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Severe acquired neutropenia in 15-month old girl – a case report

Ciężka nabyta neutropenia u 15-miesięcznej dziewczynki – opis przypadku

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Słowa kluczowe

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Neutropenia is a common problem in the practice of hematology. Acquired neutropenia is observed more frequently and mainly caused by viral infections. Described case concerns a 15 month old girl, who was hospitalized twice in the Department of Pathology Infants University Children's Hospital in Lublin because of neutropenia. During the first hospitalization hit with fever, pneumonia, inflammation of the throat and mouth. Then joined rash on the skin in type of herpes. In laboratory studies: agranulocytosis (neutrophils – 170/ μ l), elevated CRP, blood cultures negative, throat swab – *Staphylococcus aureus*, *Candida famata*. Serological tests have confirmed infection with HSV. After a week of discharge from the hospital, another hospitalization also with fever, inflammation of the throat and lungs, and neutropenia. In laboratory studies agranulocytosis (neutrophils – 70/ μ l). Expanded diagnostics of viral, bacteriological, immunological and metabolic tests. It was found a high antibody level of EBV and *Mycoplasma pneumoniae* – IgM; *Chlamydia pneumoniae* and *Pneumocystis carini* – IgG. The bone marrow aspiration biopsy of mature neutrophils was very low (1.2%). On this basis, the acquired severe neutropenia was diagnosed. For the treatment, except for those used previously (antibiotics, antifungal medicine), activated recombinant human granulocyte colony stimulating factor (rHuG-CSF), resulted in an improvement of the general condition of the child and the parameters of peripheral blood (granulocytes – 3760/ μ l). Control bone marrow examination after 7 months, showed an increase in the proportion of mature neutrophils (6.8%). Today, the girl without signs of infection with persistent neutropenia (neutrophils – 160/ μ l).

S t r e s z c z e n i e

Neutropenia jest częstym problem w praktyce hematologicznej. Ze względu na etiologię możemy wyróżnić neutropenie wrodzone i nabyte. Zdecydowanie częściej obserwujemy neutropenie nabyte, których dominującą przyczyną są zakażenia wirusowe. Opisany przypadek dotyczy 15-miesięcznej dziewczynki, która dwukrotnie była hospitalizowana w Oddziale Patologii Niemowląt Uniwersyteckiego Szpitala Dziecięcego w Lublinie z powodu ciężkiej nabytej neutropenii. Podczas pierwszej hospitalizacji trafiła z gorączką, zapaleniem płuc, gardła i jamy ustnej. Następnie dołączyły się zmiany skórne o typie opryszczki. W badaniach laboratoryjnych stwierdzono agranulocytozę (neutrofile – 170/ μ l), podwyższone CRP, posiewy krwi ujemne, wymaz z gardła – *Staphylococcus aureus*, *Candida famata*. Badania serologiczne potwierdziły zakażenie HSV. Po tygodniu od wypisu ze szpitala, ponowna hospitalizacja – również przebiegająca z gorączką, zapaleniem gardła i płuc oraz neutropenią. W badaniach laboratoryjnych agranulocytoza (neutrocyty – 70/ μ l). Poszerzono diagnostykę o badania wirusologiczne, bakteriologiczne, immunologiczne i metaboliczne. Stwierdzono wysokie miano przeciwciał EBV i *Mycoplasma pneumoniae* w klasie IgM, *Chlamydia pneumoniae* oraz *Pneumocystis carini* w klasie IgG. W wykonanej biopsji aspiracyjnej szpiku odsetek dojrzałych granulocytów obojętnochłonnych był bardzo niski (1,2%). Na tej podstawie rozpoznano ciężką nabytą neutropenię. Do leczenia, poza lekami stosowanymi poprzednio (antybiotyki, lek przeciwgrzybiczy), włączono rekombinowany ludzki czynnik wzrostu kolonii granulocytarnych (rHuG-CSF), uzyskując poprawę stanu ogólnego dziecka oraz parametrów krwi obwodowej (granulocyty – 3760/ μ l). Kontrolne badanie szpiku wykonane po 7 miesiącach, wykazało wzrost odsetka dojrzałych granulocytów obojętnochłonnych (6,8%). Obecnie dziewczynka bez cech infekcji, z utrzymującą się jednak neutropenią (neutrocyty – 160/ μ l).

INTRODUCTION

Neutropenia is a common problem in the practice of hematology. Congenital neutropenia is observed extremely rare (1). It may be the only symptom of disease or a component of the syndrome. More frequently we can see acquired neutropenia. Globally, the most common cause of this type of neutropenia is considered malnutrition (2). The dominant cause of acquired neutropenia are also viral and bacterial infections (3). Equally toxic operate certain drugs, chemicals contained in paints, solvents, detergents and pesticides (1, 4). Other major causes of acquired neutropenia include proliferative diseases, displacement correct weaving bone (5).

