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THE ENDOCRINOPATHIES OF MALE ANOREXIA NERVOSA: CASE SERIES

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Abstract

Objective—Anorexia nervosa (AN) is a serious disorder with associated morbidity and mortality, most commonly diagnosed in females. Existing literature on male anorexia is sparse, and a review of the endocrine effects of AN in males has not previously been published. Our objective is to highlight the clinical characteristics of AN in males as a routinely overlooked cause of multiple endocrinopathies and systemic illness in hospitalized patients.

Methods—We present 4 cases (2 cases at The Mount Sinai Hospital; 2 cases at Long Island Jewish Hospital) of young men with hormonal dysfunction due to underlying AN. Pertinent de-identified data were collected from a chart review of cases seen on the endocrinology consult service at both hospitals. Institutional Review Board approval was not required for an observational report of the cases presented.

Results—Four young men with AN demonstrated evidence of multiple systemic complications from severe caloric and protein malnutrition. Varying degrees of endocrinopathies were present, including hypogonadotropic hypogonadism, hypercortisolemia, and nonthyroidal illness syndrome, resulting in bradycardia, gastroparesis, hypothermia, acute systolic heart failure, and erectile dysfunction. Ages at diagnosis were 20, 24, 23, and 20 years, with mean age 21.75 years. Most of the clinical effects from these endocrinopathies resolved with improved caloric intake and nutrition, although symptoms of hypogonadism persisted.

Conclusion—This small case series highlights the importance of AN as a potential cause of multiple endocrinopathies in males. The heterogeneous presentations and varying degrees of clinical manifestations in our cohort emphasize the challenge in diagnosis. Increased awareness of

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DISCLOSURE

The authors have no multiplicity of interest to disclose.

AN in males is vital, as its prevalence is likely underestimated and appropriate diagnosis and treatment can ameliorate the metabolic dysfunction in a majority of cases. Further studies on males with eating disorders are needed to help guide diagnostic and therapeutic decisions.

INTRODUCTION

Anorexia nervosa (AN) is a serious psychiatric disorder characterized by abnormal eating behaviors, resulting in weight loss and increased mortality. The Diagnostic and Statistical Manual of Mental Disorders (DSM) IV diagnostic criteria included: a) failure to maintain weight above 85% of ideal; b) distorted body image or denial of seriousness of low body weight, fear of gaining weight; and c) amenorrhea (1). AN can be further categorized into three types: restricting, binge and purging, and as yet not classified (2). Although more common in females, an estimated 5 to 10% of affected patients are males. This number may be underestimated and may constitute as much as 25% of the total AN population, as male AN is less frequently recognized and diagnosed (3). In fact, a female bias is evidenced by previous diagnostic criteria, which include amenorrhea but not low testosterone or decreased libido. The more recent DSM V diagnostic criteria have been revised to exclude amenorrhea (4).

AN is associated with significant morbidity and mortality. Serious consequences involve the endocrine system, including the hypothalamic-pituitary-gonadal axis, hypothalamic-pituitary-thyroid axis, hypothalamic-growth hormone (GH)-insulin-like growth factor 1 (IGF-1) axis, hypothalamic-pituitary-adrenal axis, effects on bone metabolism, and neuroendocrine signaling mechanisms in the modulation of appetite. The influence of AN on these endocrine pathways is frequently missed, especially in male patients. We present 4 male patients with AN and significant endocrine dysfunction at 2 hospitals between 2010 and 2014, to highlight the challenges associated with their medical management.

