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Mellova Amir Amir
Pharmaceutical Science Department, Faculty of Mathematics and Natural Sciences, National University of Sciences and Technology, Jakarta 12640, Indonesia, masrizaldt@yahoo.com

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Mellova Amir Masrizal

Pharmaceutical Science Department, Faculty of Mathematics and Natural Sciences,
National University of Sciences and Technology, Jakarta 12640, Indonesia

E-mail: masrizaldt@yahoo.com

Abstract

Protein-Energy Malnutrition (PEM) is believed to lead to an increased susceptibility to infection, or cause impaired immunity. Infection, occurring with malnutrition, is a major cause of morbidity in all age groups and is responsible for two-thirds of all death under 5 yr of age in developing countries. Many cells of the immune system are known to depend for their function on metabolic pathways that employ various nutrients as critical factors. The most consistent changes in immune competence in PEM are in cell-mediated immunity, the bactericidal function of neutrophils, the complement system, the secretory immunoglobin A, and antibody response.

Keywords: protein-energy malnutrition, immune system, cell mediated immunity, amino acid deficiency, antibody responses

Introduction

Millions of people, in every generation from rural areas of developing countries, live in poverty, which leads to malnutrition. Malnutrition, known as Protein-Energy Malnutrition (PEM), is recognized by two syndromes, kwashiorkor and marasmus.

Malnutrition and infection have an impact on health and survival. Malnourished people are believed to have an increase susceptibility to infection. Infection, occurring with malnutrition, is a major cause of morbidity in all age groups and is responsible for two-thirds of all death under 5 yr of age in developing countries [1].

There are many causes of increased susceptibility to infection among the underprivileged, malnourished community. Although primary protein-energy malabsorption is not commonly seen in medical or surgical worlds, physicians are becoming more aware of the fact that malnutrition can be secondary to renal, hepatic, or cardiopulmonary disease and malabsorption problems.

Malnutrition is one of the most widespread causes of secondary immunodeficiency. A significant impairment of the cell-mediated immune system has been demonstrated by many investigators [2-4].

Most often, malnutrition involves a composite syndrome of multiple nutrient deficiency. It is obvious, because single nutrients such as amino acids, lipids, vitamins, minerals, may have rather specific effects in host resistance, and they frequently complicate PEM and many diseases. Several animal studies have begun to investigate the aspect of nutrient and immune proficiency.

Protein-Energy Malnutrition

Protein-energy malnutrition has been considered a range of pathological conditions arising from a coincident lack of varying proportion of proteins and calories. Occurring most frequently in infants and young children, and commonly associate with infection.

The most obvious feature of PEM is reduction or failure of growth. Different organ systems are altered to varying degrees by PEM, with tissues, which have the highest rates of turnover being most severely affected. Two types of tissue expedient especially high rates of turnover, and therefore are particularly susceptible to deprivation of essential nutrients. First, tissues with a high-rate of all turnover, such as intestine, testes, and bone marrow. The other type of tissue is susceptible to an insufficiency of essential nutrient contents, liver and pancreas, which are metabolically very active and experience a high rate of cytoplasmic turnover.

Two major categories of PEM are kwashiorkor and marasmus. Kwashiorkor and marasmus are different events during homologous dietary deficiencies. The symptomology of marasmus is thought to be the result of the extreme degree of adaptation of the body to a deficient diet. In this situation, essential organs and function are protected at the expense of fat and muscle tissue. kwashiorkor results after the host can no longer adapt to the nutritional stress.

Nearly all aspects of homeostasis in the malnourished organism are affected by metabolic and biochemical abnormalities, such as altered metabolism of proteins and amino acids. Perhaps the best indication of altered protein metabolism in PEM is a reduction in the level of circulatory plasma protein, the albumin fraction being particularly affected [5].

It is known that the polysomal profile is markedly affected by nutritional condition, which would certainly have a major effect on the rate of protein synthesis and degradation [5].

Host Immune Response in Protein-Energy Malnutrition

The immune system is enormously complex and highly integrated, with "built-in" checks and balances to regulate each antigen-specific response. This complexity reflects a system that is rapidly responsive, continually vigilant, highly precise and sensitive in terms of antigen recognition and detection, capable of amplification, and possessed of a superb capacity for memory [6]. However, this complexity also permits a variety of extraneous factors to influence or impair immune system functions. Nutritional status and intercurrent infections are among the most important of the extrinsic influencing factors [1,6,7].

