

# Nutrition Therapy on Cutaneous Lymphoma Patient with Anemia and Hypoalbuminemia: A Case Report

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## ABSTRACT

Nutrition is a part of cancer management during therapy, recovery, remission, and recurrence prevention. Malnutrition and cachexia often occur in cancer patients and influence morbidity, mortality, and quality of life, especially in the advanced stage of malignancy. We reported a case of cutaneous lymphoma with anemia and hypoalbuminemia in the terminal condition. This case report focuses on nutritional therapy and palliative care on nutrition. We reported a case of a 40-year-old-man with Cutaneous Lymphoma (CL) and moderate protein-energy malnutrition that was developed to severe protein-energy malnutrition due to difficulty in dietary access. He had an eating problem because of multiple tumors and ulcers on his mouth. We provided access for parenteral nutrition from Central Venous Catheter (CVC) and orogastric tube (OGT) for enteral feeding. Even though the dietary target was never accomplished, there was a slight recovery on hypoalbuminemia and renal function during hospitalization. This case showed a considerable challenge in nutritional therapy due to limited dietary access. Since death was inevitable, we have tried different dietary access to provide adequate intake.

**Keywords:** Nutritional support; cachexia; hypoalbuminemia; quality of life

## Article history:

Received: 30 June 2020

Accepted: 15 August 2020

Published: 30 August 2020



GREEN MEDICAL  
JOURNAL  
E-ISSN 2686-6668

**Published by :**  
Faculty of Medicine  
Universitas Muslim Indonesia

**Mobile number:**  
+62822 9333 0002

**Address:**  
Jl. Urip Sumoharjo Km. 5, Makassar  
South Sulawesi, Indonesia

**Email:**  
greenmedicaljournal@umi.ac.id

## **Introduction**

Cutaneous lymphoma is a heterogeneous group from extra nodular Non-Hodgkin Lymphoma (NHL) from the malignant clonal transformation from T cell or B cell skin-homing or skin resident. Cutaneous lymphoma is defined as a heterogeneous group with many variabilities from clinical picture, histopathology, immunophenotyping, and prognosis<sup>1,2</sup>. A study about malnutrition that occurred in NHL patients has been conducted in Hasan Sadikin Hospital, proved that all NHL patients experienced malnutrition<sup>3</sup>.

Nutritional status in a cancer patient is related to therapeutic response, prognosis, and quality of life. Cancer patients are at high risk of malnutrition and cachexia. Cachexia is defined as a loss in muscle mass with or without lipolysis. This condition is intractable to conventional nutrition support. In terms of symptoms, cachexia is a syndrome of anorexia, early satiety, and general weakness<sup>3</sup>.

The goals of nutritional therapy for cancer patients are to prevent nutritional deficiency, to preserve lean body mass, to minimize side effects on nutritional status, and to maximize the quality of life. Nutrition is an integral part of cancer patients since diagnosed, getting therapy, and recovery period. Nutritional screening should be performed regularly to all cancer patients as early nutrition status evaluation and assessment<sup>3,4</sup>. It is expected that nutritional therapy could improve biochemical values such as serum albumin levels and kidney function.

## **Case**

A 40-year-old man was consulted from the Department of Dermatovenereology with CL, suspect a malignancy, post-biopsy day-2, lung tuberculosis with positive bacteriology on anti-tuberculous treatment continuous phase with unknown HIV status, anemia and severe hypoalbuminemia.

From the physical examination, we found that he was weak, moderate illness, compos mentis with GCS E4MV5. The vital sign was within normal limits, without respiratory modalities. There were multiple tumors with purulent ulcers, nodules, excoriations, and generalized erythema all over his body, as seen in Figure 1. On his nose, we found a tumor with purulent ulcers covered bilateral nostrils. He had lip swelling, and a tumor with purulent ulcers on his lips. His tongue looked dirty, covered with a white layer, and some ulcers. On his chest, we found normal symmetrical expansion of both sides, no retraction, prominent rib, loss of subcutaneous fat was present. From auscultation, he had vesicular breath sounds, no rhonchi or wheezing, normal sound of S1 and S2. His abdomen was soft with peristaltic sound within the normal limit. There was wasting in all extremities and edema on the right arm. From anthropometry, we found his body length was 167 cm, with an ideal body weight of 60.3 kg. The middle upper arm circumference was 22 cm, so the estimated body weight was 50.44 kg.

