INTERNAL MEDICINE

□ CASE REPORT □

Near-fatal Anorexia Nervosa in a Middle-aged Woman

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Abstract

Anorexia nervosa (AN) is a serious psychiatric disorder which typically occurs in young women; however, more and more cases in middle-aged women are being reported. The management of this complex disease requires a team approach, and full recovery occurs only in 50% of patients. Endocrine and metabolic complications are commonly observed, the latter of which may even be life-threatening, and require prompt and proper management. Infections, albeit reported, are not usually a major clinical problem in these patients. We herein report the case of a severely malnourished middle-aged woman with long-standing AN who was hospitalized with marked hypokalaemia (1.5 mEq/L) and rhabdomyolysis; during hospitalization she developed septic shock and acute respiratory distress syndrome, which required urgent admission to the intensive care unit. She underwent sedation and tracheal intubation for mechanical ventilation and was managed with combined therapies, which eventually led to a successful outcome. Life-threatening medical complications can occur not only in young women but in middle-aged women with AN as well and require a combined multidisciplinary approach.

Key words: anorexia nervosa, hypokalaemia, ARDS, intensive care unit

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Introduction

Anorexia nervosa (AN) is a psychiatric disorder which can result in life-threatening medical complications (1-3) and multifaceted endocrine abnormalities (4, 5). Its prevalence is 0.2-0.9% among young women, with a peak age ranging between 14 and 25 years (1). However, a significant number of middle-aged women have this disorder as well, including those who never recovered from adolescent AN and, to a lesser extent, those who develop this disorder for the first time in middle age (6).

The treatment of AN is difficult and requires a multidisciplinary team that includes a psychiatrist or psychologist, an internist/endocrinologist, and a nutritionist. Despite multidisciplinary treatment efforts, the overall prognosis is quite poor, with only 40% to 50% of AN patients progressing to complete recovery (1, 5). Despite being severely malnourished, AN patients have fairly well-preserved immune function and are relatively free from infectious diseases (7-9). However, cases of infections, some severe and mostly in the lung, have been reported (10-12).

We herein report the case of a severely malnourished middle-aged woman suffering from long-standing AN who was hospitalized with very severe hypokalaemia and subsequently required admission to intensive care unit (ICU) owing to septic shock and acute respiratory distress syndrome (ARDS).

Case Report

A 46-year-old woman was taken to the emergency department of our hospital by the territorial emergency team after she had been found on the floor in her house by a friend; the patient reported that she had fallen because her legs "had given way" and that she was unable to stand up. A physical examination showed that the patient was fully conscious but cachectic and dehydrated, and she had low blood pressure (75/50 mmHg) with bruises on the chin and right hip. Electrocardiography (ECG) revealed sinus bradycardia (60 bpm) with a prolonged corrected QT interval (0.60 sec). Hemogasanalysis showed metabolic hypokalaemic hypochloraemic alkalosis (pH: 7.7, n.v. 7.35-7.45, PO_2: 100 mmHg, n.v. 80-100, pCO_2: 38 mmHg, n.v. 35-45, K: 1.7

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mEq/L, n.v. 3.5-5, Cl: 73 mEq/L, v.n. 98-106, HCO_3-: 45.7 mEq/L, n.v. 24-28). Emergency laboratory tests confirmed extremely severe hypokalaemia (1.5 mEq/L), hyponatraemia, acute renal failure, rhabdomyolysis, increased C- reactive protein (CRP), and normocytic anaemia (Table). The findings from an X-ray examination of the chest (Fig. 1a), pelvis, and facial bones proved unremarkable. The psychiatrist advised admission to a medical facility. A potassium infusion (90 mEq) in saline was started, and the patient was hospitalized in the Internal Medicine Department. Anamnesis ascertained a long history of AN, diagnosed about 20 years earlier, and several previous hospital admissions for malnutrition, alcoholism, and suicide attempts. She had been supervised by a psychiatric centre until two years prior and regularly took benzodiazepines as well as laxatives for constipation. In addition, she reported self-induced vomiting, albeit infrequently. Overall, the patient's habits characterized AN purging subtype.

