A CASE OF SEVERE HYPOALBUMINEMIA ASSOCIATED WITH CHRONIC CONGESTIVE HEART FAILURE: THE ROLE OF THE TRICUSPID REGURGITATION

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A CASE OF SEVERE HYPOALBUMINEMIA ASSOCIATED WITH CHRONIC CONGESTIVE HEART FAILURE: THE ROLE OF THE TRICUSPID REGURGITATION (Abstract): Hypoalbuminemia is considered an independent predictor of mortality, especially in elderly patients. It is common in patients with congestive heart failure, when is due to several mechanisms: increased volume of distribution, significant stasis in the mesenteric circulation and altered protein metabolism in the liver. These alterations are even more pregnant when tricuspid regurgitation is associated or aggravated by different risk factors (recent infections, anemia, hyperthyroidism). We present the case of an elderly patient with severe hypoproteinemia and important hypoalbuminemia associated with congestive heart failure and aggravation of tricuspid regurgitation. The differential diagnosis concluded that hypoalbuminemia was influenced by tricuspid regurgitation as it enhanced liver dysfunction and enteral protein absorption due to increased stasis in mesenteric system. On the other hand, hypoalbuminemia contributed to the progression of heart failure by favoring myocardial edema, volume overload, and diuretic resistance. This is why correct management of this situation should include removal of subclinical excess of fluid and renutrition. A multidisciplinary approach is needed in order to achieve a good control of the symptoms and a significant improvement of quality of life. Keywords: HYPOALBUMINEMIA, CONGESTIVE HEART FAILURE, TRICUSPID REGURGITATION.

Hypoalbuminemia can be caused by various conditions, including acute and chronic inflammation, heart failure, malnutrition, hepatic cirrhosis and nephrotic syndrome (1). Low serum albumin is considered an independent predictor of mortality, especially in elderly patients (2). However, albumin or prealbumin are not considered as defining characteristics of malnutrition in elderly (even if Mini Nutritional Assessment is part of the Comprehensive Geriatric Evaluation) because recent evidence show that serum levels of these proteins do not change in response to changes in nutrient intake (3).

CASE REPORT
We present the case of a 87-year-old
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woman with a history of numerous cardiovascular diseases (atrial fibrillation, deep venous thrombosis with repetitive pulmonary embolism, severe pulmonary hypertension and chronic congestive heart failure) and thyroid hyperfunction (with normal function under medication). She was admitted in the Geriatric Clinic for aggravating signs of congestive heart failure. She was referred to our clinic for the first time 6 months previously. Ever since, she is under adequate diet and chronic medication: diuretics, digoxin, aspirin and carvedilol, which she takes regularly.

Clinic examination and exhaustive investigations were performed in order to diagnose the main cause that induced her present symptoms and the comparative results with previous hospitalization revealed the following: recent onset of pruritus; dysphonia for the last 3 months; progression of tricuspid regurgitation (grade II → grade III on echocardiography); aggravation of hypoproteinemia (45 mg/l → 38 mg/l) and hypoalbuminemia (21 mg/l → 18 mg/l).

Based on these elements, we considered that this episode of heart failure could be due to the following causes: 1. onset of a new medical condition: neoplastic (dysphonia, pruritus), parasitic infection (pruritus), new alteration of thyroid function; 2. new episode of pulmonary thromboembolism (D-dimers were negative); 3. natural evolution of her ischemic cardiomyopathy; 4. aggravation of hypoalbuminemia.

Exhaustive investigations did not detect any of these suppositions, so we concentrated on the possible causes of hypoalbuminemia as risk factor for heart failure other than the heart failure itself:

- intake deficit – the MNA (Mini Nutritional Assessment) was normal and the Comprehensive Geriatric Assessment (ADL, IADL, GDS, sarcopenia test) revealed a normal nutritional behavior;
- protein loosing enteropathy, a medical condition difficult to prove in very old patients; anyway, the aggravation of tricuspid regurgitation could have increased stasis in venous circulation and decreased normal absorption of nutrients;
- deficit of protein synthesis due to hepatic failure, but the liver tests were normal and abdominal ultrasound and CT were within normal ranges; however, liver function could have been modified by increased stasis due to tricuspid regurgitation;
- increased catabolism due to acute/chronic inflammation (in our case we considered cancer, tuberculosis, hyperthyroidism, acute hepatitis) but we found no data to confirm these suppositions;
- increased losses due to an unknown renal problem, but renal function was normal.