To assess functional status, we used a handgrip. The patient handgrip strength was 12 kg (weak). Nutritional status was assessed using Subjective Global Assessment (SGA)<sup>4</sup>. We assessed this patient had B on his SGA score.



**Figure 1. The patient condition when he was consulted**

From history-taking, he complained about decreased oral intake since the previous four months due to loss of appetite and worsened in the last one week due to nausea, that occurred after he took medicine. He had vomited three days before, twice a day, consist of leftover food and gastric juice. Intermittent epigastric pain in daily, no abdominal pain, intermittent fever since four months ago worsen in the last one month, cough with thick white phlegm since six months ago, and intermittent shortness of breath. Weight loss in the last month was challenging to assess because of the swollen in several regions of the body. He had no defecation in two-days, his urination was within normal limit, yellowish colored urine.

From past medical history, he had no hypertension or diabetes mellitus. He was diagnosed with chronic eczema for the last 20 years, with spontaneous resolution, but the lesion never really disappear. He had a history of radiochemotherapy three years ago, unfortunately, we could not assure the regimen therapy due to a lack of information from the family. He had not finished a cycle of course regimen. At that time, he was diagnosed with skin cancer. He was on TB therapy for three months. He stopped the anti-TB drugs for several days due to severe nausea. However, after the symptoms decrease, he started to consume it again. He had no history of malignancy in his family. He used to smokes one pack of cigarettes/day for 20 years, quit two years ago, and drink alcohol bottle/week, quitted, and drink alcohol one bottle/week, quitted one year ago.

From food history, we knew that at his healthy times, he ate 2-3 times daily, 2-3 portion of rice, with a variety of side dishes and vegetables. He ate fruit 1-3 times a week. He liked instant noodles, grilled fish, and soda four months ago. The oral intake was decreased and worsen in last week due to nausea and vomitus. He had no food allergy or lactose intolerance. He restricted egg and chicken consumption because he felt itchy after he consumed it. From 24-hours food recall, he consumed: Energy: 587.5 kcal; Protein: 27.7 grams; carbohydrate: 105.6 grams; Fat 5.4 grams coming from the different variety of foods.

**Table 1. Laboratory values during the rest of the patient's hospitalization period**

Parameters	Pre Treatment		Post Treatment	
			5th day	16th day
Hb (g/dL)	9.3	10	9.2	10.2
WBC ( $10^3/L$ )	27.16	37.12	39.59	25.6
TLC ( $sel/mm^3$ )	2100	2430	2100	3610
PLT( $10^3/L$ )	572	696	158	15
Urea (mg/dL)	42	28	94	85
Creatinine (mg/dL)	1.69	1.14	2.4	1.53

Note : Abbreviations: Hb, Hemoglobin; WBC, White Blood Cell; TLC, Total Lymphocyte Count; PLT, Platelet

**Table 2. Albumin value during the rest of the patient's hospitalization period**

Parameter	Pre Treatment	Post Treatment			
		2nd day	4th day	6th day	16th day
Albumin (g/dL)	1.6	1.7	1.8	1.8	1.9

Our working diagnosis was Moderate Protein Energy Malnutrition (Subjective Global Assessment Score B) on cutaneous lymphoma post-biopsy day 2 with lung tuberculosis on treatment (continuous regimen) with positive bacteriology findings with unknown HIV status, anemia, and severe hypoalbuminemia. Our prognostic nutritional index was 26.5.

This patient was consulted due to a decrease in food intake, appetite loss, swallowing difficulty, and inflammation, mainly due to infection and the underlying conditions of cancer. The target of nutritional therapy was to overcome dysphagia, prevent disease-related hypercatabolism, nutrient deficit (hypoalbuminemia), improve nutritional status, fasten wound healing, and give nutritional education to patient and his family about nutritional support for this disease.