Her last menses dated back 13 years. The physical parameters revealed severe malnourishment [height: 155 cm, body weight: 25.7 kg, body mass index (BMI): 10.7 Kg/m^2], dehydration and low blood pressure (80/60 mmHg). The woman, who was poorly cooperative, reported not having eaten or drunk in the previous few days.

Further laboratory testing was carried out for biochemical and hormonal evaluations (Table). Her gonadotropin levels, which were associated with undetectable 17β-estradiol levels, were unexpectedly elevated given the patient's extreme malnutrition and were compatible with a menopausal state; in addition, reduced IGF-I levels, sick euthyroid syndrome and secondary hyperparathyroidism with undetectable vitamin D levels were ascertained. Her cortisol levels were surprisingly normal for a severely malnourished subject, whereas the nutritional parameters were obviously reduced.

Her resting energy expenditure (REE) was calculated using the Harris-Benedict formula as 965 kcal/day. Saline (250 mL/day) and partial parenteral nutrition (PPN) (volume: 1,500 mL, 1,000 kcal, with glucose, amino acids, lipids, and electrolytes supplemented with vitamins) was started at a low infusion rate, with the total caloric amount administered in 72 hours for the first 3 days, in 48 hours from days 4 to 6 and every 24 hours thereafter. In addition, a balanced diet was started and was slowly increased up to 1,500 kcal/day with good tolerance. Prophylactic low-molecular weight heparin, proton-pump inhibitors, intravenous ceftriaxone, and oral colecalciferol (100,000 IU as initial load and 10,000 IU/week thereafter) were also started. Large amounts of infused potassium (up to 120 mEq/day) were required to normalize serum levels in 5 days; the corrected QT interval subsequently normalized on ECG. Her haemoglobin (Hb) levels dropped to 7.3 g/dL without apparent blood loss, probably as a result of haemodilution, and 1 unit of packed red blood cells was transfused which increased the Hb levels (8.7 g/dL). A central venous catheter was positioned in order to properly continue the combined therapies, and a slow but constant improvement in the patient's clinical condition was observed, although mild oedema occurred in her legs. Owing to this appropriate management, no refeeding syndrome occurred, and the patient gained 2 kg in weight in 2 weeks. However, over several days, the patient developed acute urinary retention with marked bladder overdistension (1,700 mL), for which she was catheterised, and an acute confusional state requiring urgent computed tomography (CT) of the brain, which showed cerebral atrophy and cerebrovascular disease (Fig. 2). However, these symptoms vanished spontaneously.

Three weeks after admission, the patient became febrile, and septic shock with acute respiratory failure and oliguria rapidly ensued; she appeared to have multiorgan failure syndrome. Hemogasanalysis with ambient air revealed hypoxaemia (PO_2: 51 mmHg) with normocapnia (PCO_2: 29.4 mmHg), PO_2/FiO_2: 242, SO_2: 88%, reduced HCO_3-: 20.4 mEq/L, and pH: 7.45. An urgent chest X-ray examination showed bilateral interstitial pneumonia (Fig. 1b), and urgent laboratory testing revealed markedly increased CRP levels (30.9 mg/dL) and procalcitonin levels (17.1 ng/mL), increased creatinine levels (2.4 mg/dL), and reduced Hb levels (7.6 g/dL) (Table). Blood and urine cultures were negative for HIV antibodies, *Mycoplasma pneumoniae* antibodies, and urinary antigen for *Legionella pneumophila*. One unit of packed red blood cells was transfused, and colloids, crystalloids, broad-spectrum antibiotic therapy (intravenous piperacillin/tazobactam), steroids, and oxygen were started. The patient's respiratory condition, as assessed by hemogasanalysis (PO_2: 46.3 mmHg, PCO_2: 38.3 mmHg, PO_2/FiO_2: 193, SO_2: 83%, HCO_3-: 22.1 mEq/L, pH: 7.37), worsened further. ARDS was diagnosed, and continuous positive airway pressure [CPAP, FiO_2: 60%, positive end-expiratory pressure (PEEP): 5 cm H_2O] was started but proved unsuccessful.