We concluded that hypoalbuminemia was an important factor in the aggravation of heart failure but, in the same time, aggravation of tricuspid regurgitation and severe heart failure were key causes for hypoproteinemia and hypoalbuminemia. These conditions were tightly interconnected and we took these aspects into consideration when devising therapeutical management. We combined high doses of diuretics, adequate doses of anticoagulants and digoxin with intense treatment of hypoalbuminemia (recombinant human albumin, intravenous amino acids and parenteral nutrition) and we registered a good evolution, with significant decrease of symptoms and important amelioration of quality of life.

**DISCUSSION**

Low serum albumin is an important predictor of clinical outcome and mortality
in elderly patients. For every 10 g/L decrease in serum albumin level, mortality increases by 137% and morbidity by 89% (1). This is why diagnosis of hypoalbuminemia and, more importantly, identification of the causes that led to this condition, are very important for practitioners.

Hypoalbuminemia is quite common in elderly population due to several causes closely related to aging itself (4). Dietary intake deficit is frequently encountered due to:

- Undernutrition, particularly in institutionalized patients. This age-associated physiologic reduction in appetite and food intake, which has been termed "the anorexia of aging," contributes to the development of pathologic anorexia, and is associated with substantial adverse effects. (5);

- Depression-associated anorexia. Even if depression is not an inevitable part of aging, it is definitely more frequent in old people due to several causes (retirement, the death of loved ones, increased isolation, and medical problems). Geriatric Depression Scale (GDS) is also an important compound of Geriatric Assessment and should alert the practitioner if psychological therapy is needed;

- Drug-induced anorexia: antiparkinson agents (levo-dopa), antibiotics (co-trimoxazole metronidazole), diuretics (clopamide), chemotherapeutic agents (cytarabine, dacarbazine), anti-Alzheimer’s agents (tacrine), anticonvulsants (zonisamide) are known for their negative effect on appetite (6);

- Age-induced changes of digestive system, including dental and hepatic functions (1).

Other frequent causes of hypoalbuminemia in elderly patients are: chronic heart insufficiency, liver cirrhosis, nephritic/nephrotic syndrome, and acute or chronic inflammatory syndrome. If liver and renal problems are relatively easy to identify, inflammation is quite a challenge for physicians.

Inflammation, either acute (burns, infections) or chronic (arthritis, dementia, Crohn’s disease) are more often associated with vague symptoms as malaise, fatigue and lack of appetite than with classic symptoms such as fever, headaches, chills, muscle stiffness, and fatigue. Chronic inflammation is typically detected with lab tests including C-reactive protein, complete blood count (CBC) and complete metabolic panel (CMP). Sodium level should be reviewed to see if it is low, in which case, the albumin level may be diluted due to overhydration. The source of chronic inflammation could take a while to identify but anti-inflammatory treatment should be considered in order to influence hypoalbuminemia.

There are several mechanisms that lead to hypoalbuminemia in congestive heart failure (7). If the synthesis of albumin is normal, hypoalbuminemia results from an increased volume of distribution (which will increase hydrostatic pressure and favor migration of fluids in interstitium). There are many situations when right heart failure is accompanied by significant stasis in the mesenteric circulation, which would affect protein absorption from digestive tube and protein metabolism in the liver; these additional mechanisms for hypoalbuminemia are even more pregnant when tricuspid regurgitation is associated or aggravated by different risk factors (recent infections, anemia, and hyperthyroidism).

