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Infectious complications in patients with hematological malignancies

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Abstracts: The analysis of infectious complications in cancer patients receiving chemotherapy in soft hematology department of the Amur Regional Hospital were conducted in 2002 - 2011 years. In patients with acute lymphoblastic leukemia infectious complications reported in 88% of cases at the time of induction of remission, during the re-induction of remission and consolidation in 40%, in patients with acute leukemia non lymphoblastic 90% of cases at the time of induction of remission, during the consolidation of remission in 80% and during maintenance therapy in 10% of cases in patients with chronic lymphocytic leukemia in 85% of multiple myeloma is 40%, with 50% of NHL cases. The most frequent complication of Leukemia is febrile neutropenia, mucositis, and pneumonia. The most severe complications are pneumonia, sepsis and necrotizing enteropathy. The features of the course and prognosis of these diseases were analyzed.

Keywords:hematological malignancies, infectious complications.

Modern cytostatic therapy can achieve long-term remission and, in some cases, even cure many patients with blood diseases [2, 8]. However, these results are achieved through intensification of chemotherapy [8]. In the process of software hematological malignancies treatment in the majority of patients develop serious complications associated with hematologic and non-hematologic toxicity of chemotherapy. Joining infection can cause death of patients even in the absence of progressive tumor growth. The main factors determining the development of infection in patients with hematological malignancies were neutropenia (depth, duration, and speed of development), impaired cellular and humoral immunity, mucosal lesion of the gastrointestinal tract, central venous catheter [4, 6]. The most dangerous are the infections that have joined in the presence of neutropenia. By reducing the white blood cells less than 1×10^9/L and / or granulocytes less than $0{,}75 \times 10^9$/L (agranulocytosis), the risk of infectious complications increases significantly, they take an atypical, severe and protracted course [1, 2, 9]. In addition to bacterial infections in these patients are more often diagnosed with invasive fungal infections [3, 5].

In this context, the problem of diagnosis and treatment of infectious complications in patients with hematological malignancies receiving chemotherapy program is very important.

The aim of the study was to investigate the characteristics of infectious complications in patients with hematological malignancies who underwent chemotherapy program.

Materials and methods.

Studied history and hospital records 284 patients with acute leukemia (AL) over the age of 18 years, 180 with chronic lymphocytic leukemia (CLL) in stages B and C by Binet, 125 with non-Hodgkin's lymphoma (NHL), 123 with multiple myeloma (MM), 10 patients with chronic myeloid

leukemia (CML) and 14 with chronic idiopathic myelofibrosis (IMF) in blast crisis stage, treated in the hematological separation of the Amur Regional Hospital (AOKB) in 2002 - 2011.

The results of the study.

In patients with acute lymphoblastic leukemia in remission induction of infectious complications occurred in 88% of cases during reinduktion and consolidation of remission in 40%. Dominated by febrile neutropenia (35%), mucositis (30%), pneumonia (13%), less frequent herpes infection (6%), upper respiratory tract infection (5%), the defeat of the intestine (5%), urinary tract infection (2 %), abscesses and cellulitis (2%), sepsis (2%). Patients with acute nonlymphoblastic (myeloid-governmental) leukemia in remission induction of infectious complications occurred in 90% of cases during the consolidation of 80% remission and maintenance therapy at step 10% of patients. The most frequently reported febrile neutropenia (30%), mucositis (30%), pneumonia (15%), less frequent herpes infection (6%), the defeat of the intestine (5%), upper respiratory tract infection (5%), sepsis (3%), urinary tract infection (2%), abscesses and phlegmons (2%), invasive fungal infections (2%).Table 1.

Infectious complications were recorded in 85% of patients with CLL treated with chemotherapeutic treatment, the incidence has increased in the tumor progressions, 75% of infectious complications reported in patients in the terminal stage of CLL. Prevailed bronchopulmonary disease (pneumonia and bronchitis - 38.8%) and upper respiratory tract pathology (29.6%), less likely to have - herpes infection (18.3%), raw abscess and phlegmons (6.3%), erysipelas (5.7%), sepsis (1.3%). Table 1.

In 40% of patients with MM registered infectious complications. Basically diagnosed pneumonia (35%) and mucositis (25%). There were also of febrile neutropenia (15%), upper respiratory tract infection (10%), herpes infection (5%), and the expression of the intestine (4%), urinary tract infection (3%), abscesses and phlegm-us (2%), sepsis (1%).Table 1.

Infectious complications were diagnosed in 50% of patients with NHL: febrile neutropenia (25%), mucositis (20%), infectious diseases of the upper respiratory tract (20%), pneumonia (15%), herpes infection (11%), damage to the intestine (4 %), infection of the urinary tract (3%), erysipelas (2%).Table 1.