After an anaesthesiological evaluation of the patient, whose clinical condition was by now critical, she was urgently transferred to the ICU, where she underwent sedation and endotracheal intubation for mechanical ventilation. In addition to the therapies she was already receiving, she was started on a dopamine and norepinephrine infusion due to persistent hypotension. She also received intravenous albumin, calcium, sodium bicarbonate, and diuretics. The hemogasanalysis values deteriorated (CPAP, FiO_2 60%, PEEP: 7 cm H_2O) and revealed respiratory acidosis (pH: 7.187, PO_2: 46.2 mmHg, PCO_2: 75.6 mmHg, HCO_3-: 28.6 mEq/L, PO_2/FiO_2: 71, markedly reduced). A further chest X-ray examination revealed a worse picture than that seen 2 days earlier, showing bilateral diffuse interstitial-alveolar consolidations with no evidence of ventilation (Fig. 1c). PEEP was progressively increased to 12 cm H_2O and, in order to improve oxygenation and mitigate the harmful effects of mechanical ventilation, cycles of ventilation in the prone position were started. Blood cultures proved positive for *Enterococcus faecalis* and *Candida albicans*, and antibiotic therapy was implemented with parenteral linezolid and fluconazole on the advice of an infectivologist. Echocardiography was normal.

Table. **Main Laboratory Tests thoroughout Hospitalization in the Middle-aged Woman with Anorexia Nervosa Studied.**

	IM Admission	IM Day 1	IM Day 2	IM Day 3	IM Day 5	IM Day 6 after 1 HT	IM Day 10	IM Day 14	IM Day 20	IM Day 21 after 1 HT	IM Day 22	ICU Day 22	ICU Day 23	ICU Day 24	ICU Day 25	ICU Day 26	ICU Day 27
Glucose (n.v. 70-115 mg/dL)	91	65	71	144	73		78	64	72	56	89	118	194	178	121	119	100
Creatinine (n.v. 0.6-1 mg/dL)	1.4	1.2	1.3	1.9	1.8		0.7	0.8	2.4	2.3	1.6	1.5	1.2	1.7	1.5	1.3	1.1
Na (n.v. 135-145 mEq/L)	125	134	138	133	138		139	137	137	138	146	147	152	145	141	137	138
K (n.v. 3.5-5 mEq/L)	1.5	2.4	2.2	2.6	4.2		4.6	4.7	4	3.2	2.9	2.9	3.6	2.7	3.9	3.9	3.8
AST (n.v. 4-37 IU/L)	107	-		67	42							71	53	166	77	68	103
ALT (n.v. 4-41 IU/L)	32	-		27	29							32	20	72	52	47	52
