

Edema can be a handicap in treatment of anorexia nervosa

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Anorexia and bulimia nervosa are common in western civilized countries. They are among the psychiatric disorders in that they are often accompanied by a variety of life-threatening physical abnormalities. These patients need a close follow-up of the pediatrician in collaboration with the psychiatrist since the changes in bodily functions affect the psychiatric therapy. The challenge to the physician is to use the traditional tools of medicine to diagnose and treat these physical abnormalities using careful medical history, a complete physical examination and appropriate laboratory testing. Peripheral edema is seen as a physical finding in anorexia nervosa (AN) and it is not rare. The estimated frequency is up to 20% among adolescent patients. Peripheral edema in this setting can be easily confused as weight gain. There are five possible mechanisms for its occurrence: hypoproteinemia, electrolyte imbalance, hormonal changes, rapid refeedings, and abuse of laxative, diuretics and diet pills. Patients with eating disorders may ingest a large number of drugs in an attempt to control their weight. We present a case of a female adolescent with AN and peripheral edema who terminated her psychiatric treatment during the refeeding phase because of the unbearable anxiety caused by this edema that affected her body image dramatically. With this case study, we point out the importance of assessing peripheral edema and discriminating it from true weight gain.

Key words: anorexia nervosa, peripheral edema, weight gain.

Anorexia nervosa (AN) and bulimia nervosa (BN) may be associated with serious medical complications. The restoration of metabolic and physiological homeostasis is the first step in the treatment of a patient with eating disorder. Fluid retention in AN can be quite dramatic, particularly after withdrawal of laxatives or diuretics. There are five different possible mechanisms for peripheral edema: 1) hypoproteinemia, 2) electrolyte imbalance, 3) hormonal changes, 4) rapid refeeding, and 5) sudden discontinuation of laxatives, diuretics or diet pills. Diuretics are often misused by patients with eating disorders. Despite the fact that the use of diuretics is contraindicated in patients with eating disorders, one study found 10% of bulimic patients to be using diuretics daily¹. Caffeine, usually in the form of beverages such as coffee or diet cola, is also ingested in large quantities because of its appetite suppressant, diuretic, and stimulant effects². Patients with AN and BN may also abuse

thyroid medications in an attempt to increase their basal metabolic rate and to facilitate weight loss. In one study, approximately 7% of patients with eating disorders were found to have at one point abused thyroid medication to further weight loss³. Persistent purging behaviors can result in a hypovolemic state, which stimulates the renin-angiotensin-aldosterone system as the body's homeostatic mechanisms attempt to conserve fluid. Patients who abuse diuretics or laxatives are particularly at risk of developing overstimulation of this hormonal axis⁴. Localized edema can often be confused as weight gain in this clinical setting. In this case presentation, we will review the occurrence of peripheral edema in a female adolescent with AN.

Case Report

OE was a 17-year-old girl who was diagnosed with AN two years prior to presentation. She was consulted with our unit by her psychiatrist when after a year of psychiatric outpatient

treatment she accepted to make small changes in her strict eating schedule. She was reported to be on fluoxetine 20 mg daily for a year but she refused to take it any more as her fears about gaining weight increased. She was highly intellectual and was very keen on the side effects of drugs. She refused to increase the dose of fluoxetine and refused to take any other psychotropic due to her fears about their side effects that would lead to weight gain. She had shown no particular signs of psychopathology prior to diagnosis with AN at the age of 15 years. She was an overweight girl till age 13 and began dieting at that time. She was described by her parents as a perfectionist, skillful and hard working, but it was understood that she was emotionally dependent on her parents. Although she was very successful in her academic life, she had refused to attend school since the last term. She had a family history on the paternal side of mental illness; her aunt was described by our patient's mom as a severe obsessive compulsive disorder. She is still under treatment.

For the last year, she was reported to be eating very small amounts of food at the same place and time every day in a ritualistic manner. Her situation had never become serious enough to require hospitalization. Though she had never permitted anyone to weigh her, she reported her body mass index (BMI) as less than 13. When she presented for the first visit, her BMI was accepted as 13 according to her report, and after psychiatric follow-up, she accepted the psychiatrist's suggestion to increase her BMI up to 17. When the edema appeared, she started to take protein by herself. Although she was given information about edema development, it nevertheless caused increased panic attacks, crying spells, refusal to wear clothes, and refusal to leave the house. At the beginning of psychiatric examination, she was complying with all the rules, but when the edema appeared, her attitude changed and she started skipping her visits. She had amenorrhea for more than a year, which began three months after starting her diet. She attempted to purge by vomiting, used diuretics and laxative to induce weight loss, and exercised excessively. Our patient drank enormous amounts of green tea (over 30 mugs a day) for its diuretic effects and also took diuretic and rarely laxative pills.

