J Tokyo Wom Med Univ
69 (6) 289~295 (1999)

A Young Male with a Hypothalamic Tumor Mimicking Anorexia Nervosa

Mari HOTTA[1], Tamotsu SHIBASAKI[2], Kanji SATO[1], Osami KUBO[3], Hiroshi DEMURA[1] and Kazue TAKANO[1]

[1]Department of Medicine, Institute of Clinical Endocrinology, and [3]Department of Neurosurgery, Neurological Institute, Tokyo Women's Medical University, School of Medicine

[2]The Department of Physiology, Nippon Medical School

(Received Jan. 27, 1999)

A 20-year-old Japanese man with a hypothalamic tumor which caused hypopituitarism and diabetes insipidus was mistakenly diagnosed as anorexia nervosa because of anorexia, weight loss, denial of being ill, changes in personality, and abnormal behavior resembling the clinical characteristics of anorexia nervosa. After irradiation therapy, he gained weight and is behaving normally under replacement therapy. Unlike in hypopituitarism, anorexia nervosa patients often have elevated plasma levels of growth hormone (GH), cortisol or adrenocorticotropin (ACTH). Careful testing and examination must be performed to distinguish between anorexia nervosa and other organic disorders.

Introduction

The diagnosis of anorexia nervosa is based upon the presence of weight loss unexplained by physical illness or other psychiatric disorders. Psychological characteristics include fear of gaining weight, distortion of body image, preoccupation with food, and denial of cachexia. The diagnostic criteria for anorexia nervosa as determined by the Survey Committee for Eating Disorders of the Japanese Ministry of Health and Welfare in 1990 are ①weight loss of 20% below that expected, lasting longer than 3 months, ②abnormal eating behavior including food restricting, bulimic episodes, and stealth eating, ③a disturbance in the perception of body weight or shape and intense fear of gaining weight, despite being underweight, ④onset at under 30 years of age, ⑤amenorrhea in females, and ⑥negation of other illness including psychiatric disorders, that could account for anorexia and weight loss. In practice, it is difficult in many patients to determine whether or not they have a fear of gaining weight. The incidence of male anorexia nervosa has recently been increasing, although anorexia nervosa still occurs 10 times more frequently in girls than boys [1]. This report describes a male patient whose clinical presentation resembled that of anorexia nervosa, but who was eventually diagnosed with a hypothalamic tumor. Prior to the correct diagnosis, the misdiagnosis of anorexia nervosa had endangered his life.

Case Report

A 20-year-old Japanese man, the elder of two siblings, was emergently admitted to our department on July 4th, 1995, due to poor nutrition and disturbance of consciousness. He had had no serious illnesses in the past. He was not aggressive and was considered highly intelligent at school.

On March 1st 1995, he caught a cold after skiing and lost his appetite with nausea and vomiting. He had frequently drunk water with ice in late March, but the polydipsia disappeared in April. However, he did not voluntary disclose his polyuria. Laboratory tests were performed at a general hospital on April 10th, which revealed that the serum values for urea nitrogen, sodium and chloride were slightly higher than normal. No abnormal findings were observed in a computed tomographic (CT) scan of the head. He was mistakenly diagnosed as suffering from anorexia nervosa both at the general hospital as well as outpatient department of a psychiatry unit of a university hospital. He denied being ill and showed resistance to seeing a doctor. He was inhibited and rather uncommunicative.

In June, he entered another psychiatric hospital because of dehydration and abnormal behavior, such as intentional vomiting accompanied by moaning in a toilet room for long periods of time. He rejected laboratory tests as well as an intravenous drip, and was discharged from the hospital at his discretion. He was then admitted to our department because of poor nutrition and a disturbance of consciousness. He lost 6.4 kg in weight in 4 months.

On admission, he was seriously dehydrated. He was emaciated, with a height of 169 cm and a weight of 45 kg, which was more than two standard deviations below the mean for his age. His pulse was 78/min and blood pressure 106/70 mmHg. His consciousness was 10 as estimated by the Japanese Coma Scale, with hallucinations. The extragenital organs appeared normal and his pubic hair was of the female-type shape. Visual field examination showed no abnormalities.

The results of routine laboratory studies (Table 1) revealed proteinuria, a mild degree of anemia, a severe degree of dehydration, hypoproteinemia, hypoalbuminemia, hypernatremia, hypercalcemia in spite of hypocalciuria and renal failure. Hormonal studies were performed (Tables 2 and 3).

