ENDOCRINE CHANGES IN A MECHANICALLY VENTILATED GIRL WITH ANOREXIA NERVOSA

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Abstract

Introduction: Anorexia nervosa (AN) is an eating disorder and also a psychiatric disorder, characterized by a weight well below the standard weight due to a distorted image of the body with obsessive fear of weight gain. ***Material and method:*** We present the case of a 10 years old girl weighing 16 kg (body mass index BMI = 8.16 kg/m2), who was hospitalized in the Pediatric Clinic for loss of appetite, inability to walk and maintain orthostatism, with motor deficit on the right side of the body. The onset was affirmative five months ago, after separation from the mother (gone abroad), the child being left in the care of a grandmother. Twenty-four hours after admission, the girl experienced periods of voluntary apnea, requiring endotracheal intubation and mechanical ventilation. ***Results:*** Endocrine balance showed in this case: elevated cortisol levels, low levels of follicle stimulating hormone (FSH), estradiol and testosterone; high levels of growth hormone (GH) and low levels of insulin-like growth factor (IGF-I); low levels of thyroid hormones (T3 and T4) and slightly decreased thyroid-stimulating hormone (TSH). During the 96 days of hospitalization, the patient required the placement of a tube tracheostomy to continue mechanical ventilation and a PEG (percutaneous endoscopic gastrostomy tube) for enteral nutrition. Weight gain was 4 kg. The patient died due to infectious complications after 6 months following hospitalization in another center. ***Conclusions:*** Endocrine changes that occur in AN are secondary to physiological adaptation of the body to a state of starvation. AN and the associated malnutrition that occurs through self-imposed starvation can cause severe organic and psychological complications and can even lead to death.

Introduction

Anorexia nervosa (AN) is an eating disorder, and according to ICD-10 (international classifications of disease), diagnostic criteria for AN are: (a) Body weight is consistently 15% less (or lower) than that expected for height and age, or body mass index is 17.5 or less. This can be due to either weight loss, or failure to gain weight during growth. (b) Weight loss is caused by the avoidance of foods. (c) Distorted body image perception driven by an intense, irrational fear of becoming fat, leads to the desire to remain at a low body weight. (d) Amenorrhea in women, and loss of libido in men. There may be changes in growth hormone, cortisol, thyroid hormone and insulin. (e) Puberty in girls and boys may be delayed if the onset of anorexia nervosa is prepubertal, but once recovery from the illness is made, it will often progress normally.

AN affects 0.3-0.6% of the female population worldwide (1) and has the highest mortality rate of any psychiatric disorder, between 5-18% (2,3,4). AN is more common seen in female patients between the ages of ten to thirty years, with the greatest incidence at seventeen to eighteen years of age (5).

Over the last few years, many epidemiological and risk factor international studies have provided solid evidence on the role that genetic factors play in AN as well as on the influence of socio-cultural factors (6,7).

Endocrine disturbances in AN are complex and aims the hormones secreted in pituitary –adrenal, –thyroid, and –gonadal axes and represent a body response to starvation. For a better understanding of the physiology of AN it is essential to understand the physiology of starvation (8). The starvation response consists of three phases (9,10). Phase one is short and represents the period when the consumed meal has been digested. In this phase glycogen is not stored for energy. Phase two appears when glycogen stores completely deplete and this stage is responsible for many of the physiological and biochemical alterations in the body. Increase in free fatty acids (FFA) lead to an increase level of fibroblast growth factor-21 who mediates growth hormone (GH) resistance and reduces (insulin-growth-factor-1) IGF-1 levels (11). Further, if starvation continues, the fat stores exhaust and the body enters phase three of starvation. During this phase, there is a breakdown of muscle tissue and the amino acids liberated are used in the formation of glucose for maintaining brain function. Therefore, adapting to starvation involves reducing energy expenditure by suppressing metabolic rate, body temperature and delaying growth (12,13).

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Table I. Summary of vital signs from the initial physical examination in ICU.

Initial vital signs	
Pulse (bpm)	120
Blood pressure (mmHg)	120/65
Breathing (bpm)	0
Weight (kg)	16
Height (cm)	140
BMI (kg/m2)	9.18
Body temperature (°C)	36.2

Table II. Summary of the initial laboratory screening.