CASE REPORT

Patient 1

A 20-year-old male without available past medical history presented to The Mount Sinai Hospital with severe progressive weakness and bradycardia. According to his parents, he had always been thin and a “poor eater” but recently lost weight from 115 to 70 pounds at a height of 63 inches over the past few months. He had come to medical attention for complaints of erectile dysfunction and was started on testosterone replacement therapy. He also complained of worsening fatigue and constipation. Vital signs were significant for a temperature of 34.4°C, a pulse of 30 to 40 beats per minute, and a blood pressure of 90/50 mm Hg. His BMI was 12.9 kg/m^2. On physical examination, he appeared severely cachectic, with sarcopenia and short stature. He was arousable but would not converse, bradycardic, and with acrocyanosis on his hands. Capillary blood glucose was 50 mg/dL. His laboratory workup was significant for hypokalemia, azotemia, an albumin of 4.3 mg/dL, and a transaminitis. Repeat finger-stick glucose was 15 mg/dL. Endocrine evaluation revealed a thyroid-stimulating hormone (TSH) 2.6 μIU/mL (normal, 0.34 to 5.60), free thyroxine (T4) 0.8 ng/dL (normal, 0.6 to 1.1 ng/dL), free triiodothyronine (T3) 1.8 pg/mL (normal, 2.5 to 3.9 pg/mL), total T3 20 ng/dL (normal, 87 to 178 ng/dL), morning cortisol 25.1 μg/dL

(normal, 6.7 to 22.6 μg/dL), adrenocorticotropic hormone (ACTH) 24 pg/mL (normal, 0 to 46 pg/mL), testosterone 88 ng/dL (normal, 170 to 780 ng/dL), IGF-1 <25 ng/mL (normal, 116 to 358 ng/mL), and prolactin 11.5 ng/mL. He was given a dextrose infusion for hypoglycemia and then started on parenteral nutrition (PN) and enteral nutrition (EN) with a presumptive diagnosis of AN. The EN formula was slowly increased to a goal of 21 kcal/kg/day, and the PN was tapered off with no evidence of refeeding syndrome. Blood pressure remained stable without the use of vasopressors, and the bradycardia slowly improved over the course of weeks. On the 26th hospital day, the patient was discharged home on an oral diet along with supplemental EN via a gastrostomy tube. A repeat total testosterone at discharge was 141 ng/dL. His mental status was back to baseline with a flat affect, and his hypoglycemia resolved.

Patient 2

A 24-year-old male with a history of AN was transferred from an outside hospital to The Mount Sinai Hospital. He was admitted 4 weeks earlier for bradycardia with a hospital course complicated by transaminitis, pancreatitis, pneumomediastinum, and refeeding syndrome. He had lost 141 pounds over the past 1 year (220 to 79 pounds) with Hydroxycut™, decreased oral intake, and excessive exercise (ran 10 miles daily). Vital signs were significant for a temperature of 35.9°C, a pulse of 60 beats per minute, and a blood pressure of 74/48 mm Hg. His BMI was 12 kg/m^2. On physical examination, he appeared severely cachectic, with bitemporal wasting, scleral icterus and jaundice, severe generalized weakness, crepitus along the right supraclavicular region, and decreased pedal pulses bilaterally. His lab work was significant for azotemia, an albumin of 2.8 g/dL (normal, 3.3 to 5.0 g/dL), aspartate aminotransferase (AST) 433 U/L, alanine aminotransferase (ALT) 1,754 U/L, alkaline phosphatase 394 IU/L, total bilirubin of 11.8 mg/dL (direct 7.4 mg/dL), and pre-albumin 6.1 mg/dL. Endocrine labs revealed a TSH of 1.28 μIU/mL (normal, 0.34 to 5.60), free T4 0.7 ng/dL (normal, 0.6 to 1.1 ng/dL), free T3 1.1 pg/mL (normal, 2.5 to 3.9 pg/mL), total T3 31 ng/dL (normal, 87 to 178 ng/dL), cortisol at noon 217 μg/dL (normal, 6.7 to 22.6 μg/dL), 24-hour urinary collagen cross-link 1,564 nmol bone collagen equivalents (BCE)/mmol creatinine (normal, 11 to 103 nmol BCE/mmol creatinine). Two-dimensional echocardiogram revealed an ejection fraction of 19%. He was started on vasopressors for hypotension, developed episodes of hypoglycemia, and PN was initiated. His hospital course was further complicated by hypercapneic respiratory failure requiring mechanical ventilation, development of sacral decubitus ulcers, aspiration pneumonia, recurrent pneumothorax, and severe anemia and thrombocytopenia requiring blood and platelet transfusions. Eventually tracheostomy and percutaneous gastrostomy tubes were placed in anticipation of discharge to a rehabilitation facility after 7 months of hospitalization.

