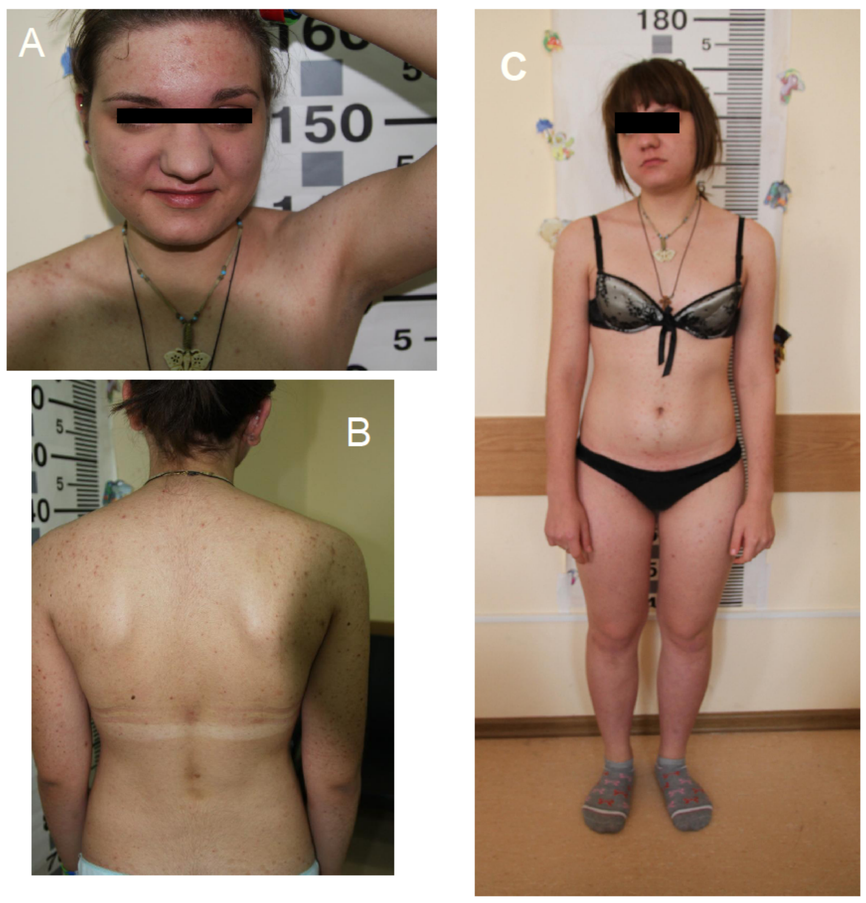

Figure 1. Patient's phenotype: A ,B severe acne C normal weight and height

Table 1 Clinical and laboratory data

Test name		Result
Testosterone	nmol/l	5.0
DHEA-S	nmol/l	10.0
17-OHP	nmol/l	6.5
Cortisol 08:00	nmol/l	643.6
Cortisol 23:00	nmol/l	463.0
ACTH 08:00	pg/ml	71.5
ACTH 23:00	pg/ml	62.8
Cortisol after 1-mg DST	nmol/l	719
Cortisol after 8 mg DST	nmol/l	167
24-hour urinary cortisol secretion	nmol/day	2091
Genetic test: found	**Mutations in NR3C1 gene were not**	

Treatment and follow-up

STEP 1 — Dexamethasone 0,5 mg/day orally was started

Table 2. Laboratory and clinical changings on dexamethasone treatment

	Before the treatment	10 days	6 month	10 month
Testosterone, nmol/l	5.27	2.5	2.49	12.3
DHEA-S, mmol/l	10.39	5,7	7.69	
Mensis	Amenorhea	Oligomenorhea	Regular	Oligomenorhea
Acne	Diffuse		Without change	
Weight	Normal	Normal	normal	Weight gain (+5 kg)
Signs of Cushing syndrome	no	no	no	round face
Blood pressure	Normal	Normal	Normal	Normal
TSH, mu/l	0,3		0.45	0.05
T4 free pmol/l	14.5		14,5	35
Signs of thyrotoxicosis	no	no	no	no
Dose of DEX, mg/day	-	0.5	0.5	0.5

STEP 2: **Dexamethasone was discontinued**
Flutamide 250 mg/day was started

Three months of treatment
- Normal menstruation
- Normal blood pressure
- Improvement of androgen dermatitits
- Weight – without change
- Testosterone 3.5 nmol/l
- Liver enzymes - normal

STEP 3: ?
Oral contraceptives?
Other antiandrogene drugs?
Dexamethasone?

Conclusion: Severe hyperandrogenia in adolescents could be caused by GC resistance. Other mechanisms of glucocorticoid resistance, than hGR gene mutations, remain to be elucidated. The reason for subclinical thyrotoxicosis in our patient is not clear, but could be the result of multireceptor resistance.

References **Lipsett, M. B., Tomita, M., Brandon, D. D., De Vroede, M. M., Loriaux, D. L., Chrousos, G. P. Cortisol resistance in man.In: Chrousos, G. P.; Loriaux, D. L.; Lipsett, M. B. : Steroid Hormone Resistance: Mechanisms and Clinical Aspects. New York: Plenum Press (pub.) 1986. Pp. 97-109. Charmandari, E., Kino, T., Ichijo, T., Chrousos, G. P. Generalized glucocorticoid resistance: clinical aspects, molecular mechanisms, and implications of a rare genetic disorder. J. Clin. Endocr. Metab. 93: 1563-1572, 2008. [PubMed: 18319312]**

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