Table 1 Initial laboratory data

Peripheral blood		Urine examination	
Red blood cell	374×10^4 /mm^3	Gravity	1.007
Hemoglobin	11.1 g/dl	Protein	(+)
Hematocrit	28.2 %	Glucose	(−)
White blood cell	7,340 /mm^3	Ocult blood	(+)
Platelets	9.0×10^4 /mm^3	Red blood cell	1 /HPF
Blood chemistry		White blood cell	6 ~ 10 /HPF
Total bilirubin	0.4 mg/dl	Urine chemistry	
AST	20 IU/*l*	Total volume	955 ml
ALT	12 IU/*l*	Protein	0.04 mg/dl
LDH	242 IU/*l*	Na	40 mEq/*l*
ALP	129 IU/*l*	K	44 mEq/*l*
CK	36 IU/*l*	Cl	46 mEq/*l*
Total protein	5.9 g/dl	Creatinine	61 mg/dl
Albumin	3.7 g/dl	BUN	335 mg/dl
Total cholesterol	144 mg/dl	Ca	0.8 mg/dl
Triglyceride	141 mg/dl	P	31.1 mg/dl
Glucose	72 mg/dl	NAG	27.9 U/*l*
BUN	42 mg/dl	α_1 microglobulin	84.1 mg/*l*
Creatinine	3.9 mg/dl	β_2 microglobulin	30,300 mg/*l*
Uric acid	10.5 mg/dl	Uosm	274 mOsm/kgH_2O
Na	164 mEq/*l*	Posm	342 mOsm/kgH_2O
K	3.9 mEq/*l*	FENa	0.54 %
Cl	125 mEq/*l*	FECa	0.73 %
HCO_3	25.6 mEq/*l*	24h CCr	13.2 ml/min
Ca	13.7 mg/dl		
P	3.9 mg/dl		
Mg	2.2 mEq/*l*		

AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase, CK: creatine kinase, BUN: blood urea nitrogen, NAG: N-acetyl- β-D-glucosaminidase, Uosm: urinary osmolality, Posm: plasma osmolality, FENa: fractional excretion of Na, FECa: fractional excretion of Ca, 24hCCr: 24 hour creatinine clearance.

The basal levels of plasma ACTH, cortisol, aldosterone, gonadotropins, and testosterone were depressed. Although plasma GH increased in response to GH-releasing hormone (GRH) and plasma ACTH increased in response to corticotropin-releasing hormone (CRH), the responses of those hormones to insulin-induced hypoglycemia were impaired. Gonadotropins did not show any responses to luteinizing hormone-releasing

Table 2 Endocrinological and related data

	Normal range	Present patient
T_3	(90 ~ 170)	100 ng/dl
T_4	(5.1 ~ 11.4)	8.9 μg/dl
Free T_3	(2.5 ~ 4.3)	4.0 pg/ml
Free T_4	(1.0 ~ 1.8)	1.5 ng/dl
TSH	(0.2 ~ 4.0)	0.1 > μU/ml
Thyroglobulin	(30 >)	46.7 ng/ml
TBII	(−15 ~ 15)	4.5 %
TGHA	(100 × >)	100 × >
MCHC	(100 × >)	100 × >
GH	(5 >)	0.5 ng/ml
PRL	(15 >)	40 ng/ml
ACTH	(10 ~ 60)	5.7 pg/ml
Cortisol	(4.5 ~ 24)	1.1 μg/dl
Urinary free cortisol	(10 ~ 100)	44.7 μg/day
17OHCS	(2.9 ~ 11.6)	2.0 mg/day
17KS	(4.6 ~ 16.4)	2.0 mg/day
LH	(1.6 ~ 9.5)	0.5 mIU/ml
FSH	(1.2 ~ 8.2)	0.9 mIU/ml
Testosterone	(250 ~ 1,100)	5.0 ng/dl >
ADH	(0.3 ~ 4.2)	0.47 pg/ml
Renin	(0.5 ~ 3.0)	11.5 ng/ml/hr
Aldosterone	(2.2 ~ 15)	2.7 ng/dl
1, 25(OH)$_2$D	(20 ~ 60)	12 > pmol/*l*
25(OH)D	(25.0 ~ 62.4)	24.5 nmol/*l*
ACE	(8.3 ~ 21.4)	17.2 IU/*l*
Intact PTH	(23 ~ 73)	8 ng/*l*
PTHrP	(1.1 >)	1.1 > pmol/*l*

