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# Touch on the Brake at Edge of Uremia Cachexia: A Case Report

**Xin Pan, Juan Cai,Pan Xie, Yan Zhuo,Shuang Hu and Kan-fu Peng***

Department of kidney, Army Military Medical University, China

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**Corresponding author:**
Kan-fu Peng,
Department of Kidney, Southwest Hospital, Army Military Medical University, Chongqing 400038, China,
Tel: +023-68754239;
Email: 392906786@qq.com

## ABSTRACT

Different from ordinary Protein-Energy Wasting (PEW), cachexia of uremia aggravates the complications of uremia in the vicious circle of low protein, volume overload and inflammatory response, which seriously affects the quality of life and survival rate of patients. Uremia cachexia is rare in dialysis center of our hospital. This case is an 81-year-old female who has been on dialysis regularly for two years. From April to September in 2019, she repeatedly developed pulmonary infection, lost much weight, diagnosed as uremic cachexia. After strong anti-infection and nutrition support treatment, respiratory failure and cardiac insufficiency were corrected, infection index decreased and nutrition index increased. In this difficult process, we found more worthy of attention factors: body weight, (Body Mass Index) BMI, calf circumference, grip strength, prealbumin, and inflammatory indicator. Strengthening the attention to the relevant indicators may prevent the progress of cachexia uremia.

## INTRODUCTION

Protein–Energy wasting (PEW) is the state of decreased body stores of protein and fat masses, which was proposed on the International Society of Renal Nutrition and Metabolism (ISRNM) in 2008[1]. PEW, also called malnutrition, occurs in patients with chronic renal failure (CRF) as high as 40%, and is defined as an independent risk factor that increases cardiovascular mortality [2]. PEW is commonly caused by intake loss for example in anorexia nervosa. However in chronic kidney disease there are multiple factors related to loss of lean body mass including poor food intake because of anorexia, nausea and vomiting due to uremic toxicity, hormonal derangements [3], academia [4,5] and increased Resting Energy Expenditure(REE) in dialysate [6,7]; transient, intercurrent catabolic illnesses [8] and so on. Malnutrition in CRF is divided into two subgroups as malnutrition type 1 and type 2 with different features listed in (Table 1) [3].

High levels of high-sensitive C-Reactive Protein (hs-CRP) and proinflammatory cytokine IL-6 have a negative effect on protein synthesis, and a reliable predictor for determining malnutrition and cardiovascular disease [9,10]. A multiple regression analysis [11] conducted in pre-dialysis patients proved that, the relationship between volume and malnutrition is stronger than the relationship between inflammation and malnutrition. The elimination of volume excess would ameliorate both inflammation and malnutrition. How to manage chronic inflammation and excess volume needs to be supported or proved with prospective clinical studies.

The uremic cachexia syndrome consists of anorexia, increased energy expenditure, hypo-albuminemia, and loss of protein stores, as well as sarcopenia (muscle wasting),

and is reported to have a prevalence of 30–60%. Uremic cachexia is an important risk factor for mortality in patients with end-stage renal disease, which is 100-fold to 200-fold higher than in the general population [12,13]. There is no obvious distinction between cachexia and PEW from a pathophysiologic standpoint [14]. Koppe and colleagues [15] suggest a new term 'kidney disease cachexia' to encompass both cachexia and PEW as part of a spectrum of the same nutritional disorder, treating cachexia as the most severe stage of PEW.