Patient 3

A 23-year-old male presented to the Long Island Jewish Medical Center emergency department due to his mother’s concerns of disorganized behavior and starving himself with a 35-pound weight loss over the past 2 months. The patient claimed he had no current weight problem. Upon presentation, his vital signs were significant for a temperature of 33.9°C, a pulse of 30 beats per minute, and a blood pressure of 94/68 mm Hg. His BMI was

13 kg/m^2. On physical examination, he appeared cachectic and lethargic with a flat affect. A capillary blood glucose was 50 mg/dL. His laboratory evaluation was significant for sodium of 146 mmol/L, prerenal azotemia, an albumin of 5.3 mg/dL, and total bilirubin of 1.8 mg/dL. Endocrine labs revealed a TSH of 0.82 ìIU/mL (normal, 0.34 to 5.60), free T4 0.62 ng/dL (normal, 0.6 to 1.1 ng/dL), free T3 0.2 ng/mL (normal, 0.8 to 2.0 ng/mL), random cortisol (12 pm) 18 µg/dL (normal, 6.7 to 22.6 µg/dL), ACTH 21 pg/mL (normal, 0 to 46 pg/mL), testosterone 198 ng/dL (normal, 249 to 836 ng/dL), luteinizing hormone (LH) 1.4 IU/L, follicle-stimulating hormone (FSH) 3.1 IU/L, IGF-1 147 ng/mL (normal, 116 to 358 ng/mL), GH 1.33 ng/mL (normal, <5.0 ng/mL), and prolactin 17.7 ng/mL. Two-dimensional echocardiogram revealed an ejection fraction of 55 to 60%. His blood pressure remained stable with intravenous fluid hydration, but he remained hypoglycemic, requiring a continuous infusion of dextrose. He was transferred to the coronary care unit for persistent bradycardia with pauses on telemetry. A nasogastric tube was placed, and his caloric intake was gradually increased with close monitoring of electrolytes and for possible refeeding syndrome. Throughout his hospital stay, he was seen by psychiatry, maintained on olanzapine, and received haloperidol and lorazepam occasionally. Electroconvulsive therapy was scheduled for refractory depression but was never performed, as the patient suddenly began to eat full meals. At the time of discharge, his bradycardia and hypothermia resolved.

Patient 4

A 20-year-old male with no significant medical history presented to the Long Island Jewish Medical Center with persistent nausea and vomiting. He had lost 130 pounds over 6 months and had been taking “Reduced Fat Fast” pills (*Camelia Sinensis* and *Orthosiphon Stamineus*) for 2 weeks. He also complained of dizziness, poor appetite, and malaise. His BMI was 18 kg/m^2. On physical examination, he appeared cachectic with temporal wasting, dry mouth, and a flat affect. Initial laboratory evaluation revealed severe hypokalemia of 2 mmol/L (normal, 3.5 to 5.1 mmol/L), hypochloremia of 88 mmol/L (normal, 96 to 108 mmol/L), and elevated bicarbonate to 34 mmol/L (normal, 22 to 31 mmol/L). Subsequently, the patient became bradycardic (pulse 39 to 40 beats per minute), hypothermic (temperature 36.4°C), and hypotensive (blood pressure 90/60 mm Hg). Additional laboratory evaluation revealed hypophosphatemia 2.2 mg/dL (normal, 2.5 to 4.5 mg/dL), hypoalbuminemia 3.1 g/dL (normal, 3.3 to 5.0 g/dL), total protein 4.9 g/dL (normal, 6.0 to 8.3 g/dL), blood urea nitrogen 3 mg/dL (normal, 7 to 23 mg/dL), pre-albumin 14 mg/dL (normal, 20 to 40 mg/dL), and normal liver transaminases. Endocrine workup revealed TSH 2.0 µIU/mL, free T4 1.72 µIU/mL (normal, 0.8 to 1.8 µIU/mL), hemoglobin A1c 5.5% (36.6 mmol/mol), 25-hydroxyvitamin-D 35.5 ng/mL, ACTH 8 pg/mL (normal, 0 to 46 pg/mL), cortisol 5.4 µg/dL at 6 am, with stimulation to 29.7 one hour after cosyntropin (250 µg) administration (normal, 6.7 to 22.6 µg/dL). Total testosterone was 614 ng/dL (normal, 249 to 836 ng/dL), and free testosterone was 5.4 pg/mL (normal, 9.3 to 26.5 pg/mL), with FSH 1.9 IU/L (normal, 4.7 to 21.5 IU/L) and LH 6.3 IU/L (normal, 2.4 to 12.6 IU/L).