CPK (n.v. 39-308 IU/L)	1,159		392	142							48	21	11	10	11	14	12
Calcium (n.v. 8.2-10.2 mg/dL)		7	7.6	8.4	9.1			8.1			7.3	7.8	8.8	9.3	9.2	9.9	9.4
Phosphorus (n.v. 2.7-4.5 mg/dL)		2.3	2.4		2			5									
Magnesium (1.6-2.6 mg/dL)		1.4	1.5		2.1			2.9									
White blood cells (n.v. 4,000-11,000/mL)	12,280		6,520	4,540	5,060	6,220	7,850	7,440	4,690	4,350	11,270	17,050	22,460	24,570	22,710	19,870	14,650
Neutrophils (n.v. 2,000-8,000/mL)	10,450		4,790	2,950	2,700	3,710	5,610	4,640	3,670	3,500	9,230	14,570	18,470	22,160	19,410	17,570	13,050
Haemoglobin (n.v. 14-17 g/dL)	8.8		9.5	9.1	7.3	8.7	10.4	9.6	7.6	9	11.2	13	10.9	10.2	10.3	10.3	8.7
Hematocrit (n.v. 42-50%)	22.8		25.9	23.9	20.3	24.8	31.5	28.4	22.6	26	32.4	36.7	32.5	30.5	30.1	29.8	25.1
MCV (n.v. 80-96 fL)	88.4		90.6	96.5	91	90.8	89.2	91.5	88.6	90.2	84.4	84	88.6	86.2	85	85.9	85.7
Platelets (n.v. 150,000-400,000/mL)	123,000		137,000	134,000	88,000	91,000	92,000	301,000	149,000	107,000	131,000	138,000	130,000	86,000	147,000	187,000	158,000
Iron (30-200 μg/dL)		90															
Ferritin (n.v. 30-400 ng/L)		1,006													1,315		
Prothrombin time (n.v. 70-120%)	62	79									42	42	90		80	91	88
Albumin (n.v. 3.5-5.2 g/dL)		2.3							2.5			1.7	1.2	2.1	2		2.2
Transferrin (n.v. 200-400 mg/dL)		84													66		
Haptoglobin (30-200 mg/dL)		104															
IGF-I (n.v. for age 90-360 ng/mL)		52.1															
FT4 (n.v. 0.93-1.7 ng/dL)		0.68															
FT3 (n.v. 1.8-4.6 pg/mL)		0.99															
TSH (n.v. 0.3-4.2 μU/mL)		2.6															
LH (7.7-78.5 mIU/mL for menopause)		77.2															
FSH (25.8-134.8 mIU/mL for menopause)		168.9															
17-beta-estradiol (<20 pg/mL for menopause)		<5															
PRL (n.v. 3-20 ng/mL)		15.8															
Cortisol (n.v. 6.2 -19.4 μg/dL, 7-10 a.m.)		14.5															
25-OHD (n.v. > 30 ng/mL)		<4															
PTH (n.v. 15-65 pg/mL)		174.4															
CRP (n.v. 0-0.5 mg/dL)	3.1	2.2							30.9	33.5		28	26.6	9.3	11.1		
PCT (<0.5 ng/mL)									17.1	22.8		8.5		4.6			
pro-BNP (< 500 pg/mL)														70,000	70,000		
Ethanol (g/L)		negative															
HIV test									negative								