Table 1: The differences between malnutrition type1 and type 2.

| | Type 1 | Type 2 |
|---|---|---|
| serum albumin | Normal/low | Low |
| Co-morbidity | Uncommon | Common |
| Presence of inflammation | No | Yes |
| Food intake | Low | Low/Normal |
| REE | Normal | Elevated |
| Oxidative stress | Increased | Markedly increased |
| Protein catabolism | Decreased | Increased |
| Reversed by dialysis and nutritional support | Yes | No |

Table 2: The differences of criteria between PEW and Cachexia in dialysis patients.

| Criteria | | PEW | Cachexia |
|---|---|---|---|
| Serum chemistry | Albumin | <38g/L | <32g/L |
| | Pre-albumin | <3g/L | — |
| | Cholesterol | <1g/L | — |
| Body mass | BMI | <23kg/m2 | <20kg/m2 |
| | Unintentional weight loss | 5% over 3 months 10% over 6 months | ≥5% over 12 month |
| Muscle mass | Reduced mid-arm muscle circumference area | reduction >10% in relation to 50th percentile of reference population | <10th percentile for age and gender |
| Dietary intake | Unintentional low DPI | <0.80 g /kg/day for at least 2 months | |
| | Unintentional low DEI | <25 kcal/kg/day for at least 2 months | <20 kcal/kg/day |
| Definition of PEW/cachexia | | At least three out of the four listed categories (and at least one test in each of the selected category) | Weight loss of at least 5% in 12 months or BMI <20 kg/m2, plus three of the other criteria |

The differences of criteria between PEW and cachexia were shown in (Table 1) [14]. It reflects distinctions in clinical manifestations, which can also be regarded as a disease course of progress. In PEW, fat is lost first, while Lean Body Mass (LBM) is preserved. In cachexia, muscle is wasted and fat is relatively underutilized. Cachexia is Often accompanied by anorexia, which means losing an adaptive response [16]. The abnormality of malnutrition can usually be overcome by providing more food or changing the die [17]. Cachexia carries a very poor prognosis. There approves to be almost no therapies for its treatment, apart from that for Acquired Immune Deficiency Syndrome (AIDS) induced cachexia [18]. Uremic cachexia is same as the characteristics of malnutrition type 2, difficult to be reversed by dialysis and nutritional support, which leads to a bottleneck in treatment. It is necessary to increase the ultrafiltration volume of dialysis to reduce the volume load of patients, but it will increase the REE caused by dialysis. The daily protein intake recommended is at least 1.2 g/kg body weight/day in dialysis patients [19]. Meanwhile, to prevent protein from being utilized as an energy source via gluconeogenesis, a sufficient energy intake is needed [20]. To be more specific, an energy intake of 35-40kcal/kg is not enough, regarding the increased energy expenditure in chronic dialysis patients [21]. With the progress of the severity of malnutrition, the treatment has also turned to be more complex.

## CASE PRESENTATION

The patient was an 81-year-old woman who was diagnosed as uremic phase of chronic renal failure (CKD5 stage) in 2016 at local hospital, she went to the outpatient clinic of our department, for the first time, to solve the problem of access, with the outpatient clinic examined serum creatinine at about 948.6 umol/L, which met the indications for hemodialysis. The left arteriovenous fistula was operated on March 2017. Regular dialysis treatment (three times a week) was arranged in our dialysis unit. The concentration of serum creatinine decreased gradually. On December 4, 2018, the patient coughed repeatedly with sputum and shortness of breath after activity. The patient was treated in the local clinic, and felt the symptoms improved after oral administration of antibiotics. Later, the above symptoms occurred repeatedly, and the patients did not pay attention to them. The patient's appetite was normal, but her food intake decreased significantly.

The patient developed a fever (39.1℃) in March 2019, with current wheezing, shortness of breath, fatigue, and loss of

appetite, mainly the liquid diet, no supplement of enteral and parenteral nutrition. The results of blood gas analysis suggest type I respiratory failure. (Oxygen inhalation 4L/min: pH 7.51, pCO2 28.8mmHg, pO2 69.6mmHg, Lac 2.1, HCO3- 24.2mmol/L). The chest CT hinted: 1.bilateral pulmonary inflammation, with bilateral pulmonary edema; 2. pericardial effusion, bilateral pleural effusion and interlobar fissure increased, with bilateral pulmonary edema. Acinetobacter baumannii found in sputum culture.The white blood cells and CRP of the patients were higher than normal.