She complained of dizziness, constipation and insomnia. Her physical examination showed decreased temperature (usually below 36 °C), bradycardia at 52 beats per minute (which did not increase with exercise), and hypotension (usually below 80/50 mmHg). We were unable to scale her weight due to her refusal. Her general appearance was excited, hyperactive and distrustful. She had edema of her face, abdomen, hands and feet (pitting), acrocyanosis of the skin, abdominal pain, fatigue, muscle weakness and cramps, postural changes (walking as if she has truncal obesity), and ecchymosis on her feet. She did not have any abnormality on examination of head, eye, ear, nose and throat (HEENT), neck and thyroid, heart, lung, abdomen, back, or extremities. She had breast and pubic hair with Tanner V staging. Her neurologic examination was normal including description of gait, deep tendon reflexes, strength, and balance.

Laboratory findings showed: white blood cells 6,400/mm³, platelet count 292,000/mm³, hemoglobin 13.4 g/dl, erythrocyte sedimentation rate 5 mm/h, normal cholesterol 184 mg/dl (was 271 mg/dl, normal level was <200 mg/dl according to the lab results one month ago), no electrolyte imbalance but mildly increased potassium 4.74 mEq/L (range: 3.4-4.4 mEq/L), normal liver function tests, normal protein and albumin levels, and urine Na 21 mEq/L, K 52 mEq/L and Cl 61 mEq/L (normal ranges: 40-220 mEq/L, 25-125 mEq/L and 110-250 mEq/L, respectively). After she stopped taking diuretics and laxatives, her blood and urine electrolyte tests were repeated one month later at a different lab. The results were as follows: Na 136 mEq/L (130-150), K 4.15 mEq/L (3.5-5.5), Cl 106 mEq/L (95-110), and phosphorus 4.1 (2.7-4.5) in blood and Na 101 mEq/L (54-150), K 49.22 mEq/L (20-80) and Cl 158 mEq/L (110-250) in urine. Phosphorus level of 72 g/24-hour urine (normal range: 0.4-1.3) was noted, but her EKG was normal. Urinalysis showed proteinuria and sterile pyuria. Blood protein and albumin level were in the normal range (7.2 g/dl (6-8.7), 4.71 g/dl (3.2-4.8), respectively). We thus did not assess for hypoproteinemia during follow-up. She was very sensitive about gaining any weight. She tried to eat meals that were high in protein because she knew that hypoproteinemia could

be one of the reasons for her weight gain. Her thyroid function tests, gonadotropins, estradiol, progesterone, cortisol, and growth hormone were within normal range; however, the prolactin was elevated at 38 ng/ml (normal range: 1.3-25). Her T4 and thyroid stimulating hormone (TSH) levels were found to be low and thyroid supplement was recommended by a family physician. We did not recommend thyroid hormone for our patient because these lab abnormalities were due to her eating disorder, not to a thyroid abnormality. In addition, folic acid, ferritin and 25(OH)D₃ vitamin were within normal limits. She refused other tests for evaluation of osteoporosis like bone mineral density (Dexa Scan) and magnetic resonance imaging (MRI) for cortical atrophy.

Although the psychiatrist had informed our patient about the edema development, she was highly anxious about it, experiencing crying spells and becoming agitated when she had to dress to leave the house. Her weight was localized in a different body area each day. Her mother agreed with her daughter, and was very upset with her daughter's daily change in body shape. Her mother also reported that her body appearance changed every morning; each morning she awoke with an enlarged belly that made it impossible for her to wear any of her usual dresses. Just prior to this period, she had made significant improvement in her psychiatric treatment and even began to go to school. The edema around her belly made it impossible to wear her school uniform so she again stopped attending school. Her agitation increased, until she finally refused to go out and began not to attend her sessions. This period was followed by a worsening of her anorexic symptoms, with the patient returning to her strict ritualistic eating behavior and terminating her treatment.

Discussion

Anorexia nervosa is characterized by marked loss of weight, amenorrhea, intense fear of gaining weight, and body image disturbances. Anemia, peripheral edema and pronounced muscular weakness due to electrolyte imbalance may be observed in advanced cases. The disease commences in puberty with more or less obvious loss of weight followed by reduced food intake. Anorexic patients are usually resistant to treatment and they deny their need for help.

Therapy should be initiated as a team by the psychiatrists, dietitian, and an expert adolescent physician. In severe cases, parenteral nutrition and intensive care may be required. This is particularly true in complicated cases such as occurrence of infection and serious electrolyte disorders or coagulation defects. The earlier a diagnosis is made the better the prognosis. Manifestation of the disease for more than five years' duration considerably decreases the chances for cure. In our case, although diagnosed two years before, the patient was not followed up by a physician due to her reluctance. Only when her psychiatric treatment resulted in some progress and she began to eat, could she be persuaded to be seen by a pediatrician. She agreed that her increased weight was because of the edema and accepted the help of a physician only to reduce this edema. When she was weighed, her weight fluctuated in both directions by 2 or 3 kg, but these changes were not consistent from day to day. The peripheral edema caused her to feel overweight despite being underweight. Although she intellectually understood that her increased weight was because of the edema, and even understood the mechanism of this edema, the changes in her body shape created so much anxiety and agitation that her anorexia relapsed and she terminated the treatment.