The resistance of the host animals against bacterial infection is dependent on lymphocytes, antigen specific, that participate in the humoral, the beta-cell system of antibody production, and the T-cell system of cell mediated-immunity. These systems work in conjunction with several nonspecific factors of resistance, such as, skin, mucous membranes, complement, phagocytic cells, lysozyme, and bactericidal capacity of blood and tissue phagocyte [1,6]. T-lymphocytes, predetermined clone proliferate, produce molecules responsible for increasing the phagocytic and bactericidal ability of monocytic blood cells and also directly participate in graft rejection, cytotoxicity against cancer cells, delayed-type hypersensitivity, suppression of the autoimmune phenomenon, and regulation of the immune response [6].

Malnutrition, Infections, and Immunity

Most attention during the period of immunonutritional reemergence focused on effects of PEM on the immune system and other host defensive mechanism. The myriad observations, some quite old and some quite new clearly show that the immune system can not function optimally if malnutrition is present. Malnutrition also produces adverse effects on antigenically nonspecific mechanism of host defense. Careful observation showed a correlation between nutritional status and morbidity and mortality largely due to infections.

The initial work on interaction between nutrition and immunity was carried out in young children with PEM [7-9]. It was seen that infection and malnutrition were invariably linked together, each aggravating the other. It can be caused by several factors, such as lack of health education, illiteracy, contaminated food and water, poor sanitation and over crowding are important in worsening the situation. The hypothesis that depressed immune system in malnutrition enhances the risk and severity of infections are compatible with the consistent impairment of immunity in PEM and hospitalized patient with primary immuno-deficiencies.

The Effect of Protein Energy Malnutrition on the Immune System

Malnutrition can cause disfunction of various organ systems. The degree of severity on these organs depends on several factors, including the amount and rate of protein synthesis, the rate of cell proliferation, and the role of individual nutrients in metabolic pathway. Lymphoid tissues are very vulnerable to these damaging effects.

Many cells of the immune system are known to depend for their function on metabolic pathway that employ various nutrients as critical factors. The most consistent changes in immune competence in PEM are in cell-mediated immunity, the bactericidal function of neutrophils, the complement system and the secretory immunoglobulin A (IgA) antibody response [2,5,7-9].

According to modern definitions, "Cell-mediated immunity is immunity whose induction and expression is T-cell dependent. " Cell-mediated immune is regarded as non humoral immunity having to do with delayed-type hypersensitivity in the skin test and T-cell functions . Many of these parameters have been used in malnourished host studies, including the anatomy of lymphoid organs, allograft rejection, transfer of delayed hypersensitivity, in vitro test of T-cell function and T-cell dependent antibody synthesis.

A variety of investigations have been carried out in children with PEM to estimate the degree of depletion of the thymolymphatic system and its effect on cell-mediated immune [8, 10].

Tonsil Size

The tonsil is the only visible lymphoid tissue in the body and it may play a significant role in lymphatic function. Tonsils were measured using longitudinal histological section the length and depth of the tonsil. When adjusted for age, the tonsils of children with PEM were significantly smaller than those of control children [5,8,9]. It has created the impression that lymphoid areas were reduced in PEM. kwashiorkor is associated with the greatest reduction in bulk of these lymphoid tissue.

Estimation of the degree of paracortical depletion of lymph nodes in result marked paracortical depletion was noted about 30% in kwashiorkor cases and 29% of cases with thymic atrophy. This depletion indicates an exhaustion of immunocytes concern with cell-mediated immunity and the association between marked depletion, severe thymic atrophy and PEM, particularly kwashiorkor, is strong histological evidence that an acquired deficit in cell-mediated immunity is present in PEM [9].

Delayed Hypersensitivity Reaction

The capacity to react to 2,4-dinitro chlorobenzene sensitization of the skin was compared in children with PEM and control [5, 8]. In the PEM group, there was no reaction of blastogenic activity [5].

