

DEPRESSION OF NEUTROPHIL FUNCTION FOLLOWED BY SEVERE INFECTION IN A CHILD WITH MARASMIC KWASHIORKOR

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Abstract

Malnutrition in childhood continues to be one of the most important risk factor for secondary immunodeficiency in the world; therefore one should think of existence of malnutrition in a child suffering of frequent infections, not only in developing country, rarely but still possible in developed country also.

Undernourishment in the early childhood is a trigger for starting a vicious cycle of impaired immunity, recurrent infections, and worsening malnutrition. Taking out from that cycle is an urgent and complex process, in which in parallel the infection should be controlled and the nutritional status solved out, and then, slowly follows the restoration of the immune system.

We present a patient at the age of 13 months, with marasmic kwashiorkor accompanied by severe infection manifested with sepsis. The laboratory investigations revealed severe anaemia, hypo-proteinemia and impaired immunological response, first of all neutrophil dysfunction with decreased oxidative metabolic response during the phagocytosis, paralyzed first line of defense of the organism and open possibility for bacterial or fungal invasion, multiorgan failure and high risk for fatal outcome. Because malnutrition and infections had many causes, only multiple and synergistic interventions embedded in true multisectoral programs, fortunately, were effective and got positive outcome.

Key words: malnutrition, marasmic kwashiorkor, neutrophil dysfunction, NBT test, infections.

Introduction

Malnutrition continues to be a major public health problem throughout the developing world, and indirectly is responsible for about half of all deaths in young children [12]. The risk of death is directly correlated with the degree of malnutrition [7, 18].

Protein-energy malnutrition (PEM) usually manifests early, in children between 6 months and 2 years of age, when the immune system is still not completely mature, associated with early weaning from breast-feeding, delayed introduction of complementary foods, a low-protein

diet and severe or frequent infections [12]. Severe malnutrition, typified by wasting, edema or both, occurs almost exclusively in children [3]. Marasmic kwashiorkor is defined as malnutrition with severe wasting in the presence of edema [3, 9].

After insufficient supply of protein, carbohydrates and fat, the next major cause of protein-energy malnutrition is severe and chronic infections, particularly those producing diarrhea.

It is well known that undernourished children have impaired immune responses. The abnormalities are seen more or less in all compo-

nents of the immune system, such as significant impairment of cell-mediated immunity, phagocyte function, complement system, secretory immunoglobulin A antibody concentrations, and cytokine production. [1, 5, 6, 11, 13, 14, 16].

The pathologic changes that caused immunologic deficiency are result of protein deficiency and lack of immune mediators. Metabolic disturbances also play a role in impaired intercellular degradation of fatty acids because of carbohydrate deficiency [12].

As a result of vicious cycle of impaired immunity, recurrent infections, and worsening malnutrition, secondary immunodeficiency is developed [10].

Most children with severe protein-energy malnutrition have asymptomatic infections, because the polymorphonuclear phagocytes, which are the effector cells that play the main role in the first line of defense, fails to respond with chemotaxis, opsonization and phagocytosis of bacteria, viruses or fungi [5, 6, 12, 15]. The neutrophils function is so much depressed, that the body cannot even produce the fever that is typical sign of inflammation [2].

Despite the intensive care and manifold dietary and therapeutic approaches to severe malnutrition and infections that have been tried, patients with marasmic kwashiorkor are of high risk to die [12, 17].

We present a patient at the age of 13 months, with marasmic kwashiorkor followed by anaemia, and severe hypoproteinemia and severe infection manifested with sepsis. The laboratory investigations revealed immunological disturbances, but first of all neutrophil dysfunction with decreased oxidative metabolic response during the phagocytosis. Prompt management was required and long follows up afterword in achieving the best outcome.