(continue)

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Table. continued

	ICU Day 28	ICU Day 29	ICU Day 30	ICU Day 31 after 1 HT	ICU Day 32	ICU Day 34	ICU Day 36	ICU Day 37 after 2 HT	ICU Day 38	ICU Day 39	ICU Day 41	IM Day 42	IM Day 43 after 1 HT	IM Day 47	IM Day 52	IM Day 60
Glucose (n.v. 70-115 mg/dL)	108	94	116	127	96	98	103	107	97		92			87	133	83
Creatinine (n.v. 0.6-1 mg/dL)	0.9	0.9	0.7	0.6	0.5	0.5	0.5	0.5	0.4		0.5			0.5	0.5	0.5
Na (n.v. 135-145 mEq/L)	136	135	137	136	135	133	137	138	134		133			138	136	135
K (n.v. 3.5-5 mEq/L)	4.2	4.5	4.5	4.6	4.1	5	4.4	4	4.2		3.6			4	3.7	4.4
AST (n.v. 4-37 IU/L)	125	87	58	37	21	18	13	12	17		15					
ALT (n.v. 4-41 IU/L)	66	57	51	43	19	22	16	15	14		10					
CPK (n.v. 39-308 IU/L)	14	17	10	9	8	8	12	8	17		6					
Calcium (n.v. 8.2-10.2 mg/dL)	9	9	8.8	8.8	7.9	9.1	8.2	8.2	8.4		8.9				9.2	
Phosphorus (n.v. 2.7-4.5 mg/dL)															3.7	
Magnesium (1.6-2.6 mg/dL)															1.8	
White blood cells (n.v. 4,000-11,000/mL)	12,590	15,110	11,040	10,790	12,920	11,630	10,050	11,570	12,880	18,700	12,900	11,340	13,760	9,570	10,550	7,610
Neutrophils (n.v. 2,000-8,000/mL)	10,800	13,780	9,190	8,590	9,910	8,730	7,760	8,770	9,480	15,730	9,400	7,100	9,050	4,610	6,800	3,590
Haemoglobin (n.v. 14-17 g/dL)	8.2	7.8	7	8.1	7.7	7	6.6	8.8	9	9.8	8.2	7.6	8.3	9.7	10	9.7
Hematocrit (n.v. 42-50%)	24.1	23.7	20.9	24	23.2	21	20	26.2	27	29.4	24.5	23.4	25.6	29.1	29	29.7
MCV (n.v. 80-96 fL)	85.2	85.3	86	86	86.6	87.5	84.4	84.5	85.2	85	86.9	88	88	87.1	87.5	87.6
Platelets (n.v. 150,000-400,000/mL)	166,000	164,000	137,000	132,000	120,000	123,000	249,000	352,000	402,000	395,000	358,000	309,000	314,000	290,000	272,000	372,000
Iron (30-200 µg/dL)									9,480							
Ferritin (n.v. 30-400 ng/L)																
Prothrombin time (n.v. 70-120%)	105	107	101	93	80	99	85									
Albumin (n.v. 3.5-5.2 g/dL)	2		2.1			2.3										
Transferrin (n.v. 200-400 mg/dL)												122				
Haptoglobin (30-200 mg/dL)																
IGF-I (n.v. for age 90-360 ng/mL)															150.5	
FT4 (n.v. 0.93-1.7 ng/dL)															0.98	
FT3 (n.v. 1.8-4.6 pg/mL)															2.6	
TSH (n.v. 0.3-4.2 µU/mL)															1.9	
LH (7.7-78.5 mIU/mL for menopause)															38.5	
FSH (25.8-134.8 mIU/mL for menopause)															82	
17-beta-estradiol (<20 pg/mL for menopause)															<5	
PRL (n.v. 3-20 ng/mL)																
Cortisol (n.v. 6.2 -19.4 µg/dL, 7-10 a.m.)															13.1	
25-OHD (n.v. > 30 ng/mL)																
PTH (n.v. 15-65 pg/mL)																
CRP (n.v. 0-0.5 mg/dL)			13.4		9.1	8.4			4.9		13			5.6	4.5	1.4
PCT (<0.5 ng/mL)			1.87		0.88				0.4					0.2		
pro-BNP (< 500 pg/mL)		9,838	6,788													
Ethanol (g/L)																
HIV test																

CRP: C-reactive protein
HT: hemotransfusion
IGF-I: insulin-like growth factor-I
PCT: procalcitonin
pro-BNP: pro-brain natriuretic peptide
IM: internal medicine
ICU: intensive care unit

Over several days, 2 units of packed red blood cells were transfused in response to relapsing anemization (Hb: 6.6 g/dL). The patient's clinical condition, laboratory data (reduction in CRP and procalcitonin levels, normalization of renal