Peripheral edema is seen in 20% of patients with AN. There are different mechanisms for its occurrence, one of which is hypoproteinemia. However, we did not detect a low protein or albumin level in her blood tests. The patient was careful to consume a high-protein diet. Electrolyte imbalance is another important cause of edema; however, this patient's blood electrolyte levels were normal during follow-up. Only her phosphorus level in urine was elevated, but there was no abnormality on EKG. In AN, electrolyte abnormalities are less common and are usually due to malnutrition or, in rare cases, to purging behavior. In many cases, the frequency of electrolyte abnormalities does not seem to correlate with either the type of behaviors (starvation, vomiting, diuretics abuse, laxative abuse) or the reported frequency of these behaviors⁵. Many patients with electrolyte abnormalities are asymptomatic, and it is impossible to predict when complications might occur. It must be noted that there is high probability for multiple electrolyte disturbances

to coexist if a single abnormal electrolyte determination is found⁶. It is known that electrolyte abnormalities can be due to vomiting or laxative/ diuretic abuse as well as from low salt intake and resulting dehydration. She had been addicted to caffeinated beverages since her childhood. She drank coffee whenever she studied, and the kettle switch was on at all times. Diet coke, which is highly caffeinated, was her preferred beverage when thirsty. She commented that her urine amount was higher than usual. Thus, volume depletion leads to a secondary hyperaldosteronism (pseudo Bartter's syndrome) and reflex peripheral edema. Reflex fluid retention again causes weight gain and sustains diuretic use. Most anorexic patients who misuse or abuse diuretics use over-the-counter preparations, which usually contain ammonium chloride and caffeine. The three groups of prescription drugs most often abused by patients with eating disorders are thiazides, loop diuretics, and potassium-sparing diuretics. Thiazides and loop diuretics such as furosemide can produce potassium and sodium depletion. Elevated urine potassium levels in the presence of significant hypokalemia may indicate diuretic abuse. The aldosterone-antagonist diuretics such as spironolactone actually may be helpful for the patient with secondary hyperaldosteronism with hypotension and myocardial conduction abnormality. We did not determine any electrolyte abnormality in blood or urine except high phosphorus level in the urine. High phosphorus level in the urine shows decreased phosphorus in the blood but we did not determine any decrease in the urine. Glucose, however, inhibits fat metabolism and requires phosphate for glycolysis. Consequently, severe hypophosphatemia may occur in patients with AN during parenteral refeeding with a large carbohydrate load and without sufficient amounts of phosphate⁷. Hypophosphatemic symptoms are due to reduced cellular energy stores and tissue hypoxia, leading to cell breakdown and neuromuscular changes such as irritability and paresthesia⁸. She pointed out that she had momentarily stopped the diuretics and diet pills. Her hormonal laboratory results were normal until the last evaluation. In the last laboratory assessment, there was suppression of TSH. She wanted to use thyroid pills despite knowing its mechanism. This is a thyroid conservation response to starvation and is in no

way indicative of a primary thyroid abnormality. Treatment of this 'euthyroid sick syndrome' with thyroid is contraindicated. Such hormone therapy is often abused by patients in order to further weight loss. The normal conversion of T4 to T3 appears to be diverted to reverse T3 as a peripheral adaptation to starvation and may be closely linked to the hypersecretion of cortisol also found in AN⁹. Hypersecretion of cortisol shows negative feedback effects on secretion of vasopressin, which increases free water clearance by this mechanism^{10,11}. This may contribute to the peripheral edema. Rapid refeeding can also lead to peripheral edema. If edema occurs, it should be carefully monitored but rarely requires specific treatment. AN patients occasionally have a pattern of consuming small amounts of carbohydrate and avoiding all protein. For these patients, refeeding edema and vitamin deficiency is a particular concern¹². We stopped her from using diuretics and laxatives and from drinking green tea and other caffeinated beverages. Rarely and under extreme conditions would diuretics be required, and low-dose thiazide diuretic for 1-2 weeks would be the preferred treatment. This treatment method is controversial for peripheral edema because some authors have recommended the use of a mild sodium restriction during the first few days followed by discontinuation of diuretics. We treated our patient with low-dose thiazide and a mild sodium restriction then tapered the diuretic dose slowly. We achieved a good response with decreased peripheral edema but she still abandoned her psychiatric treatment due to her fear of looking fat again in the treatment process.

This case shows the importance of a close collaboration between the pediatrician and psychiatrist from the beginning of the treatment of AN. Patients should be informed about the consequences of their eating and drinking habits. It is very important to prepare the patient about the expected changes during the refeeding period so that peripheral edema is not perceived as weight gain by the patient or the family. Anorexic patients should be closely monitored by the pediatrician especially in this period to prevent relapses.

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