TBII: TSH binding inhibitory immunoglobulin, TGHA: thyroglobulin hemagglutination test, MCHA: microsome hemagglutination test, PRL: prolactin, 17OHCS: urinary 17-hydroxy corticosteroid, 17KS: urinary 17-ketosteroid, LH: luteinizing hormone, FSH: follicle stimulating hormone, 1, 25(OH)$_2$D: 1, 25 dehydroxy vitamine D, 25(OH)D: 25 hydroxy vitamine D, ACE: angiotensin II converting enzyme, PTH: parathyroid hormone, PTHrP: PTH-related proteins.

Table 3 Pituitary hormone stimulation tests

Rapid insulin (0.075 U/kg BW), TRH (500 μg) and GnRH (100 μg) test

		0	30	60	120 min
Blood sugar	(mg/dl)	73	29	48	
GH	(ng/ml)	0.7	0.8	0.5	0.8
ACTH	(pg/ml)	5.1	3.0 >	3.0 >	3.0 >
Cortisol	(μg/dl)	1.0	1.2	1.1	4.2
TSH	(μU/ml)	0.1 >	0.1	0.1 >	0.1 >
Prolactin	(ng/ml)	40.0	43.5	38.9	40.9
LH	(mIU/ml)	0.5 >	0.5 >	0.5 >	0.5 >
FSH	(mIU/ml)	0.9	1.0	1.1	1.0

GRH (100 μg) and CRH (100 μg) test

		0	30	60	90 min
GH	(ng/ml)	0.5	17.8	20.0	9.3
ACTH	(pg/ml)	5.7	43.9	28.7	38.5
Cortisol	(μg/dl)	1.1	7.6	8.7	9.7

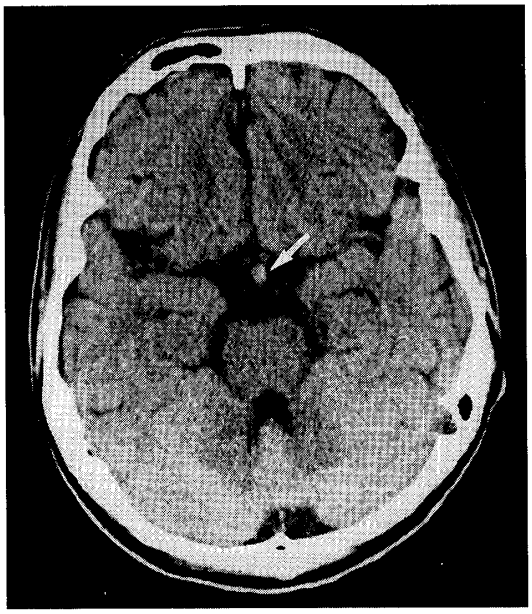

Fig. 1 CT scan of the head
Enlargement of the pituitary stalk with homogeneous enhancement was observed.

hormone. His basal levels of triiodothyronine (T_3) and thyroxine (T_4) were within the normal ranges with a slightly elevated level of serum thyroglobulin on addmision. In addition, the basal level of thyroid-stimulating hormone (TSH) was depressed and showed no response to TSH-releasing hormone. However, serum levels of both hormones gradually decreased below the lower limits of the normal ranges in spite of replacement therapy with 50 μg L-thyroxine. Despite severe dehydration with hypernatremia, his urinary output on admission was 955 ml/day, with an inappropriately low urinary osmolality and low plasma level of antidiuretic hormone (ADH), which was diagnosed as diabetes insipidus.