On April 3, 2019, meropenem was infused intravenously with 0.5g per12 hours, with ambroxol intravenous push, budesonide suspension atomization inhalation and other symptomatic treatment. The patient's body temperature was still high on April 12, and meropenem was increased to 1g per 12h. The CRP index and body temperature of the patients decreased gradually. On April 19th, piperacillin / tazobactam sodium was used for 2.25g per 12h. On April 22, the patient was discharged after the above symptoms were significantly improved. She was discharged with oral moxifloxacin hydrochloride. After discharge, the patient no longer developed fever, but the patient still had a poor appetite, gradually could not move freely, and was bedridden for a long time.

On August 3rd 2019, she was admitted to hospital again because of fever, poor spirit and anorexia, and was admitted to hospital as “uremic cachexia”, when her body weight turned to be 37kg, BMI 14.82. From April 2019 to Aug 2019, the patient's weight lost significantly, as shown in (Table 3).

Table 3: Changes in patient's nutritional status.

| Time | creatinine umol/L | Albumin g/L | Weight Kg | BMI Kg/m2 |
|---|---|---|---|---|
| 2016.09 | 948.6 | 32.9 | 50 | 20.03 |
| 2017.01 | 276 | 33.2 | 48 | 19.23 |
| 2018.12 | 584 | 27.9 | 47 | 18.83 |
| 2019.04 | 209 | 30.3 | 45 | 18.03 |
| 2019.08 | 272 | 25.6 | 37 | 14.82 |
| 2019.09 | 195 | 31.9 | 29.5 | 11.8 |
| 2019.10 | 295 | 31.7 | 33 | 13.2 |

In view of the serious illness of patients with advanced age, poor nutrition, long-term infection and long-term bedridden, the patient's overall condition is extremely poor (shown in Figure 1).

Figure 1: The condition of the uremic cachexia patient's limb.

The patient's condition was extremely poor. Gram-positive cocci were found in sputum culture. Moxifloxacin hydrochloride 400ml per day was given intravenously in the treatment. At the same time, on the basis of the usual liquid diet, the family members were instructed to increase the intake of eggs, meat, total nutrients and protein powder to strengthen enteral nutrition. Intravenous supplement 250ml of 20% medium / long-chain fat emulsion and 250ml compound amino acid are dispense with albumin to maintain daily energy intake of 1200-1400kcal and protein 50-60g.

On Aug 8 thoracic and abdominal CT showed partial atelectasis in the lower lobe of both lungs, dense nodules in the anterior segment of the upper lobe of the right lung, enlarged pericardial effusion, multiple small lymph nodes in the mediastinum, bilateral pleural and interlobar fissure effusion, partially wrapped. A large amount of water accumulates in the patient's body, which needs to be dialyzed by hemodialysis to improve the patient's respiration and heart pressure.

In terms of volume control, from Aug 3rd to Aug 5th, patients were arranged with HDF once a day, accumulating Ultrafiltration volume to 4390. On Aug 10th, half an hour before the end of dialysis, the patient showed dyspnea, sweating and decreased blood pressure, suggesting acute heart failure. Considering the dialysis intolerance caused by hemodynamic instability, we treated her with CRRT for 8 hours. To ultrafilter out the volume more stably, the treatment of CRRT was a better choice.

The dialysis scheme is listed in (Table 4).

Table 4: The dialysis session between April 3 to 13.

| Time | dialysis modality | duration(H) | Ultrafiltration volume(ml) |
|---|---|---|---|
| August 3 | CRRT | 4 | 1050 |
| August 4 | HDF | 2 | 1340 |
| August 5 | HDF | 3 | 2000 |
| August 6 | HDF | 4 | 2400 |
| August 8 | HDF | 3.3 | 2000 |
| August 10 | HDF | 3.3 | 1570 |
| August 11 | CRRT | 8 | 2318 |
| August 12 | CRRT | 10 | 2740 |
| August 13 | CRRT | 6.5 | 1402 |

On Aug 23, the infection index reached the peak and began to show a downward trend, and the levels of albumin and hemoglobin were higher than before, but still lower than normal. The patient's mental state has improved, and her diet is still poor, which can't meet his daily needs. Reexamination of pleural effusion in patients with thoracic and abdominal CT, showed that pericardial effusion was significantly less than before. When discharged from the hospital, her body weight increased to 33kg.

