Obesity in ROHHADNET syndrome: does cortisol play a role?

van Tellingen V, van Trotsenburg ASP

Department of Pediatric Endocrinology, Emma Children's Hospital, Academic Medical Center Amsterdam, The Netherlands

✓ *All authors declare no conflicts of interest*
✓ *Informed consent was given by patient and parents for use of medical information & clinical pictures*

Background

ROHHADNET syndrome is characterized by rapid onset childhood obesity, hypoventilation, variable hypothalamic-pituitary and autonomic dysfunction, and in 30-40% neuroendocrine tumors. Autoimmunity and paraneoplastic phenomena are proposed as possible pathophysiological mechanisms, but the exact etiology remains unclear.

Methods & Objective

We present the clinical course of ROHHADNET syndrome in a 17-year-old girl, with the consecutive symptoms indicated in her growth chart.

Case report

Age: *Medical diagnosis:*

4 years: The girl came under medical attention because of rapid weight gain (Figure 1) and a deflecting growth curve (Figure 2). IGF-1 was <5 nmol/L, but low growth hormone concentrations in stim tests were concluded to be false positive, secondary to obesity.

6-7 years: Endocrine investigations for obesity revealed central hypothyroidism (FT4 9.3 pmol/L, N 10-23 pmol/L; TSH 2.2 mE/L, N 0.4-4 mE/L) for which thyroxine treatment was started.

8-9 years: Polyuria and hypernatremia (serum sodium 159 mmol/L). A water deprivation test confirmed partial central diabetes insipidus with adipsia after which a fixed fluid regimen and desmopressin treatment was started. Metyrapone test: no signs of ACTH deficiency. Brain MRI: no abnormalities in the hypothalamic-pituitary area.

10 years: Because of persisting low IGF-1 concentrations, recombinant growth hormone therapy was started, followed by impressive weight loss and change in body composition (Figure 3).

12 years: Chest X-ray, performed because of M. tuberculosis exposure, showed a thoracic mass (Figure 4); diagnosis (needle biopsy): mature ganglioneuroma (benign accidental finding, no indication for treatment).

12,5 years: Hospital admittance because of pre-renal failure due to gastro-enteritis with acute dehydration. Early morning cortisol <50 nmol/L, max. cortisol 136 nmol/L in low dose ACTH test. Start of hydrocortisone treatment (8-10 mg/m2 per day) for suspected central adrenal insufficiency. Rapid weight gain (+15 kg in 9 months). Discontinuation of hydrocortisone resulted in weight loss, but an Addisonian crisis at the age of 15 years necessitated daily use again (4-5 mg/m2 per day).

14 years: No signs of puberty, low LH and FSH concentrations after GnRH administration, estrogen substitution started.

15 years: Periodic hypothermia, dysarthria and strabismus. Repeat brain MRI again no abnormalities. Autonomic dysfunction? ROHHADNET was suspected, severe central hypoventilation was diagnosed and night-time (face mask) assisted ventilation was started.