Case report

Our patient is a 13-month old girl, born with caesarean section in 36th gestational week, with 2750gr weight and 48cm height at birth. Exclusively breast – fed for only a month and a half, and afterwards with half strength milk for the following three months. Due to the fact that she vomited a lot during this period, her nutrition consisted of only tea, instant soup and biscuits until the age of 13 months. No vege-

tables, no fruit, no meat and no floury products. She suffered from frequent upper respiratory infections. For a longer period of time she was pale, refused any food, and there was no weight gain. Two weeks prior to being admitted in hospital, skin changes started, especially in the genital region, and later spread all over the legs and around the mouth. She was treated locally first with antibiotic ointment but with no success. She was admitted at our immunology department in extremely serious septic condition, somnolent, apathetic, with weak and almost silent cry, dehydrated, intoxicated, with generalized fatigue. Her body weight was 6200 grams, with edema on the distal part of the legs. She had sepsis with multiorgan failure (oral candidiasis, bronchopneumonia, hepatomegaly and diarrhea) and still had not elevated temperature as a sign for inflammation [15]. The skin was pale, translucent and radiant, with decreased turgor and elasticity, with massive dermal changes on the back, gluteal and genital region and all over the legs. He had decubitus in the sacral region. That entire region was without epithelium, dark colored, with plasma-rhea and bleeding with crusts.

It was more than obvious that it was a case of difficult protein-energy malnutrition, which requested urgent hospitalization and treatment. The laboratory tests showed severe anemia, deep hypoproteinemia (total serum protein level 25g/l, albumins 8g/l), electrolytes disturbances and sepsis caused with coagulase negative *Staphylococcus*.

The immunological tests showed extremely low values of the NBT test, spontaneous 34 fmol/fag (normal value 129 fmol/fag), and stimulated 72 fmol/fag (normal value 280 fmol/fag), which suggested severe neutrophil dysfunction with impairment of the oxidative metabolic response during the phagocytosis. The serum immunoglobulin were almost normal (IgA = 0, 89; IgG = 5, 14; IgM = 0, 76 g/l).

Hence, there was a patient who due to the age has immune system not completely mature yet, and in addition to this has depressed immune system as a result of the severe malnutrition (marasmic kwashiorkor), and recurrent infections. This condition needed urgent, multidisciplinary guidance for correction the homeostasis, dehydration, electrolyte disturbances; sub-

stitution with vitamin and micronutrient; application of parenteral antibiotic therapy; repeated transfusion of erythrocytes, universal plasma and albumins and local skin treatment. During the whole stay, the patient was intensively treated and monitored, with daily control of the parameters and substitution of concerned deficiencies.

After one month big struggle for life in this patient, we succeeded to win the severe infection and to correct the malnutrition. It took 6 months since she become completely recovered, well-nourished, with normal neutrophil response and out of infections.

Discussion

Healthy way of life style with balanced protein-energy intake, as well as minerals and vitamins is necessary for optimal functioning of the immune system especially in childhood. Importance of good nutrition for development, establishing and regulation of the immunologic competence is starting since early fetal and neonatal period. So, the immune-competence is compromised in low birth weight infants and those who are small for gestation, showing persistent immunological impairment for several months, even years [4–6]. So was the case with our patient.

Brest feeding and mother`s milk enables nutrition during the first 6 month after birth, but also has protective function from infections by the presence of immunologic factors in it. Our patient had early weaning from breast-feeding and nourishment with low-protein and calorie diet with propensity for developing secondary immunodeficiency [18].

Nutrition and immunity have been known to be linked to each other for a long time ago. Lot of studies have confirmed that nutrient deficiencies impair immune response and lead to frequent severe infections resulting in increased mortality, especially in children [12]. Protein-energy malnutrition results in reduced number and functions of T-cells, phagocytic cells and secretory immunoglobulin A antibody response. The neutrophil function is impaired, especially their capability for intracellular killing of bacteria and fungi [5, 6, 12, 16, 17]. The levels of some complement components might be reduced also. The production of immuno-

globulins is the last that will be diminished by malnutrition. It seems that the repeated exposure to infection agents, are the strong antigen stimulation for antibody synthesis and the child`s organism economically save the proteins just for that. Some micronutrient deficiencies such as trace minerals and vitamins, particularly Zn, Fe, Se, vitamins A, B6, C and E can impair the immune response. [5, 11]. Iron is an essential part of hemoglobin, myoglobin and various enzymes. Its deficiency thus leads mainly to anemia, but also to several other adverse effects [12]. Zinc plays a central role in the function of cells mediating unspecific immunity, such as neutrophils and natural killer cells, and is needed for specific immune processes, such as balancing T helper cell functions [11, 12].