Recent studies (8, 9) found that there are independent associations between anemia, hyponatremia, severe tricuspid regurgitation, low serum cholesterol and reduced serum
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albumin; interestingly, body mass index was not predictive of albumin levels; hypoalbuminemia was common among patients with acutely decompensated heart failure and was independently associated with increased one year mortality.

The direct relationship between tricuspid regurgitation and severe hypoalbuminemia is mentioned by Sekine (10); moreover, Lau (11) considers that they are not only related but the severity of tricuspid regurgitation is responsible for the severity of hypoalbuminemia because of the stasis in hepatic venous circulation and impairment of hepatic protein synthesis. In the same time, hypoalbuminemia may also contribute to the progression of heart failure by favoring myocardial edema, volume overload, diuretic resistance (12) and exacerbation of oxidative stress and inflammation. This was the case of our patient, as the specific heart failure treatment didn’t work but only when associated with treatment of hypoalbuminemia.

CONCLUSION

Hypoalbuminemia is frequently encountered in patients with heart failure and is mainly related to the malnutrition-inflammation association. Other causal factors include hemodilution, liver dysfunction, renal and enteral loss. Evidence is growing that hypoalbuminemia independently predicts incident heart failure in elderly patients, as well as mortality in patients with heart failure regardless of left ventricular ejection fraction. We report a case with severe congestive heart failure associated with important tricuspid regurgitation and hypoalbuminemia for which correct management included removal of subclinical excess of fluid and renutrition. A multidisciplinary approach is needed in order to achieve a good control of the symptoms and a significant improvement of quality of life.

REFERENCES


**IMPORTANT BIOLOGICAL ACTIVITIES OF POMEGRANATE LEAVES**

A group of researchers from University of Toulouse conducted a study that evaluated the antioxidant, anti-inflammatory, anti-cholinesterase and cytotoxic activities of different extracts (hexane, dichloromethane, ethyl acetate, ethanol and methanol extracts) obtained from *Punica granatum* leaves. The total phenolic content varied between 8.8 ± 0.3 and 127.3 ± 1.6 mg gallic acid equivalent/g dry weight. Ethyl acetate extract contained the highest value of total phenolics (127.3 ± 1.6 mg gallic acid equivalent/g dw), followed by methanol (85.2 ± 2.4 mg gallic acid equivalent/g dw) and ethanol extracts (82.6 ± 1.5 mg gallic acid equivalent/g dw). The total flavonoids content varied between 1.2 ± 0.05 and 76.9 ± 2.45 mg quercetin equivalent/g dw. The ethanol extract contained the highest level of flavonoids. The distribution of total tannins content in the extracts showed that tannins were highly concentrated in the hexane extract of pomegranate leaves (260.8 ± 11.5 mg catechin equivalent/kg dw). The dichloromethane extract was found to contain the lowest concentration of tannins (63.7 ± 1.7 mg catechin equivalent/kg dw). Anthocyanins content in the pomegranate leaves depended on the extracting solvent. The hexane extract contained the highest total anthocyanins content (3.73 ± 0.02 mg cyanidin-3-glucoside equivalent/g dw). The methanol extract showed good DPPH and ABTS scavenging effects (IC50=5.62 and 1.31 mg/L, respectively). The strongest 5-lipoxygenase (5-LOX), acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) inhibition activities were determined for the ethanol extract (IC50 values of 6.20, 14.83 and 2.65 mg/L, respectively); the best cytotoxic activity against MCF-7 cells was determined for the methanol extract (IC50 = 31 mg/L). These important biological activities showed that the methanol extract of *P. granatum* leaves is a natural source of antioxidants and might be used as a natural additive in food and pharmaceutical industries. Further *in vivo* studies should be done (Bekir J, Mars M, Souchard JP, Bouajila J. Assessment of antioxidant, anti-inflammatory, anti-cholinesterase and cytotoxic activities of pomegranate (*Punica granatum*) leaves. *Food Chem Toxicol* 2013; 55: 470-475).

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