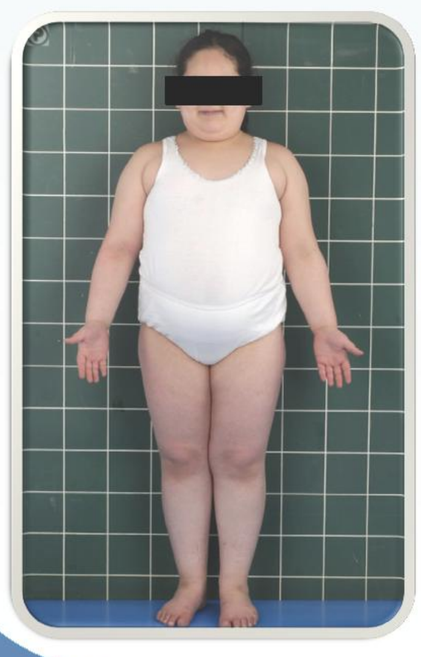

Figure 3

Before & 1,5 years after starting recombinant growth hormone therapy

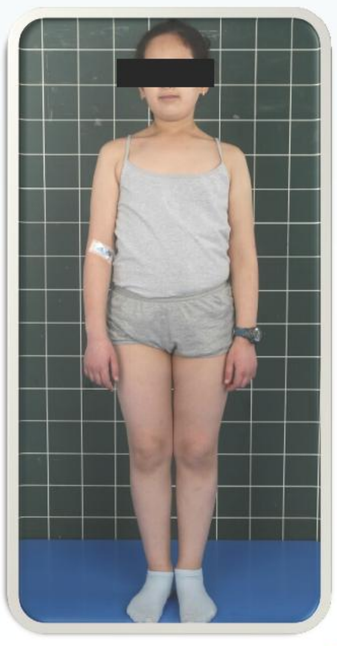

Figure 1

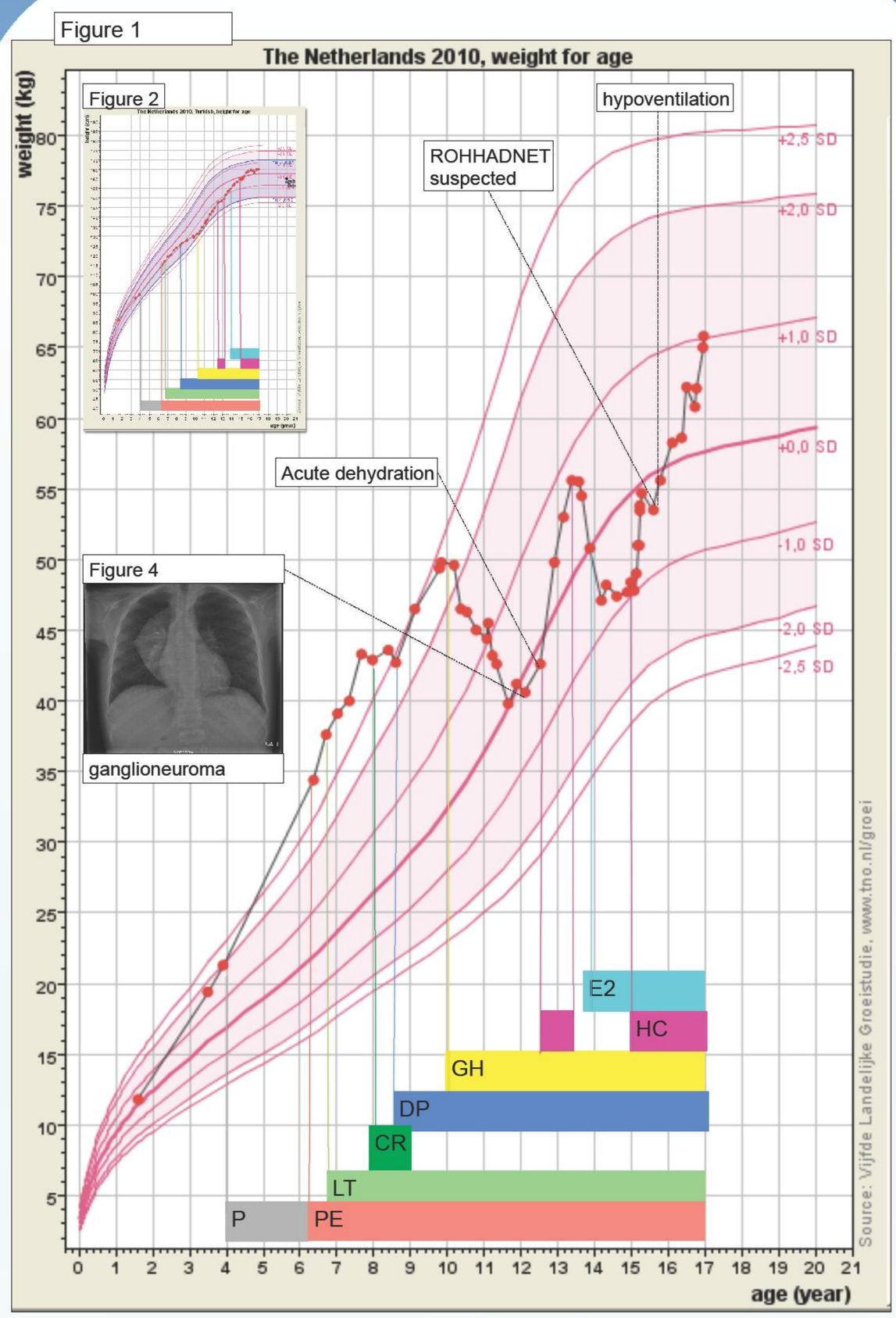

Figure 2

Figure 4

ganglioneuroma

P	Paediatrician (other hospital)
PE	Paediatric Endocrinologist
LT	Levothyroxine treatment
CR	Calory restriction by dietician

DP	Desmopressin treatment
GH	Growth Hormone treatment
HC	Hydrocortisone treatment
E2	Estrogen treatment

Conclusions

Because of the still unknown etiology of this orphan disease, every detailed case description can be helpful in better understanding the pathophysiology of ROHHADNET syndrome. This case report particularly demonstrates:

- that low IGF-1 should trigger towards the diagnosis of growth hormone deficiency in obese patients,
- that neuroendocrine tumours in combination with hypothalamic-pituitary dysfunction should point to ROHHADNET syndrome,
- an intriguing observation of enormous weight gain coincident with regular hydrocortisone treatment, weight loss after stopping this treatment, and a second period of weight gain after restarting hydrocortisone in a low dose; given the hypothesis that the weight loss between ages 10 and 12 years might be due to decreasing endogenous cortisol production, we speculate that the cause of the obesity in ROHHADNET might be related to higher than normal cortisol sensitivity.

Questions, similar patient experiences or interested in further discussion?
Contact: v.vantellingen@amc.nl

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Vera van Tellingen

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