The Paradox of Normal Serum Albumin in Anorexia Nervosa: A Case Report

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ABSTRACT
Objective: Anorexia nervosa (AN) is associated with marked decreases in caloric intake and a corresponding reduction in body weight due to abnormal self body image. Although counterintuitive, hypoalbuminemia and vitamin deficiencies are not expected consequences of this disorder. Etiologic considerations for hypoalbuminemia are discussed.

Method: The case report of a patient with AN and marked hypoalbuminemia is presented and a focused literature review is reported.

Results: Hypoalbuminemia was initially attributed to starvation. However, occult infection was ultimately responsible.

Discussion: Hypoalbuminemia should not be considered a characteristic feature of AN even in the setting of progressive weight loss. The presence of other potentially life-threatening conditions should be sought, as reduced serum albumin concentration is a marker of inflammation in AN. © 2005 by Wiley Periodicals, Inc.

Keywords: anorexia nervosa; caloric intake; hypoalbuminemia; vitamin deficiencies

Case Report
A 52-year-old White woman with a 20-year history of anorexia nervosa (AN) presented to the emergency department with 3 weeks of increasing bilateral leg pain. She described 2 months of progressive weakness, malaise, and subjective chills without fever. Review of systems was notable for mild diarrhea and a decreased appetite. Her body weight had decreased by approximately 5 kg over the course of the last month. She also reported severe bereavement in the 2 months following her mother’s recent death. One week before presentation, her husband noted that the patient was intermittently somnolent and confused.

On presentation, the patient was afebrile and weighed 49 kg with a body mass index (BMI) of 17 kg/m2. Her blood pressure was 96/50 mm Hg with a heart rate of 107 beats/min. She was afebrile. Respiratory rate was 16/min and room-air oxygen saturation was normal. In general, she appeared drowsy and cachectic but was in no acute distress. Her oropharynx was erythematous with a smooth red tongue consistent with glossitis. Lungs were clear to auscultation and cardiovascular examination was unremarkable. Abdominal examination revealed mild tenderness to palpation in the left lower quadrant, but no hepatosplenomegaly or ascites was detected. Neurologic examination revealed normal strength, reflexes, and sensation in all extremities. Skin examination was notable for an erythematous rash on the left thigh and desquamative erythema involving her hands and feet bilaterally.

Laboratory investigations revealed an elevated white blood cell count of 15.1 × 109 cells/L and a hemoglobin level of 10 g/L. The mean corpuscular volume was normal. Her serum glucose concentration normalized with antibiotic therapy despite minimal restoration of body weight.

Discussion: Hypoalbuminemia should not be considered a characteristic feature of AN even in the setting of progressive weight loss. The presence of other potentially life-threatening conditions should be sought, as reduced serum albumin concentration is a marker of inflammation in AN.

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(Received 10 June 2004
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Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/eat.20129
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Int J Eat Disord 37:3 278–280 2005
the presence of glossitis and dermatitis were presumed secondary to concomitant vitamin B deficiency. However, serum vitamin B₁₂ concentration was elevated at 2,000 pg/ml (normal range, 130–770 pg/ml) and the serum folate level was within normal limits at 15 ng/ml (normal range, 2–20 ng/ml).

An eating disorder specialist was consulted to assist with enteral feeding and commented that serum albumin levels are typically maintained in AN and suggested that other factors may be contributing to the hypoalbuminemia. Subsequently, an erythrocyte sedimentation rate and C-reactive protein level were obtained and both were abnormal (60 mm/hr and 20 mg/dl; reference ranges, 0–30 and 0–1.0, respectively). These elevated markers of inflammation coupled with a repeat leukocyte count, which had increased to 25.0 × 10⁹ cells/L, suggested an underlying infectious process. The erythema of her thigh was presumptively diagnosed as erysipelas and empiric therapy with intravenous antibiotics was initiated. Over the next week, her appetite and energy level rapidly returned to baseline and enteral feeding was discontinued. She was discharged from the hospital after receiving a full course of antibiotic therapy. A follow-up serum albumin assessment performed 2 months later was normal (4.1 g/dl) and upon review of her outpatient medical record, a baseline serum albumin level 1 year before hospitalization was identical (4.0 g/dl).

**Discussion**

This case illustrates the importance of seeking an underlying infectious or inflammatory etiology in AN patients presenting with hypoalbuminemia. Even in the most severe cases of pure AN, the serum albumin level remains normal. Clinicians must, therefore, differentiate chronic AN patients from eating disorder patients who develop concomitant medical complications.