## DISCUSSION

**Strengthen nutritional assessment**

Under the premise that there is no significant difference in dialysis adequacy, the albumin level, standardized protein metabolic rate and dietary protein energy intake in the elderly (> 65 years old) are lower than those in other age groups [22]. Because the patient is bedridden for a long time, it is difficult for the patient to monitor the body weight during the non-hospitalization period. After admission, we asked the patient's family to hold the patient's measured weight and subtract the difference of the family member's weight as the patient's body weight, which has a certain error. But the degree of fluctuation of this value has a certain significance. Therefore, we measured the middle circumference of the right upper arm as 18.9cm and the calf middle circumference (20.5cm) of calf with a tape measure (Figure 2). Because the instrument is limited, it is impossible to measure skin fold thickness and hand-grip strength. According to the nutrition guidelines of the European Dialysis and Transplant Association (EDTA), dialysis patients older than 50 should be assessed every 3 months, regardless of whether they are at risk of malnutrition [23]. Foreign research believes that the decrease of grip strength is related to protein and energy malnutrition, and grip strength is a reliable index to reflect the degree of muscle loss [24]. Therefore, the evaluation form for elderly patients to increase body weight, BMI, calf circumference, grip strength and so on is helpful for nursing to explain the nutritional status of patients to doctors, so that doctors can give dietary guidance or nutrition intervention to patients.

Figure 2: The middle circumference of the right upper arm and right calf.

**Focus on inflammation and nutritional indicators**

In this case report, we found that the change trend of C-Reactive Protein (CRP) in patients was opposite to that of prealbumin (see Table 3). In the past, we usually monitor the patient's albumin level, but ignore the index of prealbumin. When the patient's albumin level continues to be lower than the normal value (< 25), we should further monitor the patient's prealbumin level. Both of them are "acute phase reactant", decreasing when Organism facing acute or chronic inflammation, at the same time, and both are nutritional marker. Studies have shown that albumin is a poor nutritional marker also in dialysis patients [25]. However, pre-albumin has the advantages of shorter half-life and more sensitive. Although there is a correlation between pre-albumin and albumin, the former is shown to be more closely associated with mortality in many researches, in different levels of albumin. Therefore, whether it is used as an indicator of malnutrition or a predictor of poor prognosis, clinicians should pay attention to pre-albumin [26]. On the other hand, a large number of studies have shown that the inflammatory cytokines lead to increased protein catabolism and increased REE [27]. Additionally, the maintenance of immune function was estimated to account for

as much as15% of daily energy expenditure [28]. An analysis from Simone Utaka [29] showed that a significant decrease in CRP was accompanied by a significant reduction in REE. So, it is difficult for patients to correct their long-term malnutrition through simple nutritional supplement after entering the cachexia stage. This is because it is essential to control inflammation to reduce REE.

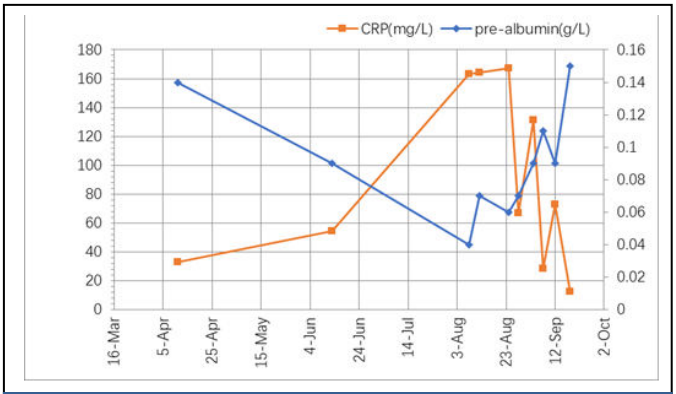


Figure 3: Changing trend between CRP and pre-albumin during March to October.