An upper endoscopy was performed to further evaluate weight loss and persistent nausea and vomiting, which revealed chronic gastritis and *Helicobacter pylori*, without evidence of malabsorption. A gastric emptying study was suggestive of gastroparesis. The patient was evaluated by gastroenterology and surgery for possible gastric pacemaker for severe (or

refractory) gastroparesis and cardiology for a cardiac pacemaker for his bradycardia prior to consultation from endocrinology. Following involvement of the endocrinology team, concern about a likely eating disorder as the etiology of his symptoms was discussed. He was interviewed by psychiatry and endorsed concerns of “being fat,” a “fear of gaining weight,” and would purge up to 5 times daily. Throughout his hospital course, he was managed with intravenous fluids, electrolyte repletion, and prokinetics and anti-emetics as needed. EN was initiated via a nasogastric tube for low caloric intake. As his nutrition was optimized, his gastroparesis symptoms improved, oral caloric intake increased, and bradycardia resolved. He was discharged to follow-up at an eating disorders day program.

RESULTS

Clinical characteristics from 4 young men with protein-calorie malnutrition and multiple endocrinopathies from AN were analyzed (Tables 1–3). The mean age of this cohort was 21.75 years (range, 20 to 24 years) (Table 1). These men had an average BMI of 13.85 kg/m^2 (range, 12 to 18 kg/m^2), weight loss of 87.75 pounds (range, 35 to 141 pounds), temperature of 35.2°C (range, 33.9 to 36.4°C), heart rate of 39.75 beats per minute (range, 30 to 60 beats per minute), and blood pressure 87/57 mm Hg (range, 74/48 to 94/68 mm Hg). All 4 patients were admitted for bradycardia and found to have multiple endocrinopathies (Table 1). The most common endocrinopathies observed were hypothyroidism, hypogonadism, and hypoglycemia, with additional endocrinopathies including elevated cortisol, increased bone turnover markers, and low IGF-1 (Tables 1 and 3). Table 2 shows the initial biochemical evaluation obtained on these patients with significant variability between subjects with respect to renal function, electrolytes, and liver function. Most of the clinical signs of these endocrinopathies resolved with optimization of nutrition, such as bradycardia, gastroparesis, and hypothermia, but symptoms of hypogonadism did not resolve prior to discharge.

DISCUSSION

This small case series highlights the importance of AN as a potential cause of multiple endocrinopathies, especially in men. The diverse clinical manifestations and hormone dysfunction make the diagnosis challenging and highlight the importance of individualizing the evaluation. Weight loss and increased stress may have led to hypothalamic dysfunction, with further adaptive mechanisms causing organ dysfunction.

In our cohort, all patients were in their early twenties and were admitted to the hospital with bradycardia. Three of the 4 patients had no previous diagnosis of AN or other eating disorder; therefore, it was not initially considered in the differential diagnosis. The average BMI was 14 kg/m^2 with an average weight loss of 16.48 pounds per month. All patients also had hypothermia (36.4°C) and hypotension. Three of the 4 patients had some evidence of elevated cortisol levels, hypothyroidism, and hypogonadism. The elevation in cortisol has been suggested to result from increased cortisol secretion following activation of corticotrophin-releasing hormone (CRH) from the hypothalamus, decreased feedback sensitivity, and downregulation of CRH corticotrope receptors (5). Anorexic patients were found to lack cortisol suppression after dexamethasone administration and failed to increase

plasma ACTH or cortisol after CRH induction (6). Despite increased levels of CRH secretion and cortisol production, plasma ACTH levels were normal. This can be explained by an intact negative feedback mechanism at the level of the pituitary but not at the level of the hypothalamus (5). Although most of the endocrinopathies improved by optimizing nutritional status in our cohort, hypogonadism did not. This may be an evolutionary protective adaptation to prevent offspring production at a time of compromised nutrition (7) or an indication that gonadal recovery is multifactorial and may also involve a psychological component (8).