The patient swallowing difficulty was occurred due to fungal infection on the oral mucosa and poor hygiene. Besides, the tumor location that was occluding nostrils made it difficult for the swallowing process. An oral gastric tube (OGT) was inserted to overcome swallowing difficulties. The OGT was detached when he was having cough and vomiting. We planned for reinsertion, but the family refused due to the patient's worsening condition. Peripheral intravenous access could not be chosen due to a high phlebitis risk. Phlebitis is preceded by thrombus on the vein wall, and its risk is higher in older age due to a decrease of elasticity of the blood vessel. A high risk of phlebitis occurred on this patient was due to comorbidities that decrease immunity and increase infection risk. Therefore, a central vein catheter was inserted for long-term parenteral nutrition access.

Nutritional therapy with diet 2050 kcal/day was programmed. We started macronutrient composition with protein 1.4 gram /ideal body weight (kg)/day = 84.42 gram (16.5%); carbohydrate 50 % = 262.25 gram and fat 33.5 % = 76.3 gram; fluid requirement 1800 mL/day.

We changed macronutrient composition on the first day of follow up due to the low level of albumin (Table 2). We decided to increase protein to 1.5 gram/ideal body weight (kg)/day = 90.45 gram (18%) with carbohydrate 50% and fat 32%. We adjusted protein intake based on kidney function. When creatinine level increased to 2,4 mg/dL at the 5<sup>th</sup> day of follow up (Table 1), we changed protein intake to 1.2 gram/ideal body weight (kg)/day until the last day of treatment. With decreased protein target, it was seen to reduce creatinine level to 1.53 mg/dL (Table 1).

Diet was initiated from 1025 kcal (50% of expected energy target) and gradually increased based on the patient's tolerance and intake. Nutritional intake was given via oral with porridge and high biological value side dishes from animal and plant-based, high protein oral nutritional support (3x 100 kcal), fruit juice (100 kcal) and virgin coconut oil (120 kcal).

Hypoalbuminemia correction was given by a high protein diet (protein up to 1.5 gr/ideal body weight (kg)/day, Human Albumin 25 % 100 ml/24 hour/intravenous (target: 300 ml, by 3 times administrations with albumin target: 3.5 g/dl) and snakehead fish extract. We gave him other supplements and medication such as zinc, vitamin B, snakehead fish extract capsule, and vitamin D+calcium hydrogen phosphate. We also added antifungal drop and anti-emetic tablets to reduce the symptoms. Nutritional and palliative management therapy for patients in terminal condition was planned. We encourage nutritional education for the patient and his family to help them understand the importance of nutritional support to improve nutrition status. We gave them information about food sources to improve nutritional status, and we taught them how to maintain food and fluid intake according to schedule and planning. We also maintained good cooperation and communication with the patient and his family, the doctor from other departments, nurses, and dietitians.

Earlier, based on the SGA score, it was categorized as moderate protein-energy malnutrition. After a reassessment of SGA on day-14, the patient had C on the SGA score. Therefore, the nutritional diagnosis became Severe Protein Energy Malnutrition. Mid upper arm circumference of the patient was 22 cm on the consultation day, and 21.8 cm after 14 days of treatment.

The albumin level increased from 1.6 mg/dl to 1.9 mg/dL during hospitalization (Table 2). We gave the patient two bottles of Human Albumin 25% 100 cc, so that albumin level increased from 1.6 mg/dL to 1.8 mg/dL. During the absence of OGT, we maximized parenteral nutrition with macronutrient content as needed, where parenteral proteins contained BCAA. Without the infusion of human albumin, it turned out that nutritional therapy with snakehead fish extract (Pujimin®) was given, which had a high dosage albumin protein, which can increase the albumin level from 1.8 mg/dL to 1.9 mg/dL (Table 2).