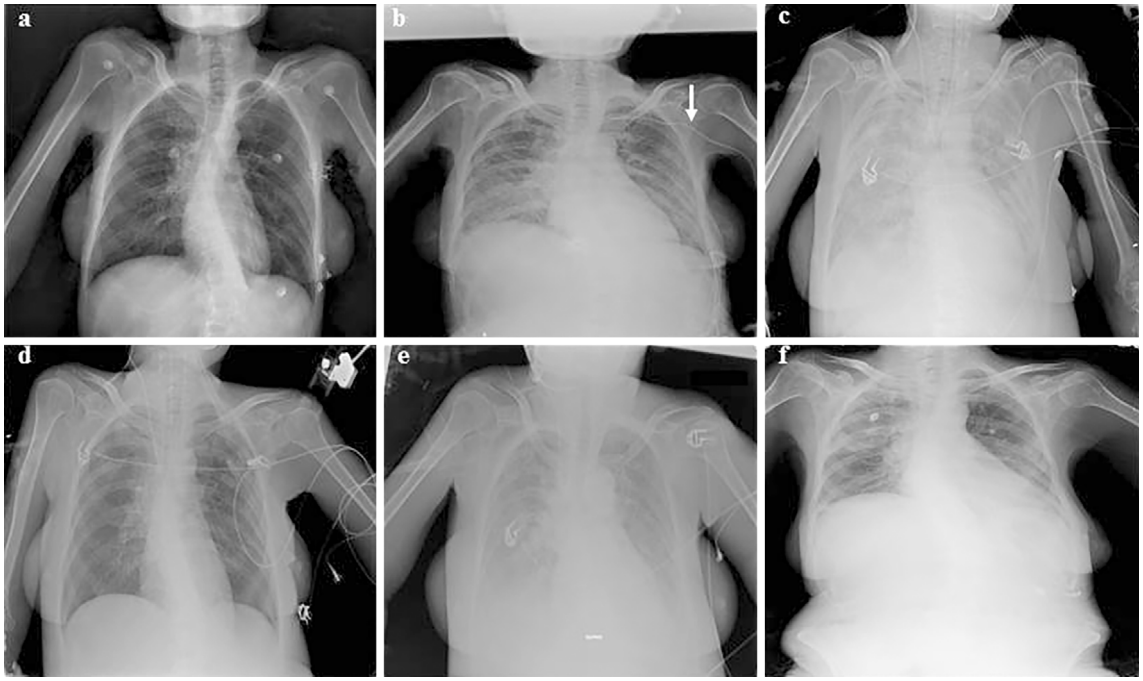

Figure 1. **The patient's chest X-ray findings throughout hospitalization. On admission, no lung pathologies were observed (a). During hospitalization, the patient developed septic shock and ARDS, and bilateral interstitial pneumonia (mainly in the right middle-basal and left parahilar regions) was found. CVC is visible along the projection of the left subclavian vein (arrow) (b). The lung condition quickly worsened after admission to the ICU, with findings of bilateral diffuse interstitial-alveolar consolidations and no evidence of ventilation (c). Following the initiation of combination therapies, the lung picture partially improved, and bilateral ventilation resumed (d). After extubation, accentuated hilar and perihilar vascular images and reduced transparency due to interstitial-alveolar consolidations, mainly in the right lung, were observed (e). Over the following days, the lung picture markedly improved, with persistence of only minor alveolar consolidations at the middle right site and stasis of the small pulmonary circulation (f). ARDS: acute respiratory distress syndrome, CVC: central venous catheter, ICU: intensive care unit**

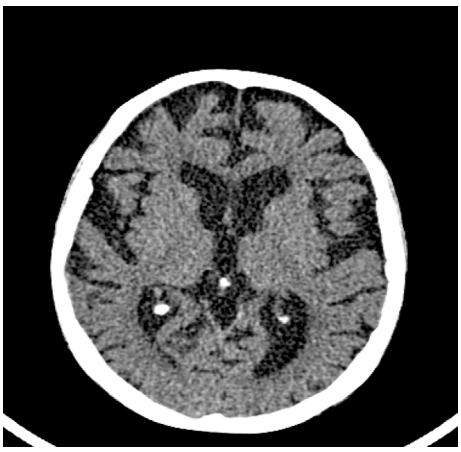

Figure 2. **The patient's basal CT of the brain showing cerebral atrophy and cerebrovascular disease. CT: computed tomography**

function, increase and stabilization of Hb levels, negativization of blood cultures) (Table), and chest X-ray findings (Fig. 1d) slowly improved. However, several attempts to wean her off sedation proved ineffective, owing to psychomotor agitation and subsequent desaturation; on one occasion, generalized seizure occurred after the withdrawal of sedation, and intravenous levetiracetam and intramuscular phenobarbital were started. Electroencephalography (significant high-grade diffuse alterations of electrical activity) and CT scan (known cerebral atrophy) were performed.

Two weeks after admission to the ICU, sedation was gradually tapered off. The patient was eventually extubated and resumed spontaneous breathing, but oxygen therapy (6 L/min by Ventimask) was necessary in order to obtain satisfactory oxygen saturation. Although reduced, interstitial-alveolar consolidations persisted on chest X-ray (Fig. 1e). A nasogastric tube was placed, and enteral nutrition was started. The patient was transferred to the critical-care medicine ward, where, after a few days, the nasogastric tube was removed and medical therapies (parenteral nutrition, antibiotics, antiepileptics, proton-pump inhibitors, benzodiazepines, oxygen therapy) were continued. Careful oral realimentation with a balanced diet was started. The chest X-ray findings markedly improved, showing only small right alveolar consolidations (Fig. 1f). Oxygen therapy by nasal cannula was withdrawn, and the oxygen saturation in the air

remained normal. One more unit of packed red blood cells was infused due to anemization (Hb: 7.6 g/dL); afterwards, her Hb levels remained stable (Table). One week later, the patient was transferred back to our internal medicine ward.