CML patients and MFIs in blast crisis stage of the program during chemotherapy diagnosed pneumonia, worn protracted and recurrent course, mucositis and necrotizing enteropathy.At the same time, many patients, especially in the period of neutropenia, but it was diagnosing multiple infectious complications. The most serious complication is pneumonia-mi, sepsis and necrotizing enteropathy.Specific course of pneumonia in the period of agranulocytosis was a predominance of extrapulmonary manifestations. In all cases, pneumonia began to raise the temperature of the body, from 38 to 40 ˚ C. All patients had tachypnea: the average respiratory rate was 31,8 ± 6,4 in 1 minute. Cough with little phlegm observed 20% of patients. Complaints of shortness of breath are bringing all of the patients. Only 5% of patients in the agranulocytosis period able to listen to finely wheezing over the zone of destruction. In all other cases, auscultation in the affected area only listens to decreased breath.

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Most of the patients was determined by the sound of the blunting of the pulmonary lesions. None of these patients, a period of lower white blood cell count less than 1,0 × 109 / L, with the traditional X-ray examination failed to reveal infiltrativeor focal changes. In the diagnosis of pneumonia occurring in the presence of neutropenia, has provided significant assistance to computed tomography (CT). When conducting CT could diagnose infiltrates even a very small scale. In the absence of being able to perform CT diagnosis of pneumonia is exposed only in clinical manifestations. In 30% of patients with inflammation of the lungs debut full-blown bacterial toxic shock to the development of multiple organ insufficiency. The agents of pneumonia in patients with agranulocytosis were: S. pneumoniae, S. aureus, K. pneumoniae, Escherichia coli, Enterobaster spp., H. influenzae, P. aeruginosa. Monoinfection occurred in 12 cases, the association of microorganisms were isolated in 8 cases. In 41% of cases the causative agent has not been identified, despite the use of the modern methods of laboratory diagnosis.

Prior to the identification of the causative agent and determine its sensitivity to antibiotics, as well as in situations where the set etiologic diagnosis of pneumonia is not possible, use broad-spectrum antibiotics: 1. as monotherapy - carbapenems or ceftazidime / sulbactam 2. Combination therapy - III-IV cephalosporins of generations (ceftazidime, ceftazidime, ceftriaxone, cefepime, cefoperazone / sulbactam) in combination with an aminoglycoside (amikacin, tobramycin, netilmitcin) in the absence of renal failure or respiratory fluoroquinolones (levofloxacin, moxifloxacin). If you suspect a river. aeruginosa used antipsychotic domonadny-β-lactam (ceftazidime, cefepime, imipenem, meropenem, doripenem) in combination with an aminoglycoside or ciprofloxacin. With the deterioration of the patient's condition or appearance of new lesions lenii on radiographs additionally administered vancomycin, amphotericin B or fluconazole. Conducted an anti-inflammatory and detoxifying on therapy. Used drugs granulocyte and granulocyte-macrophage colony-stimulating factors.

When the level of white blood cells more than 1,0 × 109 / L condition of the patients improved: Docked fever, became less pronounced symptoms of intoxication, starting secede sputum, etc. At the same time, in this period, in the light began to appear classical auscultation picture pneumonia (hard breathing, moist rales of various sizes) and was determined polysegmental infiltration on traditional radiographs. Clinical and radiological features of pneumonia in agranulocytosis attributable to the significant decrease in the number of neutrophils in this period, resulting in the lungs does not form a dense inflammatory focus, giving a clear physical and radiological picture. When the number of neutrophils in the lungs arise manifestations of inflammatory cell reaction, whereby there is a characteristic X-ray pattern auscultation and pneumonia. In all patients with agranulocytosis and severe pneumonia was of prolonged duration.

With timely diagnosis of pneumonia, and the appointment of an adequate antibacterial therapy prognosis in most cases (70%) were benign. The exceptions were patients with CML and IMF in blast crisis stage, in all cases it was a polyclonal tumor and death occurred as a result of the progression of lymphoblastic leukemia when joining pneumonia.

By "febrile neutropenia" are now realizing increased body temperature above 38 ° C, at least two times during the day, or one-time increase in body temperature above 38,3 ° C in patients with neutrophil content of less than 0,5 × 109 / L or less than 1,0 × 109 / L with a tendency toward rapid decrease in [7, 10]. These patients were unable to identify a clear focus of infection in a thorough physical, instrumental and laboratory studies. Everyone was conducted blood tests for sterility - the infectious agent could not be identified. In all cases of febrile neutropenia administered broad-spectrum antibiotics, according to testimony antifungal, antiviral drugs, drugs of granulocyte colony-stimulating factor. Weather in all cases was favorable.

Second place in the structure of infectious complications of leukemia is mucositis - the defeat of the oral mucosa. To treat mucositis, in most cases used anti-anaerobic agents (metronidazole or clindamycin), antifungal agents, local disinfectants.