Total Lymphocyte Count and Immunoglobulin Levels

In eight cases the antemortem and post-mortem immunoglobulin levels were not below normal (IgG, IgM). IgA was raised in four cases and complement was below normal in seven cases [8]. Another researcher found that IgM level is decreased in mildly malnourished children, and higher in moderately malnourished children at 2 yr of age and albumin level, C3 complement, and total protein are decreased in mildly and moderately malnourished children [5]. The frequency of rosette framing thymus-dependent lymphocytes was reduced in the peripheral blood of malnourished infant and children, which is paralleled the impairment if delayed hypersensitivity response to 2,4-dinitrobenzene and decreased DNA synthesis by lymphocyte challenge with phytohaemogylutinin [2].

Effect of Single Amino Acids in Correlation to PEM in Immunity

Concomitant deficiencies of one or more micronutrients normally occur with severe PEM. It can be seen in kwashiorkor or marasmus patients, that are often accompanied by problems of energy deficiency. It is virtually impossible to define causal relationships between individual nutrients and specific abnormalities in host defense clinically. Nonetheless, studies and analyses suggest that a single nutrient deficiency may have rather specific effects in host resistance. A few studies have determined whether single amino acids have an individual role. Although many observations attest to the importance of sufficient protein nutrition for maintaining the immune system. Several animal studies investigated the aspect of nutrient and immunocompetence. Such as the effect of essential amino acids, branch-chain amino acids

(BCAA), lipoprotein amino acid on immune response, which are deficient tryptophan and niacin [11] Chandra, tryptophan [2], combine deficiency of phenylalanine and tryptophan.

Branch-chain amino acids, which are leucine deficiency, combination of 7% dietary leucine overload in rats with protein-poor diet (4% casein), lipoprotein, methionine, choline. In patients with kwashiorkor (PEM), the concentration of individual plasma free amino acids become depressed to varying degrees.

Single amino acids deficiencies in animals have marked defect on antibody production and little defect on T-lymphocyte function. But in underdeveloped countries, children with kwashiorkor or PEM show normal to high immunoglobulin concentration and increased immunoglobin G synthesis, and have impaired in cell-mediated lymphocyte. It is probably caused by chronic parasitism plus repeated and prolonged infection episodes in those children, even though they are able to divert sufficient amino acids from other potential uses to manufacture plasma immunoglobins and acute-phase reactant protein [12].

Discussion

Depression of cell mediated immunity by PEM could be the result of an absolute or relative deficiency of amino acids for cell multiplication. Alternatively, children with PEM are known to have raised levels of plasma cortisol, which can decrease the thymolymphatic system and repeated infection may also play a part. Decreased T-cell numbers in protein-malnourished animals is caused by decreased synthesis of thymic hormones. Thymic hormones are responsible for the development of the cell-mediated immune response.

Clinical and hispathological studies have shown that the most consistent changes in immuno-competence are impaired cell mediated immunity and humoral immunity moderate or severely. The lympoic tissues, particularly the thymus were found to be atrophied, reduction in delayed cutaneous hypersensitivity, fewer T-cells, decreased thymulin activity. Impaired secretory immunoglobulin A antibody response and reduced concentration and activity of complement components. The mechanism by which the T-lymphocyte population is gradually depleted from the thymus or lymphoid organs during malnutrition is not readily apparent.

The effect of several nutrients, particularly trace elements and lipids on the afferent and effector limbs of the immune response should be studied, because a number of observations indicate the crucial role of several nutrient in key metabolic pathways and cell functions, that frequently complicate PEM and many systemic diseases. Moreover, human malnutrition is usually a complete syndrome of multiple nutrient deficiencies, in addition, PEM children have clinical, biochemical, and hematological changes (e.g., weight loss, muscular atrophy, enlarged liver, loss of subcutaneous tissue, and edema) depending on the degree of malnutrition.

The analysis of the molecular basis of immunodeficiencies in PEM is in its infancy, also is needed for future research. The influence of nutrition on antigen-non-specific mechanism of host resistance has also been inadequately studies and the biological relevancies of impaired immunity on malnutrition.

Summary

Protein-energy malnutrition increases susceptibility to infection, or cause impaired immunity. Many cells of the immune system depend for their function on metabolic pathways. The most consistent changes in immune competence in PEM are in cell-mediated immunity, the bactericidal function of neutrophils, the complement system, the secretory immunoglobin A, and antibody response.

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