Her clinical condition was significantly improved, respiratory function was satisfactory, body weight had increased (to 32.6 kg; +25% vs. baseline, BMI: 13.6 kg/m^2), and nutrition and endocrine parameters were consequently enhanced (Table). After a few days, during which her therapies were continued, the patient, still severely malnourished but in a stable cardio-respiratory condition and with satisfactory metabolic parameters (Table), was discharged and transferred to a specialized centre for rehabilitation. In total, the patient was hospitalized for two months.

Discussion

AN is a relatively common disorder among young women. While the age- and sex-adjusted incidence rates calculated from the general practice databases (4.7-7.7 per 100,000 person-years) have remained remarkably stable over the last 20 years, there has been an increase in the incidence in the high-risk-group of 15-19-year-old girls (1). However, AN among middle-aged and older women is relatively rare (6). Its prevalence in women 40-60 years of age ranges from 0.4% in Europe to 1.6% in the USA (6). AN in middle-aged and older women is therefore deemed to be mainly a chronic presentation of a disorder with earlier onset (6).

AN has the highest rate of mortality among mental disorders, with an overall standardized mortality ratio ranging from 5 to 12 (1, 12, 13), a substantial portion of which (approximately 20%) is attributable to the suicide rate (13-56 times that expected for a similar age and sex) (5, 13). Alcoholism, which was present in our patient's history, is an independent risk factor for mortality (5, 13). Life-threatening medical complications (mostly metabolic and cardiac) play a major role in the increased mortality of these patients (2, 13). In our AN patient, the misuse of laxatives and occasional self-induced vomiting caused metabolic hypokalaemic hypochloraemic alkalosis, with dramatically low potassium levels (<2 mEq/L). These metabolic findings indicate Pseudo-Bartter's syndrome, which is characterized by the activation of the renin-angiotensin-aldosterone system secondary to volume depletion triggered by purging/vomiting (14). However, the plasma renin activity and plasma aldosterone concentration were not measured in the present case.

A peculiar feature of AN patients is their gradual adaptation to weights which may even be dramatically low (BMI in the range of 9-12 kg/m^2) together with a fairly adequate availability of macro- and micronutrients; this distinguishes AN from the protein-specific malnutrition observed in famines (15). Whether this capacity is due only to a reduction in lean body mass or, as is more likely, to active mechanisms that reduce energy expenditure (e.g., euthyroid sick syndrome with decreased T3 levels and increased reverse T3 levels, a decreased cardiovascular function and leptin levels) remains unclear (15). Under typical conditions of starvation, the diet is deficient in both proteins and vitamins. AN patients, however, are primarily deficient in carbohydrates and fats but have fairly adequate protein and vitamin intake (6, 8). This relatively normal protein intake might contribute to the absence of increased susceptibility to infections in AN patients, since the blunted immune response to mitogens is more related to protein deficit than to overall reduced calorie intake (7).

In this regard, interesting results have emerged from a recent study conducted in a small group (n=15) of young (age range: 15-24 years) AN women. Although these patients displayed a reduced number (and impaired bioenergetic metabolism) of several immune cell populations (leucocytes, lymphocytes and NK cells), these cells were seen to have higher antioxidant potential and greater resistance to stress than those of age-matched controls, suggesting a preserved immune function; in addition, an increased anti-inflammatory status (i.e., increased serum adiponectin levels) was found in these patients (9).