The differential diagnosis of hypoalbuminemia may be subdivided into three general categories: (1) decreased protein synthesis, (2) excess protein loss, and (3) altered distribution of albumin outside of plasma (Table 1). In chronic malnutrition unrelated to eating disorders, patients typically develop hypoalbuminemia because of a severe deficiency of protein intake or because of an underlying inflammatory disorder. This causes a decrease in cellular RNA as well as a disaggregation of ribosomal membrane proteins (Rosenoer, Oratz, & Rothschild, 1977). As a result, albumin synthesis decreases.

By contrast, several studies have shown that in patients with AN, plasma albumin levels typically remain within the normal range (Caregaro et al., 2001; Haluzik, Papezova, Nedvidkova, & Kabrt, 1999; Smith, Robinson, & Fleck, 1996). Smith et al. used autologous I-labeled albumin to measure the catabolic rate, distribution, and plasma albumin concentration in patients with chronic AN. The mean plasma albumin concentration was 3.7 g/dl in the AN patients and 4.0 g/dl in age-matched control subjects (the p value was not significant). Moreover, the catabolic rate of plasma albumin level between study groups did not differ significantly.

No study has demonstrated a biologic mechanism by which patients with severe AN (self-induced starvation) maintain normal albumin levels, whereas those who suffer from chronic malnutrition do not. In the presented case, the patient’s hypoalbuminemia was likely secondary to reduced hepatic protein synthesis in the setting of infectious stress (Table 1). Although she had been diagnosed with AN for more than 20 years, the patient’s baseline albumin level was consistently normal and treatment of the underlying cellulitis rapidly restored the serum albumin concentration to normal.

In addition to hypoalbuminemia, the patient also manifested signs and symptoms indicative of B vitamin deficiency. Most concerning was the possibility of pellagra (niacin deficiency) given the presence of diarrhea, dermatitis, and confusion. Pellagra has been reported in AN patients, but its

**TABLE 1. Causes of hypoalbuminemia**

<table>
<thead>
<tr>
<th>Decreased albumin synthesis</th>
<th>Increased albumin loss despite increased synthesis</th>
<th>Altered albumin distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic malnutrition</td>
<td>Nephrotic syndrome</td>
<td>Ascites</td>
</tr>
<tr>
<td>Hypergammaglobulinemia</td>
<td>Protein-losing enteropathy</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>Severe burns</td>
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<tr>
<td>Waldenstrom’s macroglobulinemia</td>
<td>Hypermetabolic states</td>
<td></td>
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<tr>
<td>Stress secondary to infection, surgery, radiation, trauma</td>
<td>Cushing’s syndrome</td>
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<tr>
<td>Carcinoma</td>
<td>Hyperthyroidism</td>
<td></td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>Hepatic toxins</td>
<td></td>
</tr>
</tbody>
</table>

aPlasma oncotic pressure is believed to have a regulatory control on hepatocyte albumin synthesis.

bIn ascites, newly synthesized albumin from hepatocytes is transported directly into ascitic fluid rather than into the systemic circulation.

cDue to increased circulating plasma volume.
occurrence in this setting is extremely rare and limited to case reports (Caregaro et al., 2001; Judd & Poskitt, 1991; Prousky JE, 2003). Although our patient had an erythematous desquamative rash similar in appearance to the dermatitis observed in pellagra, the absence of a rash on sun-exposed areas such as the face and neck argued against this diagnosis. The findings of glossitis are consistent with vitamin B12 and folate deficiency, but both values were normal in our patient and her anemia was not macrocytic (megaloblastic).

Vitamin deficiencies are also extremely rare in patients with AN. One clinical study assessed serum vitamin levels in 20 patients with AN compared with a group of healthy age-matched control subjects (Van Binsbergen, Odink, Van den Berg, Koppeschaar, & Coelingh Bennink, 1988). There were no statistically significant differences in serum vitamin concentrations between the groups. It is noteworthy that vitamin B12 and retinol (vitamin A) levels were significantly higher in AN patients compared with matched control subjects. Although it is not clear why vitamin levels are generally preserved in patients with AN, it may reflect either oral vitamin supplementation or result from specific diets that such patients tend to prefer which often include vitamin-rich foods such as fruits and vegetables. The elevated vitamin B12 level and normal serum folate level in our patient are therefore consistent with the published literature.

This case illustrates the importance of recognizing that serum albumin and vitamin concentrations remain normal in AN patients despite chronic self-induced starvation. Paradoxically, albumin concentrations in AN patients remain preserved even in the most profoundly cachectic patients. When clinically evaluating AN patients with hypoalbuminemia, a thorough investigation for an independent etiology seems mandatory.

The authors are grateful to Adriana Padget for assisting with article preparation.

References