ROHHAD Syndrome: Report Of 2 Rare Cases From Crete-Greece

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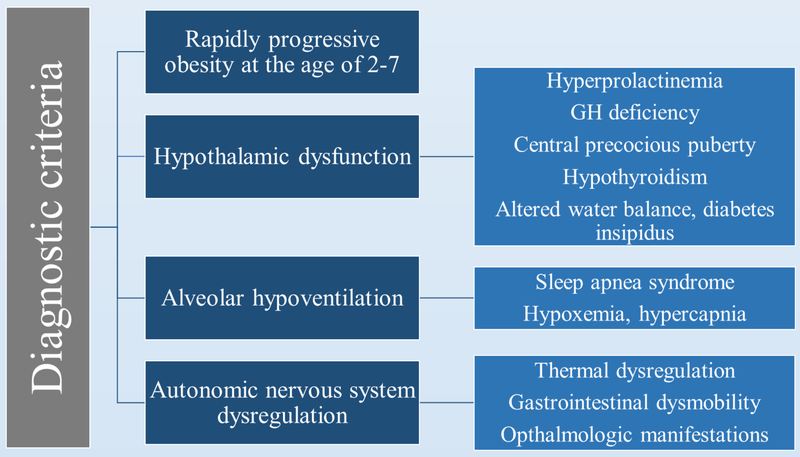
Introduction

ROHHAD syndrome (**R**apid-onset **O**besity with **H**ypoventilation, **h**ypothalamic and **a**utonomic **d**ysregulation) is a rare and complex disease with potential severe outcome. To this day there have been 158 cases reported in the literature while whole exome sequencing has not yet revealed any responsible genes. It usually presents at the age of 2-7 years. In about 40% of the patients, neuroendocrine tumors have also been reported (ROHHAD-NET).



Case report 1

A 9.5 year old female initially presented to the pediatric endocrinology outpatient care with premature menarche and rapid onset obesity (*Figure 1*).

Clinical findings:

- Height 146cm (90th percentile), weight 59kg, BMI 27.6 kg/m^2 (>97th percentile)
- Tanner stage: breast V, pubic hair V

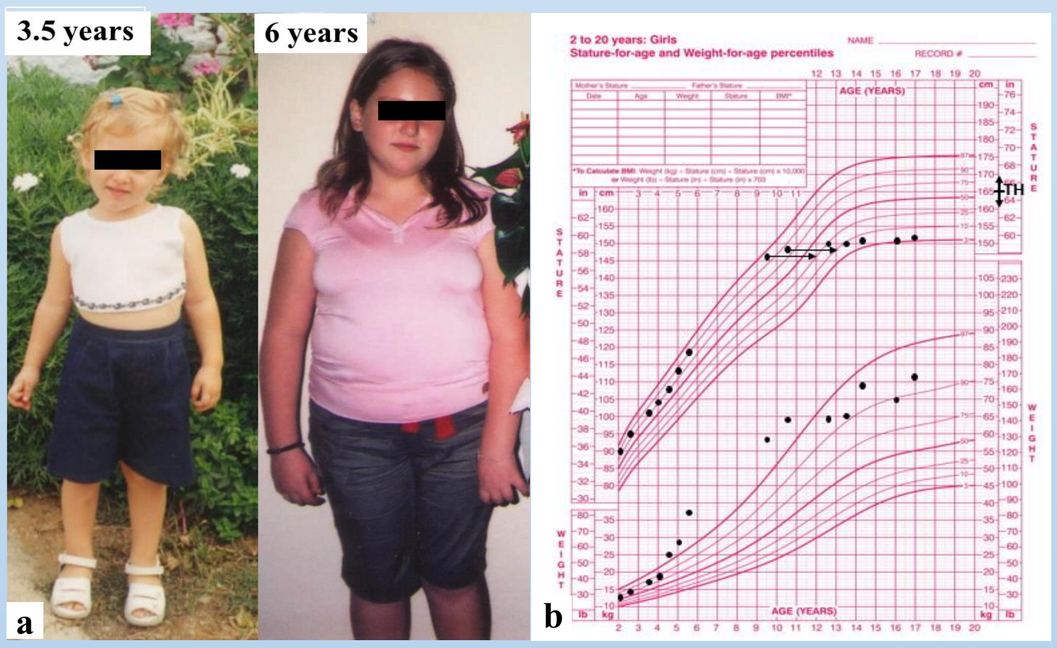


Figure 1. Photos (a) and growth chart (b) of the patient.