A majority of our cohort had preserved albumin levels despite protein and caloric malnutrition. Although one would suspect hypoalbuminemia in these patients, prior studies have shown that albumin remains typically within the normal range (9,10). Overall, pre-albumin is considered a better marker of nutritional status and, as seen in our cohort, low pre-albumin levels are more prevalent in AN (10). Furthermore, low pre-albumin was recently found to be a significant predictor of refeeding hypophosphatemic syndrome and hypoglycemia in this specific population (10). When hypoalbuminemia is present, additional evaluation may be needed to assess for other causes of inflammation or infection (11).

The lack of endocrinopathies in the fourth patient may be secondary to the patient having a higher BMI on admission (18 kg/m^2) as opposed to the other patients with a presenting BMI between 12 and 13 kg/m^2. It is possible that there may be a threshold BMI where the endocrine system fails to compensate for prolonged starvation. Evidence from patients with critical illness demonstrates a higher degree of endocrine axis suppression with increased disease severity (12). The variability between patients in clinical symptoms, endocrine dysfunction, and metabolic parameters can be attributed to differences in chronicity of protein calorie malnutrition, mechanism of weight loss (supplements, purging, starvation, etc.), total amount of weight loss, and baseline weight prior to weight loss.

The characteristics of the males in our study have some similarities to the female AN population. Similar to previously reported studies (13,14), depression, psychosis, and personality disorders were highly evident in our cohort, which parallels the high prevalence of comorbid psychiatric illness in females with AN. The age of diagnosis is similar to females as well with a mean age in our cohort of 21.75 years. In contrast to published data on females with AN where body image obsession is the driving force of the weight loss, males appear to have atypical motivating factors for weight loss (15). In our group, half of the patients became malnourished with the goal of losing weight or fear of weight gain. The other 2 patients' weight loss and starvation states were unintentional effects of underlying depression and psychosis, with less concern about their body image. Nonetheless, the failure to maintain their weight above 85% ideal, lack of recognition of the seriousness of their low body weight, and hypogonadism indicate AN in these patients as opposed to secondary anorexia. The evidence indicates that the severe multiple endocrinopathies in these patients were due to failure to seek treatment and a lack of early diagnosis, as all 4 men initially denied the severity of their weight loss. Sexual orientation was not fully assessed in our patients, although the majority had reported being in heterosexual relationships. Prior studies on male and female patients with AN showed an increased prevalence of homosexuality and asexuality compared to the general population (16).

The hypothalamic-pituitary-gonadal axis has welldescribed alterations in females with AN, which is similar to males with AN, as in our cohort. The amenorrhea seen in AN is due to hypothalamic dysfunction with low levels of FSH, LH, and estradiol. Starvation leads to impaired pulsatility of gonadotropin-releasing hormone, which suppresses the secretion of gonadotropins, particularly LH, and leads to anovulation, prolonged follicular phase with luteal phase deficiency, and hypoestrogenism (7). A decrease in normal body weight by 10 to 15% can cause amenorrhea (17). Additionally, the loss of body fat leads to decreased aromatization of androgens to estrogens. Infertility and impaired sexual function appear to be a protective adaptation to prevent pregnancy in a setting of impaired nutrition. Throughout history, luteal deficiency and infertility have been observed in times of food rationing during wars and reduced seasonal availability in nomadic populations (18). Effects in males are less described but likely have a similar mechanism leading to hypogonadotropic hypogonadism of hypothalamic origin. Low levels of testosterone and dehydroepiandrosterone may contribute to low bone mass during puberty. Leptin levels may also be involved as a regulator of reproductive function evidenced by homozygous (ob/ob) leptin-deficient mice with infertility and restoration of ovulation and pregnancy with recombinant leptin (19). Kisspeptin has also been investigated as a regulator of reproductive function. Although the role of kisspeptin in AN has not been studied, studies have shown that in women with hypothalamic amenorrhea, kisspeptin administration increases gonadotropin release (20). The gonadal effects of AN typically reverse with weight gain, and in females, menses often resume within a year of the maintenance of an appropriate weight. Body fat percentage may be predictive of menstrual restoration, as women with a higher percentage of body fat maintained menses despite low body weight (21).