## **Discussion**

The energy need for this patient was measured by Harris-Benedict Formula with an activity factor of 1.2 and a stress factor of 1.3. From the calculation, Basal Energy Expenditure was 1320,5 kcal (Harris-Benedict formula), and the total energy requirement was 2050 kcal.

Macronutrient composition was given by protein up to 1.5 gram/ideal body weight (kg)/day, which was 90.45 gram (18%) by taking hypoalbuminemia and wound healing process as a consideration. On cancer patients, it is recommended that the energy ratio from fat to carbohydrate should be higher than healthy people<sup>3</sup>.

Cytokine activation from inflammation activates neuroimmunity. An increase in cytokine levels stimulates cyclooxygenase enzyme activation and produces prostaglandin and arachidonate acid as an inflammatory mediator. Prostaglandin stimulates CART/CRF/POMC neuropeptide and inhibits NPY/AgRP neuropeptides, which decreases oral intake due to early satiety (anorexia). Moreover, cytokine can alter gaster motility by inhibiting efferent signal that regulates appetite and inhibit leptin and cholecystokinin production<sup>5</sup>.

Some of the inflammatory cytokines that released during malignancy are IL-1, TNF- $\alpha$ , IL-6, which are the main mediator from intermediate metabolism. These cytokines will stimulate inflammation mediator releases such as leukotriene and prostaglandin<sup>6</sup>. Cytokine release will make worsening and prolong of hypercatabolic condition<sup>7</sup>.

For this condition, more energy was needed. Hence, nutritional management was provided by giving a high calorie and protein intake and intensive nutritional education. Family support in terms of food provision and attention was also needed to increase food intake. Calories needed for a cancer patient should be extremely high, and protein as well. Based on nutrition management recommendation on cancer patient by ESPEN (2016), high protein intake for a cancer patient is recommended by giving a minimal 1 gram/body weight (kg)/day and target should be within 1.2 – 2.0 gram/body weight (kg)/day on a patient with normal kidney function<sup>5</sup>.

Older age and systemic inflammation have the potential to make anabolic resistance, which is a decrease protein synthesis response from an anabolic stimulus<sup>3</sup>. The wound healing process and surface area of the wound make a free amino acid loss, which makes a decrease in serum albumin level. Therefore, a low protein diet in a wound patient results in a negative nitrogen balance, hence that cancer patients are given a higher protein intake in the hope of a positive nitrogen balance. This dietary change aims to accelerate the process of forming new damaged tissue<sup>3,5</sup>.

Hypoalbuminemia in cancer is caused by decreasing albumin synthesis and increasing albumin breakdown and transcapillary leakage of albumin. The human body will respond to cancer cells as a stress condition hence increasing acute phase protein (e.g. IL-1 $\beta$ , IL-6, and tumor necrosis factor) and decreasing albumin production<sup>5</sup>. A low albumin level often occurred due to acute or chronic inflammation. Cytokines (TNF  $\alpha$ , IL6) are released as a part of an inflammatory response that decreasing albumin serum through some mechanisms<sup>5</sup>.

Based on the low level of albumin in this patient (< 3.5 mg/dL), protein intake was given up to 1.5 gram/ideal body weight (kg)/day or 90.45 gram per day. Parenteral protein given to this patient contained branched-chain amino acid (BCAA).

Oxidation of BCAA is a crucial process to provide energy for muscle and playing a role in compensatory mechanisms on high energy consumption to compensate for negative protein balance due to chronic inflammation on cancer. On normal conditions, BCAA oxidation will give 6 – 7% energy for muscle. During a high catabolic condition, the usage of this protein can be increased to 20%. On a clinical trial study that gave parenteral BCAA to patients with cachexia cancer, it is shown that BCAA could increase leucine influx, and protein synthesis while protein breakdown still in a stable condition<sup>8</sup>.

Adequate nutrition plays a vital role in anemia management of cancer patients. This patient anemia was not only due to iron intake but also an inflammatory response due to infection that was worsening the anemia<sup>3,9</sup>. Anemia in cancer can occur due to immune system activation and inflammation due to the malignancy itself. Some cytokines produced by the immune systems such as interferon (IFN), tumor necrosing factor (TNF), and interleukin-1 (IL-1) stimulate the process for anemia. Moreover, cancer itself can have a direct effect on anemia<sup>9,10</sup>.