So, we had a girl born as low birth weight infants, with immature immune system, undernourished with low-protein and calorie diet that led her into severe malnutrition and diminished immunologic response that led her to severe septic infection and big chance to die. She had severe wasting in the presence of edema, the state defined as marasmic kwashiorkor [3]. Half of her body was with denudated skin lesions (that was just open door for infections) caused by malnutrition, immunodeficiency, micronutrient deficiency and severe infection. Total serum protein and albumin level were extremely low and needed urgent multiply substitution with universal plasma and albumins. Iron deficient anemia needed urgent correction with several transfusions of erythrocytes. The immunologic disturbances in this girl correlated with those found in the literature [4–6, 8, 11]. We found completely diminished oxidative metabolic response of the neutrophils during the phagocytosis, which meant no first line of defense or any immunologic response with possibility for severe infection even from ubiquitous microorganism and lethal outcome [13, 15].

Because malnutrition and infections have many causes, only multiple ad synergistic interventions embedded in true multisectoral programs can be effective [12].

It took a long fight to put under control the severe infections, to correct all the disturbances caused by malnutrition and to allowed the immune system of our patient is recovered.

Conclusion

Lately, we rarely do meet patients with such a serious malnutrition in our country, which make possible this kind of patient being misdiagnosed and treated for other skin diseases.

Undernourishment in the early childhood is a trigger for starting a vicious cycle of impaired immunity, recurrent infections, and worsening malnutrition. Taking out from that cycle is a complex and long process, in which in parallel should be solved the infections and the nutritional status and then slowly restoration of the immune system will be done.

Malnutrition in childhood continues to be one of the most important risk factor for secondary immunodeficiency in the world; therefore one should think of existence of malnutrition in a child suffering of frequent infections, not only in developing country, rarely but still possible in developed country also.

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Резиме

НАМАЛУВАЊЕ НА НЕУТРОФИЛНАТА ФУНКЦИЈА ПРИДРУЖЕНА СО ТЕШКА ИНФЕКЦИЈА КАЈ ДЕТЕ СО МАРАЗМИЧЕН КВАШИОРКОР

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Малнутрицијата во детството и понатаму продолжува да биде еден од најважните ризик-фактори за секундарен имунодефицит во светот; токму затоа би требало да се помисли на постоење малнутриција кај дете што страда од чести инфекции, не само во земјите во развој, туку, навистина ретко, но, сепак, возможно, и во развиените земји.

Неисхранетоста во раното детство го започнува маѓепсаниот круг во кој таа е причина за нарушен имунитет, што ќе води до повтору-

вачки инфекции, а тоа уште повеќе ќе ја влоши малнутрицијата. Излегувањето од тој круг е ургентен и комплексен процес, во кој треба да биде излекувана инфекцијата паралелно со корекцијата на нутритивниот статус, за потоа постепено да следува враќање на нормалните функции на имунолошкиот систем.

Презентираме пациент на возраст од 13 месеци, со маразмичен квашиоркор придружен со тешка инфекција манифестирана како сепса. Лабораториските испитувања открија тешка анемија, хипопротеинемија и мален имунолошки одговор, пред сè неутрофилна дисфункција по-

ради намалениот оксидативен метаболен одговор во тек на фагоцитозата, парализирана прва линија на одбрана на организмот и зголемена можност за бактериска или габична инвазија, со оштетување на повеќе органи и висок ризик од фатален исход. Бидејќи малнутрицијата и инфекцијата имаа повеќе причини, само мултипната и синергичната интервенција вградена во вистинска повеќесекторска програма, за среќа, беа ефективни и имаа позитивен исход.

Клучни зборови: неисхранетост, маразмичен квашиоркор, неутрофилна дисфункција, NBT-тест, инфекции.