**Enhance muscle-building exercises**

Uremia develops resistance to Insulin-Like Growth Factor-1 (IGF-1) gene expression stimulated by Growth Hormone (GH), then impairs maintenance of muscle bulk and inhibits linear growth. This is also the pathogenesis of muscle atrophy in uremic cachexia. Work Overload (WO) [23] can effectively stimulate IGF-1 expression and muscle hypertrophy, despite the presence of GH resistance. Exercise in the form of endurance or resistance training can suppress myostatin expression and induce muscle hypertrophy [24-26].

As physical exercise can enhance immune function, it is necessary to educate CKD patients (especially elderly patients) about regular exercise. Patients who can get out of bed for 6 months of regular walking exercise (30 minutes a day, 5 times a week) have anti-inflammatory effects [20]. Long-term bedridden patients can carry out muscle-building exercises such as grip, and can also be used as an indicator of early detection of muscle atrophy.

## CONCLUSION

With the continuous development of hemodialysis, the number and survival rate of elderly patients are increasing. Maintaining a good mental and nutritional state, caused a huge burden on the family and society. It is common in patients with PEW renal failure, especially in dialysis patients, to evaluate the nutritional status of patients before the progression of PEW to cachexia, and to supplement protein and energy from enteral or parenteral nutrition in time, which is to reserve more strength for patients in the long struggle of hemodialysis. After entering cachexia, the patient's dialysis is caught in a dilemma. Choosing HDF can remove large and medium-sized inflammatory molecules as well as albumin. Therefore, it is necessary to combine nutritional support, appropriate exercise,anti-inflammation, and appropriate hemodialysis to combat the cachexia of patients. At the same time, psychological counseling and timely evaluation have an effect on the quality of life and survival rate of patients in cachexia.

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## REFERENCES

1. Fouque D, Kalantar-Zadeh K, Kopple J, Cano N, Chauveau P, et al. (2008). A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. Kidney Int. 73: 391-398.
2. Leavey SL, Strawderman RL, Jones CA, Port FK, Held PJ. (1998). Simple nutritional indicators as independent predictors of mortality in hemodialysis patients. 31: 997-1006.
3. Stenvinkel P, Heimbürger O, Lindholm B, Kaysen GA, Bergström J. (2000). Are there two types of malnutrition in chronic renal failure? Evidence for relationships between malnutrition, inflammation and atherosclerosis (MIA syndrome). 15: 953-960.
4. Bailey JL, Wang X, England BK, Price SR, Ding X, et al. (1996). The acidosis of chronic renal failure activates muscle proteolysis in rats by augmenting transcription of genes encoding proteins of the ATP-dependent ubiquitin-proteasome pathway. J Clin Invest. 97: 1447-1453.
5. Kalantar-Zadeh K, Mehrotra R, Fouque D, Kopple JD. (2004). Metabolic acidosis and malnutrition-inflammation complex syndrome in chronic renal failure. Semin Dial. 17: 455-465.
6. Wolfson M, Jones MR, Kopple JD. (1982). Amino acid losses during hemodialysis with infusion of amino acids and glucose. Kidney Int. 21: 500-506.