Old literature data suggest that malnutrition may suppress infections, while refeeding may activate them (7). Indeed, a reduction in iron intake and, more importantly, its sequestration in the liver (as indirectly inferred from our patient's increased ferritin levels on admission) and spleen can reduce bacterial proliferation. This sort of protection may be lost during the refeeding phase, as a result of the increased metabolic requests of electrolytes, micronutrients, and vitamins essential for the preservation of cellular immunity (7). After three weeks of re-alimentation (both parenteral and oral) without biochemical or clinical signs of refeeding syndrome, our patient developed septic shock due to gram-positive cocci and yeasts, as well as interstitial pneumonia (no etiological pathogen was found) causing ARDS and urgent admission to the ICU.

As described in early reports, in AN patients, the lung may be affected by microorganisms that are often non-pathogenic (*Mycobacterium* subtypes) (10) or uncommon (e.g., *Aspergillus* spp.) (11) in normonourished people. Although infrequent, lung infections in AN patients may be severe. In this regard, it has been suggested that malnutrition may i) cause sympathetic suppression and hence blunt the hypoxic ventilatory response; ii) reduce the mass of respiratory muscles (mainly diaphragm), thereby impairing respiratory dynamics; or iii) increase proteinase activity, thus damaging the connective tissue of the lung (10).

ARDS is a severe, life-threatening medical condition characterized by bilateral pulmonary infiltrates and triggered by a variety of systemic or pulmonary injuries, with severe hypoxaemia ensuing. Despite medical progress in the management of ARDS, the mortality remains high, ranging from 27% to 58%, although advances in supportive care have led to improved outcomes in recent years (16, 17).

In our AN patient, severe ARDS (PO_2/FiO_2<100) was triggered by both interstitial pneumonia and sepsis secondary to multipathogens and required urgent admission to the ICU, followed by sedation and intubation for mechanical ventilation. Combined therapies involving the administration of fluids, broad-spectrum antibiotics, antimycotics, inotropics, steroids, and antiepileptics (to treat seizures) eventually led to a successful outcome. Our patient had a long-standing history of AN and was extremely malnourished, showing several endocrine alterations found in this disorder (although also present in other types of malnutrition) such as reduced IGF-I levels and sick euthyroid syndrome (4, 5). All of these parameters improved with weight gain. Surprisingly, given her extreme underweight condition, hypergonadotropic (not hypogonadotropic) hypogonadism was found; this was associated with the patient's undetectable estradiol levels and was compatible with a menopausal state. In addition, her cortisol levels (expected to be elevated in AN) were normal, probably owing to reduced liver production of corticosteroid-binding globulin secondary to severe malnutrition (18).

With regard to refeeding management, on admission, the patient's REE was calculated using the Harris Benedict formula, which is known to be flawed in AN since it overestimates REE by up to 20% in comparison with indirect calorimetry (19). A combination of refeeding through both PPN and gradually increasing the oral balanced diet was started. As previously recommended (albeit currently under debate), the initial amount of calorie intake administered in our AN patient was as low as 10 kcal/kg/day and progressively increased to 90 kcal/kg/day without biochemical or clinical signs of refeeding syndrome (20, 21). Regarding this progressive diet, current understanding holds that AN patients (particularly those with restricting type) tend to require stepwise escalation in their caloric intake to maintain a 1- to 1.5-kg/week weight gain, starting from 20-30 kcal/kg/day and increasing to 60-100 kcal/kg/day to show sustained weight gain (22).

In her time in the ICU, the patient underwent total parenteral nutrition during the intubation phase; after extubation, enteral nutrition by means of a nasogastric tube was used. As soon as the patient's clinical condition had improved, she was returned to the internal medicine ward, where oral re-alimentation was carefully started.

In our middle-aged patient with a long-standing history of AN, combined and careful intensive medical management of severe medical complications, in both the internal medicine department and the ICU, prevented a fatal outcome. On discharge, although her clinical condition had significantly improved, the patient was still seriously underweight and was transferred to a rehabilitation centre to continue her treatment.

In conclusion, AN may have dramatic consequences on the health, even in middle-aged women, owing to the possible occurrence of life-threatening medical complications. Every effort must be made by the medical community to detect the manifestations of AN promptly and to coordinate the work of various specialists in order to implement appropriate combined therapies with long-term follow-up.

The authors state that they have no Conflict of Interest (COI).

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