A CT scan of the head indicated enlargement of the pituitary stalk (Fig. 1). Magnetic resonance

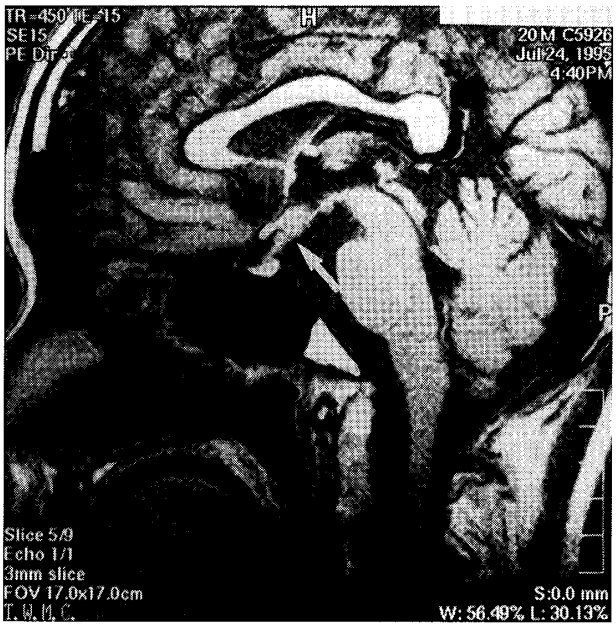

Fig. 2 MRI of the head
The infundibulum was bulked with thickening, which was isotense with white matter on T1-weighted image.

imaging (MRI) of the head showed that the infundibulum was bulked with thickening throughout, which was isotense with white matter on T1-weighted (Fig. 2) and T2-weighted images and had homogeneous enhancement. The enhanced MRI also revealed another lesion of the pineal body. Cerebrospinal fluid analysis revealed no abnormalities.

According to the above findings, he was diagnosed with a hypothalamic tumor (most likely germ-cell tumor) that caused hypothalamic hypopituitarism and diabetes incipidus. His urine volume increased once in late March, 1995 and was then normalized by adrenal insufficiency. Because of disturbance of thirst, he was severely dehydrated accompanied by acute renal failure.

Initial treatment began with administration of 3 liters of fluid to hydrate and correct elevated levels of electorolytes. The serum sodium and chloride levels then normalized. Since hypercalcemia persisted in spite of 3～4 liters/day of intravenous drip and was not suppressed by treatment with 80 U/day of elcatonin for 5 days, a single intravenous injection of 30 mg of pamidronate disodium was given on July 14th. By July 28th, serum calcium and creatinine levels normalized afterwhich hypercalcemia did not recur. He has been administrated 20 mg of hydrocortisone, 75 μg of L-thyroxine, 25 mg of methyltestosterone and 6.25 μg of 1-desamino D-arginine vasopressin (dDAVP). Radiation therapy was used to treat the hypothalamic lesions, which resulted in disappearance of the lesions and remission of his symptoms. He has gained weight to 61 kg and is behaving entirely normally under the replacement therapy.

Discussion

Hypothalamic tumors are characterized by visual disturbance, diabetes insipidus, and hypopituitalism, which can be associated with anorexia, emesis, change of mood or personality and psychiatric symptoms[2)3)]. Experimental data suggests that the lesions of the ventromedial nucleus can cause hyperphagia resulting in obesity, and that a lesion in the lateral hypothalamic nucleus can result in a lack of desire to eat and emaciation [4)～6)]. In humans, the anterior portions of the hypothalamus are associated with cachexia and cachexia is replaced by obesity when a tumor extends into other portions of the hypothalamus [7)8)]. Weight loss is a much less frequent symptom of hypothalamic dysfunction than obesity.

There has been some reports[9)～18)] of adolescents and young adults with brain tumors whose initial symptoms of the psychological disturbances as well as anorexia and emaciation has resulted in a misdiagnosis of anorexia nervosa. Chipkevitch carefully reviewed 21 cases in the literature and concluded that only a few cases fulfilled the criteria of anorexia nervosa defined by the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, 3rd edition, revised (DSM III-R)[19)]. Such misdiagnoses most

likely occurred because anorexia and psychic disturbances preceded the neurological signs or the correct diagnosis by a mean of 2.9 years [20].

Our patient fulfilled the clinical criteria of anorexia nervosa including onset age, loss of at least 20% of ideal body weight for over 3 months, abnormal eating behavior and denial of being ill. However, he had never expressed disturbed perception of body image, and had been much less active and had no history of a sense of well-being, euphoria and, shortening of sleeping time which usually occurs as starvation progresses in patients with anorexia nervosa. To our regret, laboratory test was performed once in the general hospital where he had visited at the first time. Since he did not voluntarily disclose his polyuria, the doctor in charge mistakenly considered that his hypernatremia had been resulted from dehydration due to decrease in water intake. In addition to the psychological and physical disorders, laboratory data often reveal various endocrinological disorders in anorexia nervosa. Anorexia nervosa patients often have elevated plasma levels of GH accompanied by an exaggerated response to GRH[21]. They also show elevated levels of plasma ACTH and cortisol with loss of normal diurnal rhythm, increased excretion of urinary free cortisol, inability of dexamethasone to suppress plasma ACTH and cortisol levels at a low dose, and absent or impaired responses of plasma ACTH and cortisol to CRH[22]. These are the most significant ways in which anorexia nervosa differs from hypopituitarism. Our patient had not been endocrinologically investigated until admission into our hospital.