Laboratory findings at presentation showed: hyperprolactinemia, low IGF-1 for age and sex, precocious puberty, normal cortisol secretion and thyroid function (*Table 1*).

Age	PRL (4.8-23 ng/ml)	IGF-1 (ng/ml)	LH (mIU/ml)	FSH (mIU/ml)	GnRH stimulation test	E2 (pg/ml)	UFC (5-65 mcg/24h)	Morning cortisol (6.6-27 mcg/dl)	1mg DST (<1.8 mcg/dl)	ACTH (5-46 pg/ml)	TSH (0.43-4.2 mIU/ml)	fT4 (0.79-1.39 ng/dl)	Sodium (135-145 mmol/L)
9.5 years	65	88.4 (55-233 ng/ml)	4.2	5.8		32.6	20.6	21.6	0.72	18	2.54	1.16	140
14 years	46	31 (261-1096 ng/ml)	1.05	0.17	FSH: 0.17(0') 1.61(30') 1.41(60') LH: 1.15(0') 2.81(30') 3.13(60')	<10		8.2		19.9	5.15	1.2	170

Table 1. Patient's laboratory findings at ages 9.5 and 14.

Imaging:

- Bone age: 12 years according to Greulich and Pyle
- Pituitary MRI: Rathke cyst without any other abnormal findings
- Pelvic ultrasound: pubertal ovaries and uterus

During follow up, the patient developed secondary amenorrhea, hypernatremia, severe thermal dysregulation, hypothyroidism, while further testing with sleep study revealed obstructive sleep apnea, strongly suggesting ROHHAD syndrome *(Table 1*, *Figure 2*).

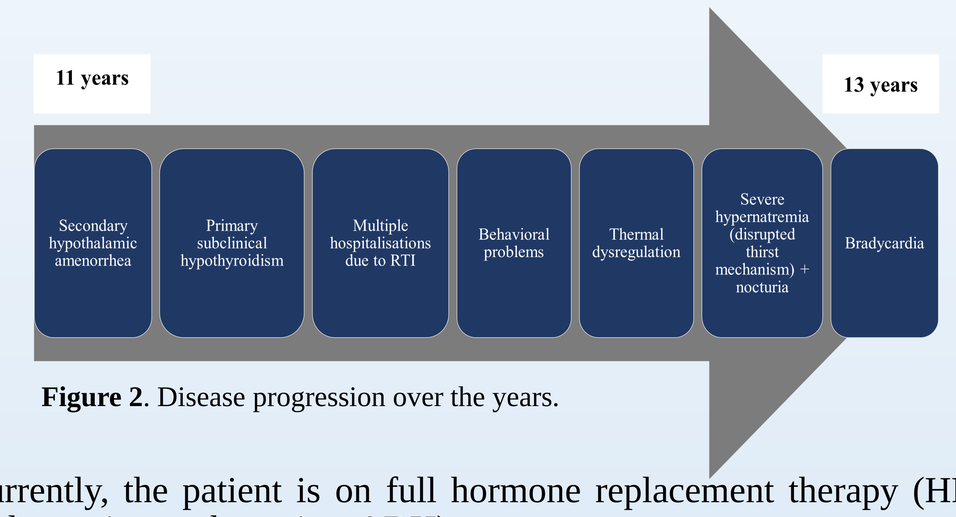


Figure 2. Disease progression over the years.

Currently, the patient is on full hormone replacement therapy (HRT, hydrocortisone, thyroxine, ADH).

Case report 2

A 14 year old boy presented for the first time to the endocrinology outpatient care with significant obesity (BMI 38.08, >97th percentile) and metabolic syndrome (*Figure 3*).