Treatment of our patients with AN required close monitoring to prevent a serious complication known as refeeding syndrome, characterized by dramatic shifts in electrolyte and intravascular fluid levels. The starved catabolic state is characterized by, among others, organ dysfunction of varying degrees, inadequate carbohydrate metabolism, insulinopenia, use of alternative energy sources, and micronutrient depletion. Upon initiation of nutrition therapy for the AN patient, the carbohydrate load (dietary sugars and starches with EN and/or dextrose with PN) results in the release of insulin, trapping of intracellular phosphate as glucose-6-phosphate, and intracellular influx of phosphorus > potassium, magnesium, and calcium. The result is primarily hypophosphatemia, the hallmark of refeeding syndrome, hypomagnesemia, and hypokalemia. When severe, these electrolyte derangements lead to arrhythmias, respiratory failure, neuromuscular weakness, hemolysis, and encephalopathy (7). On occasion, hypophosphatemia occurs in the absence of other changes, and this has recently been referred to as “refeeding hypophosphatemia.”

The high demand for phosphorylated coenzymes of glycolysis (ATP and 2,3-diphosphoglycerate) increases the risk of thiamine deficiency. The antinatriuretic effect of insulin and resulting influx of sodium can cause acute fluid retention, and coupled with a cardiomyopathy from prolonged starvation, increases the risk of life-threatening cardiac and pulmonary edema. Patients at highest risk for refeeding syndrome are those with minimal or no nutritional intake for more than 3 days, more than 15% weight loss over the past 3 months, low weight for height, and abnormal electrolytes prior to refeeding (2). The

initiation of nutrition to our patients involved conservative caloric doses of 10 kcal/kg/day and slow titration to avoid refeeding.

A main limitation of this study is the small sample size of our cohort to draw definitive conclusions. As with many other previously published studies on male AN, this is a small case series, and a larger dataset analyses would reveal more information. Nonetheless, having an increased awareness of this disease entity in men can lead to prompt diagnosis and treatment. The retrospective evaluation of these cases also has inherent limitations. Biochemical parameters such as bone turnover markers, total and free testosterone, prolactin, LH, FSH, ACTH, IGF-1, GH, and total and free T3 levels were not universally assessed in all 4 patients during their admission and would have possibly provided an opportunity for further analysis and conclusions.

Over the past few years, novel psychological treatments have emerged in the field of eating disorders, such as cognition, behavioral, and emotion-based approaches, exposure and response prevention, motivation enhancement, and family and couple-based interventions (22). Although these interventions have not been studied in large-scale randomized controlled trials, preliminary data on small case studies seem promising and an area for further investigation (22). Continuity of care in these patients is important to assess their psychologic and endocrine recovery. The patients in this study have not followed-up, which limits our ability to determine if there has been additional improvement in symptoms or biochemical parameters.

CONCLUSION

In summary, AN is not only a disease in females but should also be suspected in males with multiple endocrine dysfunction. The same endocrinopathies seen in females with AN can also occur in males. There is a need for increased awareness, as the prevalence of AN in males is likely underestimated. Males should be screened for AN if there is a history of weight loss, especially with co-existing psychiatric disorders or substance abuse, BMI below average for weight and height, symptoms of hypogonadism, or unexplained fragility fracture. Appropriate diagnosis and treatment can ameliorate the metabolic dysfunction in a majority of cases, but long-term complications include osteoporosis, infertility, and short-stature.

Further research and investigation on males with eating disorders is needed to assess the commonalities and differences between males and females with AN and determine if current diagnostic and treatment practices can be applied to the male population. Understanding male AN and the associated endocrinopathies will help guide appropriate diagnostic and treatment decisions in the future.