Initial laboratory screening		Reference values
Hemoglobin (g/dL)	14.4	11.0 – 15.0
RBC ($x10^6$ mm^3)	4.6	4.0 – 6.0
WBC ($x10^3$ mm^3)	11.3	4.0 – 12.0
Platelets ($x10^3$ mm^3)	360	150 - 400
CRP mg/L	0.26	0 – 5
Sodium (mmol/L)	135	135 - 145
Potassium (mmol/L)	4.0	3.5 – 4.5
pH	7.20*	7.35 – 7.45
PaO2 (mmHg)	46*	80 – 120
PaCO2 (mmHg)	>115*	40 – 50
Base excess (mmol/L)	-18*	-2 – 2
Glucose (mg%)	178*	80 – 120
ASAT (U/L)	25	2 – 31
ALAT (U/L)	23	2 – 32
TP (g/L)	73.9	60 – 80
Creatinine (μmol/L)	18*	45 – 75
BUN (mmol/L)	3.27	1.4 – 8.3
Lipids (g/L)	3.8*	5.0 – 8.0
Triglycerides (mmol/L)	0.5*	0.7 – 1.7
Cholesterol (mmol/L)	3.0*	3.1 – 5.20

Table III. Endocrine status

Endocrine status		**Reference values**
Cortisol nmol/L	680 ↑	171 - 536
FSH mIU/ml	0.13 ↓	0.3 – 11.1
Estradiol pg/ml	4.6 ↓	6.0 – 27.0
Testosterone ng/ml	0.02 ↓	0.050 – 0.522
GH ng/ml	34 ↑	< 20
IGF-I ng/ml	60 ↓	88 - 452
T3 pmol/L	3.7 ↓	4.1 – 7.9
T4 pmol/L	10.2 ↓	11.6 – 21.5
TSH μIU/ml	0.60 ↓(slight)	0.66 – 4.14

↑ above normal ranges
↓ below normal ranges

The onset was affirmative five months ago, after separation from the mother (gone abroad), the child being left in the care of a grandmother. The girl derived from a disorganized family (the parents are separated) and had difficulty in adaptation to a new school and a new environment.

Case report

We present the case of a 10 years old girl weighing 16 kg (body mass index BMI = 8.16 kg/m2), who was hospitalized in the Pediatric Clinic for loss of appetite, inability to walk and maintain orthostatism, with motor deficit on the right side of the body. There were reports for 2 admissions in 3 month before hospitalization in our clinic. First, in the Pediatric Neuropsychiatry Clinic for motor coordination disorder, personality disorders and depression and she was on medication with carbamazepine. At that time, the girl was weighing 23 kg (BMI = 11.73 kg/m2). The second admission, in another Pediatric Clinic for somatization disorder reveal a weight of 18 kg (BMI = 9.18 kg/m2).

Twenty-four hours after admission, the girl experienced periods of voluntary apnea, requiring endotracheal intubation and mechanical ventilation and was immediately admitted to the intensive care unit (ICU). Her mental status was altered. There were clinical signs of mild dehydration and muscle atrophy. Her breathing was voluntary stopped, with sinus tachycardia and normal blood pressure (see Table I for a summary of the initial physical examination). Electrocardiography (ECG) showed no pathological arrhythmias or signs of ischemia. An initial arterial blood gas analysis displayed severe acidosis with hypercarbia. There were no signs of infection, renal, liver functions and electrolytes were normal. Hyperglycemia and low levels of fatty acids were found. (see Table II for a summary of the initial laboratory screening).

Endocrine balance showed in this case: elevated cortisol levels, low levels of follicle stimulating hormone (FSH), estradiol and testosterone; high levels of growth hormone (GH) and low levels of insulin-like growth factor (IGF-I); low levels of thyroid hormones (T3 and T4) and slightly decreased thyroid-stimulating hormone (TSH) (see Table III for endocrine status).

Brain Magnetic Resonance Imaging (MRI) was normal and spine MRI showed signs of osteoporosis.