Clinical findings:

- Height 152cm (10th percentile)
- Delayed puberty (Tanner stage: breast II, pubic hair II, testicular volume 6ml)
- Acanthosis nigricans

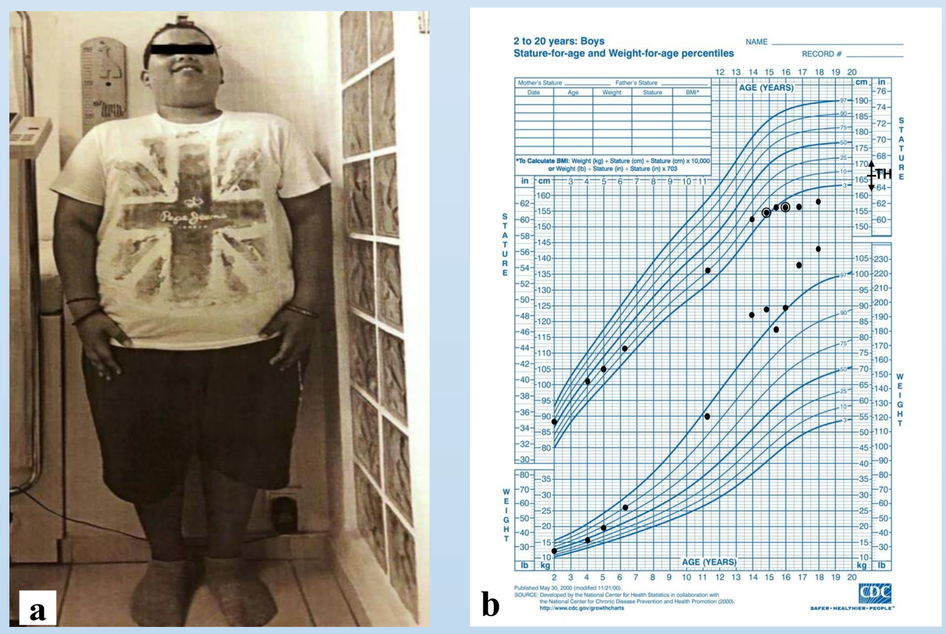


Figure 3. Photo (a) and growth chart (b) of the patient.

Laboratory findings: Hypernatremia, hyperprolactinemia, hypogonadotrophic hypogonadism, GH deficiency with normal cortisol secretion, hypothyroidism and insulin resistance (*Table 3*).

	PRL (4.8-23 ng/ml)	GH provocation test (>10 ng/ml)	IGF-1 (208-512 ng/ml)	ACTH (5-46 pg/ml)	Morning cortisol (6.6-27 mcg/ml)	UFC (5-65 mcg/24h)	1mg DST (<1.8 mcg/dl)	TSH (0.43-4.2 μIU/ml)	fT4 (0.79-1.39 ng/dl)	FSH (mUI/ml)	LH (mUI/ml)	Testosterone (0.28-11.1 ng/ml)	Sodium (135-145 mmol/l)
14 years	68.13	Gluc test <0.05 Clonid test <0.1	39	30.3	13.1	59.5	0.4	3.2	0.91	GnRH test: 0.63(0') 1.17(30') 1.17(60')	GnRH test: 0.86(0') 5.31(30') 4.87(60')	0.04	154

Table 3. Patient's laboratory findings at the age of 14.

Imaging:

- Bone age compatible with chronological age
- Pituitary MRI: without abnormal findings.

Sleep study: obstructive sleep apnea hypopnea syndrome of increased severity

Clinical and laboratory findings suggested ROHHAD syndrome.

Currently, the patient is on metformin, thyroxine, testosterone and non invasive ventilation device (C-PAP).

Conclusion

Prompt recognition of the syndrome as well as treatment of hormonal dysfunction and alveolar hypoventilation may prevent severe complications and increased morbidity mainly due to cardiopulmonary arrest.

References

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2.Rapid-Onset Obesity with Hypoventilation, Hypothalamic and Autonomic Dysregulation (ROHHAD syndrome): A case report and literature review. S.Ibanez-Mico at al., Neurologia, 2017;32(9):616-622