Decrease of red blood cell production on cancer patients occurred due to erythropoiesis interference from many factors. These factors include reduced erythropoietin production due to kidney disorders, iron, folate, and vitamin B12 folate deficiency or bone marrow suppression due to metastatic process, myelodysplasia, or any cause due to myelosuppressive from chemotherapy. The additional indirect effect includes nutritional deficiency due to loss of appetite in cancer patient<sup>10</sup>.

Nutritional intervention for cancer-related anemia is aimed to improve the underlying inflammation process and supplementing deficiencies. The nutritional intervention also gives supportive treatment by providing adequate micronutrients. It has been shown that vitamin C, zinc, and vitamin B has been depleted in cancer patients, and correlated with anemia<sup>11-14</sup>.

Immune depletion is one of the body's mechanisms to reduce the rate of inflammation. Total lymphocyte count (TLC) is an indicator of immune function (B cells and T cells) that can be used as a screening and assessment of nutritional status. However, in some circumstances, such as leucocytosis, malignancy, and steroid use, TLC levels cannot be used as an indicator of nutritional status<sup>5</sup>.

The B and T lymphocyte levels can describe the function of the body's immune system. In cancer, there is an inhibition of lymphocyte cell response, where this condition is associated with increased patient susceptibility to secondary infection complications and increased risk of patient mortality. Meeting the needs of adequate energy is a therapy to improve the body's immune system. Besides, zinc supplementation is expected to improve the immune system. It is known that zinc plays a role in the activation and proliferation of B cells and T cells<sup>11</sup>.

To get optimal wound healing is very dependent on adequate nutrition. The deficiency of certain nutrients can inhibit the wound healing process. Malnutrition is also known to be associated with an increased incidence of infection and slow healing of wounds.

The adverse effects of nutrient deficiency or malnutrition on wound healing occur by prolonging the inflammatory phase, decreasing fibroblast proliferation, and inhibiting collagen synthesis. Micronutrients are needed in small amounts per day, but micronutrients play an essential role in cell metabolism and as an enzyme cofactor that plays a role in the process of wound healing. In these patients, the addition of antioxidants sourced from food, vegetables, and also supplementation that contains micronutrients, which are essential for wound healing.

Vitamin A is known to play a role in wound healing at the inflammatory stage. Vitamin A will stimulate the immune system by increasing the number of macrophages and monocytes in the wound during the inflammatory stage. Besides, vitamin A is also known to increase epithelial cell formation and collagen deposition by fibroblasts. Therefore, vitamin A is also recommended for open chronic wounds<sup>12</sup>.

The Recommended Dietary Allowances of vitamin A is 800 RE/day or equal to 2700 IU. In wound patients, the need for vitamin A is more significant. Studies on the administration of vitamin A 10,000 IU/day to 25,000 IU/day orally for a short period (14-21 days), found faster and better wound healing<sup>13,14</sup>.

Vitamin C, or ascorbic acid, plays a role in collagen synthesis, namely hydroxylation of procollagen to collagen. Besides, vitamin C also plays a role in fibroblast proliferation, capillary formation, and neutrophil activity. Vitamin C deficiency can disrupt the wound healing process. Higher vitamin C excretion occurs in smokers and alcohol drinkers. Vitamin C supplementation of 100-200 mg/day above the RDA can accelerate the wound healing process. In patients with extensive wounds, it is recommended to administer vitamin C in the amount of 500-2000 mg orally to accelerate the wound healing process. The provision of high doses of vitamin C must be followed by adequate fluid intake to prevent the formation of kidney stones<sup>15</sup>.