In ICU, the patient was put on mechanical ventilation mode synchronized intermittent mandatory ventilation with pressure support SIMV-PS with minimal parameters (peak inspiratory pressure PIP = 20 cmH2O, positive end expiratory pressure PEEP = 5 cmH2O, respiratory rate RR = 15 bpm, inspiratory time IT = 1.2 sec, pressure support PS = 15 cmH2O, FiO2 = 0.35). A central venous catheter was mounted for parenteral nutrition. Due to the risk of re-feeding syndrome, the intake of calories was restricted to 500 kcal over the first 24 hours and then increased. The risk of re-feeding syndrome is especially high in patients with a BMI <16, recent weight loss, and electrolyte abnormalities (14). Remaining energy intake was administered on nasogastric tube as nutritional drinks with a balanced protein, fat, and carbohydrate content.

After 72 hours of mechanical ventilation the vital signs normalized and patient was extubated. Because the girl's mother did not come to see her in the hospital, the patient refused any cooperation on oral nutrition, mobilization and respiration and was placed back on mechanical ventilation. Psychiatric evaluation reveal an intelligence above average (QI Raven = 118). On examination, the girl is introverted, suspicious, depressed and shows emotional trauma and somatisation. Psychotherapy was started, but she still remains in a marked depressive state.

During the 96 days of hospitalization, the patient required the placement of a tube tracheostomy to continue mechanical ventilation and a PEG (percutaneous endoscopic gastrostomy tube) for enteral nutrition. Weight gain was 4 kg. The patient died due to infectious complications after 6 months following hospitalization in another center.

Discussions

The endocrinopathies associated with eating disorders involve multiple systems and mechanisms designed to preserve energy and protect essential organs.

Hypercortisolemia is common in AN. Elevated levels of cortisol can be found in multiple sites including the serum, urine, saliva (15,16). Some studies showed loss of normal diurnal rhythm, assessed by late-night and early-morning salivary cortisol levels (16,17). Hypercortisolemia with elevated corticotropin-releasing factor (CRH) is commonly seen in anorexic patients (18). CRH is elevated in cerebral spinal fluid (19), suggesting a central mechanism causing the elevated cortisol. Hypercortisolemia is associated with excessive fear, atherosclerosis, osteoporosis and decreased immune function (20). Possibly, the intense fear seen in AN can be explained by the rise in CRH and cortisol levels. Cortisol also regulates the negative feedback mechanism for CRH secretion.

Delayed puberty can appear if an individual develops AN during adolescence, and some girls with this disorder have primary amenorrhea (21). Low estradiol levels in AN are seen due to a lack of ovarian stimulation and altered metabolism. Amenorrhea is a predictor of osteopenia and osteoporosis with increased risk of fracture later in life. Secretion of androgens including in particular testosterone is deficient in this syndrome, suggesting that gonadal sources are compromised (22).

Growth failure has been reported and might be attributed to deficient concentrations of estrogen and IGF-I. Increased GH levels accompanied by decreased IGF-I suggest an acquired resistance to GH that reverses with refeeding (23). Acute starvation is known to block IGF-I production by the liver, and thus GH excess in AN is attributed in part to lack of IGF-I-mediated negative feedback because of low IGF-I levels (24). Potential consequences of GH resistance include muscle atrophy, growth failure and osteopenia

Malnutrition in AN is accompanied by characteristic changes in peripheral thyroid hormone values outlining an euthyroid sick syndrome. Characteristically, endogenous T3 and T4 levels are low (25). TSH levels are generally within the normal range, but there are reports of levels being lower than in healthy controls (26).

AN has a negative impact on bonn tissue. Most of the endocrinopathies described above likely contribute to the bone loss including low T3, estradiol, testosterone, IGF-I and high cortisol.

Very few studies have investigated the relationship between malnutrition and psychological symptoms in AN. Lucka I. analised a group of 30 children with AN (27) and anxiety disorders were observed in 16.7% patients; 40% of the investigated children suffered from separation anxiety in the past and depression was significantly frequent amongst children suffering from anxiety disorders and AN.

Conclusions

Endocrine changes that occur in anorexia nervosa are secondary to physiological adaptation of the body to a state of starvation. Anorexia nervosa and the associated malnutrition that occurs through self-imposed starvation can cause severe organic and psychological complications and can even lead to death.

Acknowledgement

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