Abbreviations

ACTH	adrenocorticotropic hormone
AN	anorexia nervosa

BMI	body mass index
CRH	corticotrophin-releasing hormone
EN	enteral nutrition
FSH	follicle-stimulating hormone
GH	growth hormone
IGF-1	insulin-like growth factor 1
LH	luteinizing hormone
PN	parenteral nutrition
T3	triiodothyronine
T4	thyroxine
TSH	thyroid-stimulating hormone

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Table 1

Characteristics of the Cohort

Characteristic	Case 1	Case 2	Case 3	Case 4	Mean
Age (years)	20	24	23	20	21.75
BMI (kg/m^2)	12.4	12	13	18	13.85
Weight loss (pounds)	45	141	35	130	87.75
Weight loss per month (pounds/month)	15	11.75	17.5	21.6	16.48
Temperature (°C)	34.4	35.9	33.9	36.4	35.2
Heart rate (beats per minute)	30	60	30	39	39.75
Blood pressure (mm Hg)	90/50	74/48	94/68	90/60	87/57
Admission diagnosis	Bradycardia	Bradycardia	Bradycardia	Bradycardia	
Endocrinopathies	Hypogonadism Hypothyroidism Cortisol resistance[a] Low IGF-1 Hypoglycemia	Hypogonadism Hypothyroidism Cortisol resistance[a] Hypoglycemia High bone turnover	Hypogonadism Hypothyroidism Hypoglycemia	Cortisol resistance[a]	

Abbreviations: BMI = body mass index; IGF-1 = insulin-like growth factor 1.

[a]Cortisol resistance is suspected based on elevated cortisol levels with normal adrenocorticotropic hormone levels.

Table 2

Admission Laboratory Evaluation

Lab test	Case 1	Case 2	Case 3	Case 4
INR (0.88–1.16)	1.7	1.6	1.38	1.06
Sodium (132–145) mmol/L	136	123	146	138
Potassium (3.5–5.1) mmol/L	3.2	3.8	4.4	2.0
Chloride (96–108) mmol/L	101	84	106	88
Bicarbonate (22–31) mmol/L	23	34	33	34
BUN (7–23) mg/dL	25	65	62	14
Creatinine (0.5–1.3) mg/dL	0.7	0.7	1.79	0.75
Glucose (70–99) mg/dL	148	188	108	103
Calcium (8.4–10.5) mg/dL	8.9	8.0	10.3	9.9
Magnesium (1.6–2.6) mg/dL	2.2	2.1	3.4	2.2
Phosphorus (2.5–4.5) mg/dL	2.7	2.5	2.5	2.2
Total protein (6.0–8.3) g/dL	7.2	4.1	4.5	4.9
Albumin (3.3–5.0) g/dL	4.3	2.8	5.3	4.5
Pre-albumin (20–40) mg/dL	12	6.1	16	14
T-bilirubin (0.2–1.2) mg/dL	1.8	11.8	1.8	1.4
AST (0.0–37) U/L	659	433	30	34
ALT (0.0–41) U/L	828	1,754	49	39
ALKP (30–120) U/L	186	394	52	49

Abbreviations: ALKP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; INR = international normalized ratio.

Table 3

Endocrine Laboratory Evaluation

Lab test	Case 1	Case 2	Case 3	Case 4
TSH (0.27–4.2) μIU/mL	2.6	1.28	0.54	2.00
Free T4 (0.9–1.8) ng/dL	0.8	0.7	0.62	1.72
Total T3 (0.8–2.0) ng/dL			0.2	
Total T3 (87–178) ng/dL	20	31		
Free T3 (1.8–4.6) pg/mL	1.8	1.1		
Testosterone (249–836) ng/dL	88		198	614
LH (2.4–12.6) IU/L			1.4	6.3
FSH (4.7–21.5) IU/L			3.1	1.9
Prolactin (4.0–15.2) ng/mL	11.5		17.7	
Cortisol (2.3–19.4) μg/dL	25.1	21.7	18	18.6
ACTH (0–46) pg/mL	24		21	8.0
Collagen cross-links (nmol BCE/mmol creatinine)		1,564		
IGF-1 (83–344) ng/mL	<25		147	
Growth hormone (<5.0) ng/mL			1.33	0.60

Abbreviations: ACTH = adrenocorticotropic hormone; BCE = bone collagen equivalents; FSH = follicle-stimulating hormone; IGF-1 = insulin-like growth factor 1; LH = luteinizing hormone; T3 = triiodothyronine; T4 = thyroxine; TSH = thyroid-stimulating hormone.