This patient was the first reported case of hypercalcemia in secondary hypoadrenalism due to hypothalamic tumor, as previously reported and discussed[23]. Four previous cases of hypercalcemia developing in patients with secondary hypoadrenalism[24)~27)] have been reported. All were patients with isolated ACTH deficiency due to lymphocytic hypophysitis in the post-partum period, accompanied by destructive thyroiditis. This suggests that the development of hypercalcemia in secondary hypoadrenalism requires sufficient thyroid hormone levels. In this context, the normal levels of thyroid hormones on admission in this case most likely contributed to the hypercalcemia in adrenal deficiency[23].

Hypothalamic tumors, which comprise 70% of germ cell tumors[28], are seen in the second and third decades of life. Similarly, anorexia nervosa usually occurs in the same age range. The number of male patients with anorexia nervosa has increased in Japan. In our department, the incidence was 1.3% in 320 outpatients with anorexia nervosa for 10 years. Thus, careful and comprehensive examination is required to distinguish between anorexia nervosa and other organic disorders, especially in boys or young men.

Acknowledgments

We thank Ms. Mihoko Fujii for her technical assistance.

References

1) **Fairburn CG**: Eating disorders. *In* Companion to Psychiatric Studies, 5th ed (Kendell RE, Zealley AK eds) p527, Churchill Livingstone, Edinburgh (1993)
2) **Plum F, Van Uitert R**: Nonendocrine diseases and disorders of the hypothalamus. *In* The Hypothalamus (Reichlin S ed) pp415–473, Raven Press, New York (1978)
3) **Sung DI**: Suprasellar tumors in children: a review of clinical manifestations and managements. Cancer **50**: 1420–1425, 1982
4) **Anand BK, Brobeck JR**: Hypothalamic control of food intake in rats and cats. Yale J Biol Med **24**: 123–140, 1951
5) **Teitelbaum P, Epstein AN**: The lateral hypothalamic syndrome: recovery of feeding and drinking after lateral hypothalamic lesions. Psychol Rev **69**: 74–90, 1962
6) **Baille P, Morrison SD**: The nature of the suppression of food intake by lateral hypothalamic lesions in rats. J Physiol **165**: 227–245, 1963