CASE DESCRIPTION

15-month-old girl was admitted in February 2015 to the Department of Pathology Infants University Children's Hospital in Lublin because of the fever, inflammatory lesions in the mouth and pneumonia, treated for six days on an outpatient basis with no effect. Physical examination showed: enlarged lymph nodes, mucous membrane of the mouth and throat heavily congested, thrush on the palate, erosions on the palatal arches and tonsils, liver palpable 1.5 cm below the costal margin; in laboratory tests: increased CRP – 1.9 mg/dl; the morphology of peripheral blood: agranulocytosis 170/ μ l, the X-ray of chest: in both sides the presence of bronchial densities; throat swab – *Staphylococcus* sensitive to methicillin and *Candida famata*. In treatment Amoxicillin with clavulanate, Fluconazole intravenous and topical therapy were used. In the fourth day on the back of his left hand appeared the two vesicular eruptions. Antibody titer was determined (HSV IgM and IgG) and infection with HSV was confirmed. The patient received Acyclovir. In subsequent studies of blood CRP normalized, fever subsided, but still remained agranulocytosis (100/ μ l, 40/ μ l, 20/ μ l), the total number of leukocytes was normal (6.77 thousand/ μ l, 11.54 thousand/ μ l, 7.71 thousand/ μ l). After 14 days as a result of the treatment the skin lesions and inflammation of the mouth and throat disappeared. After a week of discharge from the hospital, the girl was re-admitted to the Department of Pathology Infants with fever above 38 degrees C, moist cough, sore throat and tonsillitis. In laboratory studies agranulocytosis (neutrophils – 70/ μ l) in the chest's X-ray – both sides bronchial densities. Expanded diagnostics of viral, bacteriological, immunological and metabolic tests. It was found a high antibody titer of EBV and *Mycoplasma pneumoniae* – IgM; *Chlamydia pneumoniae*, and *Pneumocystis carini* – IgG. The bone marrow aspiration biopsy ruled out leukemia, but the percentage of mature granulocytes was very low (1.2%). On this basis, the acquired neutropenia was confirmed. The patients received recombinant human growth factor granulocyte colony (rHuG-CSF) at a dose of 100 μ g subcutaneously for 5 days, antibiotics with a broad spectrum (Ceftazidime, Amikacin), antifungal (Fluconazole), antiviral (Acyclovir), immunoglobulins, yield improvement

general child condition and parameters of peripheral blood (granulocytes 3760/ μ l). Control bone marrow examination done after 7 months showed an increase in the proportion of mature neutrophils (6.8%). Today, the girl without signs of infection, but with persistent neutropenia (neutrophils – 160/ μ l).

DISCUSSION

Sudden onset of neutropenia in our patient, with normal test results before the onset of illness, supports the acquired character of the disease. The symptoms were characteristic for neutropenia. The most common location of inflammation are: skin, mucous membranes and lungs. Especially in children under two years of age, the very severe ulcerative inflammation in the oral cavity and chronic periodontitis is observed (6). Some authors also describe atypical, insidious neutropenia, with poorly expressed local characteristics of inflammation. Almost always, there is a fever. Its absence indicates a very poor condition of the patient (7). The severity of the changes is the heavier, the smaller the number of neutrophils. While in mild to moderate neutropenia risk of infection is small, severe neutropenia carries a high risk (8). In the presented patient already diagnosed with the adoption of the very severe neutropenia, which, despite the improvement of the general condition of the child and the normalization of inflammation deepened. Commissioned serological test confirmed the presence of antibodies to HSV IgM and IgG, and EBV IgM. Infection with these viruses were most likely the causes of neutropenia. As pointed out by many authors, in European countries, the predominant cause of acquired neutropenia are the viral and bacterial infections (9). Neutropenia caused by a viral infection usually is transient. It usually begins even before the appearance of symptoms of the disease or at the onset of symptoms and lasts until resolution of viremia (10, 11). However, in young children with severe or very severe neutropenia, the condition can take the form of a chronic process (8). The etiology of infections that occur in the course of acquired neutropenia is mixed, mainly bacterial and fungal. Often they are microorganisms belonging to the normal flora of the body (12). The patient due to the low number of neutrophils, persistent fever, confirmed a mixed etiology of infection, in the treatment received antibiotics with broad-spectrum intravenous and antifungal medicine. Such therapeutic treatment is recommended in febrile children with severe neutropenia (13). In the case of the presented patient, we have made aspiration bone marrow, and after exclusion of proliferative process, we have used in the treatment of recombinant human granulocyte colony stimulating factor (rHuG-CSF). According to literature data the use of rHuG-CSF significantly reduces the time of hospitalization of patients with neutropenia and reduces the use of antibiotics (10, 14). However, be aware of the possibility of malignant transformation, especially in children with congenital immunodeficiency (15). In the case described, the use of rHuG-CSF achieved a significant increase in the number of granu-

locytes. The girl was discharged from the recommendation of the use of prophylactic antibiotics, because such conduct is indicated in children with ANC below 500/ μ l, especially in infants with recurrent bacterial infections (16). In addition, it was recommended to give vaccines against enveloped. It has been proven that patients with chronic neutropenia, in particular are exposed to such infections (17). Continued other vaccinations, except for live vaccines, as safe granulocyte count for this type of patients is 1,000/ μ l (18). In our patient, despite the correct image of the bone remains neutropenia requiring antibiotic prophylaxis. We have not observed signs of infection.

CONCLUSIONS

1. Each case of illness runs with neutropenia, due to the different course and etiology should be considered individually.
2. Regardless of the causes and duration, this condition is the cause of impaired immunity. This is related to an increased risk of infections, mainly of bacterial and fungal.
3. Postinfectious neutropenia, usually is a transitory and short-term state, however, the low number of neutrophils and the young age of the patients, could be a factor in lengthening its persistence.

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