Vitamin D is a group of fat-soluble secosteroids. Especially important are vitamin D3 (cholecalciferol), 25-hydroxyvitamin D3 (calcidiol) and 1,25 dihydroxy vitamin D3 (calcitriol; the necessary active metabolic form). Vitamin D also has anti-cancer properties by working to increase cell maturation and differentiation, inducing apoptosis, and down-regulation of telomerase<sup>16</sup>.

In this patient, although vitamin D examination was not carried out, administration of the drug OAT (Rifampicin) is known to accelerate the breakdown of vitamin D caused by the induction of the CYP450 enzyme. Vitamin D is a fat-soluble vitamin, so supplementation of this vitamin should be done during or after a meal<sup>17,18</sup>. The dose of vitamin D given to this patient is 600 IU/24 hours, due to worsening kidney function and lack of oral intake (fat), an increase in dose was not carried out. Zinc is a micromineral that plays a role in various cell metabolisms. Zinc supplementation is only given to zinc deficiency, which is often also found in patients with wounds. The zinc nutrition adequacy rate is 12.1 mg/day for healthy adult males. In patients with extensive injuries, zinc supplementation can be given up to 40 mg/day. Standard preparations for cancer cachexia patient is 10-30 mg/day<sup>11,19,20</sup>.

AKI (Acute Kidney Injury) is common in cancer patients and have medium and long term consequences because it is related to kidney function<sup>21</sup>. Patients with cancer are susceptible to the development of cancer or chemotherapy-related conditions that ultimately result in renal hypoperfusion<sup>21</sup>. In these patients, it is possible that the AKI occurs because of kidney hypoperfusion and also due to sepsis, as well as dehydration or volume depletion due to lack of intake. Besides, it is possible that this condition also a result of thrombotic microangiopathy from thrombocytosis, which causes intrinsic abnormalities of the kidneys to AKI (intra-renal AKI)<sup>21</sup>. In this patient, we adjusted the protein target based on kidney function. There was an improvement in kidney function at the end of the treatment as a result of the adjusted daily protein targets.

Nutritional education in patients and their families about the importance of nutrition after surgery (post debridement) to accelerate the process of wound healing, reduce the risk of infection, hospital length of stay, and we also gave nutritional education about diet in cancer to improve the quality of life.

Palliative care were associated with the reduction of suffering. The reduction of suffering was relieved not only physical symptoms such as pain but also psychological, social, and spiritual stress. The involvement of palliative care teams from the beginning in the care not only help the patients, but also the patient's family to understand the course of the patient's disease<sup>22</sup>.

The cause of death in the patients was due to respiratory failure. In this case, respiratory failure can occur due to anatomical abnormalities, where tumors are enlarged and obstruct the airway, making it difficult for the patient to breathe effectively. Besides, metabolic acidosis also occurred as evidenced by BGA results on 16 February 2020, almost a day before patient's death, the results of Blood Gas Analysis is in the state of "compensated metabolic acidosis". Metabolic acidosis that occurred can be caused by the accumulation of lactic acid, which is usual in cancer patients. One of the forms of acid-base disorders is lactic acidosis, which caused metabolic acidosis. Lactic acidosis occurs as a result of the accumulation of lactate caused by hypoxia or tissue ischemia<sup>23</sup>. This process was evidenced by the results of the laboratory test on 13 February 2020, where the results of arterial lactate 7.2 mmol/L. High levels of lactate due to increased glycolysis as an effect of hypermetabolism in cancer, and also as a sign of inadequate tissue perfusion/hypoxia of tissue<sup>23</sup>. The end of life is indicated by signs of brain stem death on the 17<sup>th</sup> day of treatment and respiratory failure.

In conclusion, providing adequate nutrition with the right amount of macro- and micronutrient composition is crucial for cancer patients. However, in this case, concerning the terminal condition and other difficulties, nutritional intake had never reached the expected target. Nutritional advice is an individual approach, and it requires routine follow-up to assess and adjust the macro- and micronutrient composition.

### **Conflict of Interest**

There is no conflict of interest in publishing this article

## Acknowledgments

The authors would like to thank our supervisors for useful discussions and special thanks to all the Wahidin Sudirohusodo hospital staffs for their help and support

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