7. Ikizler TA, Flakoll PJ, Parker RA, Hakim RM. (1994). Amino acid and albumin losses during hemodialysis. Kidney Int. 46: 830-837.
8. Grodstein GP, Blumenkrantz MJ, Kopple JD. (1980). Nutritional and metabolic response to catabolic stress in uremia. Am J Clin Nutr. 33: 1411-1416.
9. Stenvinkel P. (2006). Inflammation in end-stage renal disease: the hidden enemy. Nephrology (Carlton). 11: p36-41.
10. Honda H, Qureshi AR, Heimbürger O, Barany P, Wang K, et al. (2006). Serum albumin, C-reactive protein, interleukin 6, and fetuin a as predictors of malnutrition, cardiovascular disease, and mortality in patients with ESRD. 47: 139-148.
11. Kutsal DA, Kürşat S, İnci A, Ulman C, OzanÜtük I. (2016). The relationship between malnutrition subgroups and volume parameters in pre-dialysis patients. 27: 81-87.
12. Mak RH, Cheung W, Cone RD, Marks DL. (2005). Orexigenic and anorexigenic mechanisms in the control of nutrition in chronic kidney disease. Pediatr Nephrol. 20: 427-431.
13. Mak RH, Cheung W, Cone RD, Marks DL. (2006). Leptin and inflammation-associated cachexia in chronic kidney disease. Kidney Int. 69: 794-797.
14. Koppe L, Fouque D, Kalantar-Zadeh K. (2019). Kidney cachexia or protein-energy wasting in chronic kidney disease: facts and numbers. J Cachexia Sarcopenia Muscle. 10: 479-484.
15. Oliveira EA, Zheng R, Carter CE, Mak HR, et al. (2019). Cachexia/Protein energy wasting syndrome in CKD: Causation and treatment. Semin Dial. 32: 493-499.
16. Cheung WW, Rosengren S, Boyle DL, Mak RH. (2008). Modulation of melanocortin signaling ameliorates uremic cachexia. Kidney Int. 74: 180-186.
17. Mak RH, Cheung W. (2006). Energy homeostasis and cachexia in chronic kidney disease. Pediatr Nephrol. 21: 1807-1814.
18. Springer J, von Haehling S, Anker SD. (2006). The need for a standardized definition for cachexia in chronic illness. Nat Clin Pract Endocrinol Metab. 2: 416-417.
19. Kopple JD. (1998). Dietary protein and energy requirements in ESRD patients. Am J Kidney Dis. 32: S97-104.
20. Bergstrom J, Furst P, Alvestrand A, Linfholm B. (1993). Protein and energy intake, nitrogen balance and nitrogen losses in patients treated with continuous ambulatory peritoneal dialysis. Kidney Int. 44: 1048-1057.
21. Ikizler TA, Wingard RL, Sun M, Harvell J, Parker RA, et al. (1996). Increased energy expenditure in hemodialysis patients. J Am Soc Nephrol. 7: 2646-2653.
22. Burrowes JD, Cockram DB, Dwyer JT, Larive B, Paranandi L, et al. (2002). Cross-sectional relationship between dietary protein and energy intake, nutritional status, functional status, and comorbidity in older versus younger hemodialysis patients. 12: 87-95.
23. Fouque D, Vennegoor M, ter Wee P, Wanner C, Basci A, et al. (2007). EBPG guideline on nutrition. Nephrol Dial Transplant. 22: ii45-87.
24. O Heimbürger, Qureshi AR, Blaner WS, Berglund L, Stenvinkel P. (2000). Hand-grip muscle strength, lean body mass, and plasma proteins as markers of nutritional status in patients with chronic renal failure close to start of dialysis therapy. 36: 1213-1225.
25. Friedman AN, Fadem SZ. (2010). Reassessment of albumin as a nutritional marker in kidney disease. 21: 223-230.
26. Chertow GM, Ackert K, Lew NL, Lazarus JM, Lowrie EG. (2000). Prealbumin is as important as albumin in the nutritional assessment of hemodialysis patients. 58: 2512-2517.
27. Viana JL, Kosmadakis GC, Watson EL, Bevington A, Feehally J, et al. (2014). Evidence for anti-inflammatory effects of exercise in CKD. J Am Soc Nephrol. 25: 2121-2130.
28. Buttgereit F, Burmester GR, Brand MD. (2000). Bioenergetics of immune functions: fundamental and therapeutic aspects. Immunol Today. 21: 192-199.
29. Utaka S, Avesani CM, Draibe SA, Kamimura MA, Andreoni S, et al. (2005). Inflammation is associated with increased energy expenditure in patients with chronic kidney disease. Am J Clin Nutr. 82: 801-805.