7) **White LE, Hain RF**: Anorexia in association with a destructive lesion of the hypothalamus. Arch Pathol **68**: 275–287, 1959
8) **Carmel PW**: Surgical syndromes of the hypothalamus. Clin Neurosurg **27**: 133–159, 1980
9) **Lewin K, Mattingly D, Millis RR**: Anorexia nervosa associated with hypothalamic tumour. Br Med J **2**: 629–630, 1977
10) **Seaver RL, Binder HJ**: Anorexia nervosa and other anorectic states in man: general clinical considerations. Adv Psychosom Med **7**: 257–276, 1972
11) **Daly JJ, Nabarro JDN, Powell T**: A case of anorexia. Br Med J **2**: 156–161, 1973
12) **Heron GB, Johnston DA**: Hypothalamic tumor presenting as anorexia nervosa. Am J Psychiatry **133**: 580–582, 1976
13) **Swann I**: Anorexia nervosa—a difficult diagnosis in boys. Practioner **218**: 424–427, 1977
14) **White JH, Kelly P, Dorman K**: Clinical picture of atypical anorexia nervosa associated with hypothalamic tumor. Am J Psychiatry **134**: 323–325, 1977
15) **Goldney RD**: Craniopharyngioma stimulating anorexia nervosa. J Nerv Ment Dis **166**: 135–138, 1978
16) **Weller RA, Weller EB**: Anorexia nervosa in a patient with an infiltrating tumor of the hypothalamus. Am J psychiatry **139**: 824–825, 1982
17) **McClean P, Redmond AO**: Hypothalamic tumour presenting as anorexia nervosa. Ulster Med J **57**: 224–227, 1988
18) **Climo LH**: Anorexia nervosa associated with hypothalamic tumor: the search for clinicopathological correlations. Psychiatr J Univ Ottawa **7**: 20–25, 1982
19) **American Psychiatric Association**: Diagnostic and Statistical Manual of Mental Disorders. 3rd ed, revised. American Psychiatric Association, Washington DC (1987)
20) **Chipkevitch E**: Brain tumors and anorexia nervosa. Brain Dev **16**: 175–179, 1994
21) **Masuda A, Shibasaki T, Hotta M et al**: Study on the mechanism of abnormal growth hormone (GH) secretion in anorexia nervosa: no evidence of involvement of a low somatomedin-C level in the abnormal GH secretion. J Endocrinol Invest **11**: 297–302, 1988
22) **Hotta M, Shibasaki T, Masuda A et al**: The response of plasma adrenocortin and cortisol to corticotropin-releasing hormone (CRH) and cerebrospinal fluid immunoreactive CRH in anorexia nervosa patients. J Clin Endocrinol Metab **62**: 319–324, 1986
23) **Hotta M, Sato K, Shibasaki T et al**: Hypercalcemia in an euthyroid patient with secondary hypoadrenalism and diabetes insipidus due to hypothalamic tumor. Endocrine J **45**: 773–778, 1998
24) **Richtsmeier AJ, Henry RA, Bloodworth JMB et al**: Lymphoid hypophysitis with selective adrenocorticotropic hormone deficiency. Arch Int Med **140**: 1243–1245, 1980
25) **Jensen MD, Hankwerger BS, Scheithauer BW et al**: Lymphocytic hypophysitis with isolated corticotropin deficiency. Ann Int Med **105**: 200–203, 1986
26) **Vasikaran SD, Tallis GA, Braund WJ**: Secondary hypoadrenalism presenting with hypercalcaemia. Clin Endocrinol **41** : 261–264, 1994
27) **Patel MC, Clayton RN**: Secondary hypoadrenalism with hypercalcemia. Clin Endocrinol **41**: 839–840, 1994
28) **Suematsu H**: Brain tumors and anorexia nervosa syndrome commentary to Chipkevitch's paper (pp 175–179). Brain Develop **16**: 182, 1994

神経性食欲不振症に誤診された視床下部腫瘍の男性例

[1]東京女子医科大学　内分泌疾患総合医療センター　内科
[2]日本医科大学　生理学
[3]東京女子医科大学　脳神経センター　外科

堀田（ホッタ）　眞理（マリ）[1]・芝崎（シバサキ）　保（タモツ）[2]・佐藤（サトウ）　幹二（カンジ）[1]・久保（クボ）　長生（オサミ）[3]・出村（デムラ）　博（ヒロシ）[1]・高野加寿恵（タカノカズエ）[1]

20歳の男性で，食欲不振，体重減少，自己嘔吐などの行動異常，病識のなさ，精神症状および人格の変化から最初の医療機関で神経性食欲不振症と誤って診断された．その後，複数の医療機関を受診したが，本人の精神および行動異常から十分な内科的検査がされず，全身状態の悪化と意識障害で当科に緊急入院した．胚細胞腫と考えられる視床下部腫瘍で，それによる下垂体機能低下症と尿崩症と診断された．患者は多飲多尿を申告せず，副腎皮質ホルモンの低下によって経過中に多尿は改善していたことが判明し，視床下部腫瘍による口渇感の喪失が明らかになった．

Chipkevitchによる今まで報告された神経性食欲不振症に酷似した視床下部腫瘍21例の再検討では，やせをきたす身体疾患がないという項目以外の診断基準を完全に満たすものは2例であったが，行動および人格異常は，視床下部腫瘍による神経症状の出現に平均2.9年先行して出現しており，注意深い経過観察が必要なことを報告している．

神経性食欲不振症患者数は増加しており，女子高校生や大学生の1%と推測されている．男性例も稀ではなくなり，全患者の1～5%で，当科でも1.3%である．しかし，本症の診断には器質的疾患の鑑別は非常に重要である．下垂体機能低下症と異なり，神経性食欲不振症では，血漿成長ホルモン，ACTH，コルチゾールが高値となることが多く，鑑別に有用である．