Herpes infection in CLL diagnosed significantly more frequently than in other hematological malignancies - in 33 patients (18% of patients with CLL). In all cases it was herpes

zoster. In 30 patients, the disease began acutely with pain, later joined by elements of the skin, and fever. All the elements of the skin localized on the trunk and extremities. In 18 patients the size of bubbles reach a considerable size. High incidence of herpes zoster in patients with CLL is due to a significant inhibition of all parts of the immune system in this disease and leukemic skin lesions.A serious complication during chemotherapy program was necrotic enteropathy that all patients developed against the background of agranulocytosis, mostly in patients receiving high-dose chemotherapy (ALL, ANLL, malignant lymphoma). In 90% of the development of necrotic enteropathy preceded mucositis (damage to the mucous membranes of the mouth). The first symptom of malabsorption was hyperthermia, then appeared diarrhea or mushy stools, later joined by bloating and severe cramping pain, symptoms of peritoneal irritation. In the treatment of necrotizing enteropathy was prescribed starvation and antibiotic therapy. Receive the same antibiotics as in the treatment of pneumonia. In the case of timely diagnosis of necrotizing enteropathy and destination of complete starvation, weather in all cases was favorable (except for blast crisis CML and IMF).

With modern methods of diagnosis and treatment of focal infections, sepsis is rare, usually at untimely and \ or inadequate treatment of febrile neutropenia and pneumonia in patients treated with high-dose chemotherapy (ALL, ANLL, malignant lymphoma), in the presence of a central venous catheter. Often, this diagnosis was established in 11 patients. Among gram-negative sepsis pathogens microorganisms in 5 patients diagnosed, and 5 gram, and in one case was the fungal pathogen infection. In 5 patients with sepsis arising in the presence of neutropenia, has been ascertained death.

Discussion of the data.

Conducting modern software therapy can achieve remission and, in some cases, even cure many patients with blood diseases. However, this result is achieved through intensification of chemotherapy. Among the many side effects of chemotherapy occupy a special place infectious complications that may lead to death of the patients, even in the absence of progressive tumor growth. According to the literature the frequency and severity of the infection depends on the intensity of chemotherapy and neutropenia. However, analysis of the incidence of infections bronchopulmonary cancer patients treated at the hematology unit AOKB over the past 10 years, you showed a somewhat different trend. In patients receiving aggressive (often high-) chemotherapy (ALL, ANLL, malignant lymphoma) is a serious complication such as pneumonia are much less common than in patients with CLL and MM, which takes place less intensive courses of chemotherapy (Table 1). This is primarily due to three important reasons. First, in patients with acute leukemia and malignant lymphoma in the course of aggressive chemotherapy, doctors predict in advance the development of agranulocytosis, such courses are usually held in isolated wards, broad-spectrum antibiotics, and on the testimony and antifungal agents, are appointed by proactively reducing the number of leukocyte least 1 × 109 / L, or at the stage of febrile neutropenia. Patients with CLL, MM receiving treatment in the majority of cases in the general wards, where the risk of infection and preventive antibiotic therapy is not available to them. Second, it is Leukemia CLL, in which there is a pronounced secondary immunodeficiency, even in the absence of tumor progression of the process. Third, CLL MM and in most cases of pneumonia developed in the terminal stage of the disease (75%), when there is an uncontrolled growth of the tumor and severe immunodeficiency, in the first place that, instead of chemotherapy due to high incidence of bronchopulmonary infections.

The highest incidence of pneumonia was observed in patients with CML and IMF in blast crisis stage. However, this is polyclonal stage occurs when progressive tumor growth and pneumonia is only one of many complications resulting in death of such patients.

Features of infectious complications Leukemia explains severe immunodeficiency, especially the development of agranulocytosis. Due to reduction in the number of neutrophils in this period, in the tissue does not form a dense inflammatory focus, giving a clear clinical picture of infectious complications. Therefore, against the background of agranulocytosis fever (febrile

neutropenia) is the basis for the appointment of broad spectrum antibiotics. With modern antibacterial drugs, granulocyte colony-stimulating factor and other adjuvant therapy, the prognosis of infectious complications of neutropenia Leukemia in most cases favorable.

Conclusion

1. In carrying out the program of modern treatment protocols hematological malignancies, the risk of infection is very high: in ALL - 88% at the time of induction of remission, during the re-induction of remission and consolidation - 40%, with ANLL - 90% of the time during the induction of remission, during Consolidation remission - 80% and in step supportive therapy - 10%, with 85% of CLL at MM 40%, with 50% of NHL patients.

2. The most frequent complications of Leukemia are febrile neutropenia, mucositis and pneumonia. The most serious complications are pneumonia, sepsis and necrotizing enteropathy.

3. The features of pneumonia developed on the background of agranulocytosis is their atypical, severe and protracted course, often complicated by sepsis and bacteriology toxic shock. During the period of agranulocytosis in the lungs due to a deficiency of neutrophils does not form a dense inflammatory infiltrate, which gives a clear picture of the clinical and radiological pneumonia. Therefore, these patients often lack the characteristic auscultation picture of pneumonia in conventional X-ray examination reveal infiltration in the lung is also not possible. In these patients, the presence of fever, a CT scan should be performed regardless of the lung auscultation picture and without prior exposure.

4. With appropriate sanitary-hygienic regime modern antibacterial drugs, granulocyte colony stimulating factor and other adjunct therapy, prognosis of infectious complications Leukemia, without the uncontrolled growth of tumors, in most cases advantageous.

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Table 1

The structure of infectious complications in patients with hematological malignancies

Nosology / Complication		ALL n=145	AML n=139	CLL n=180	MM n=123	NLL n=125	CMLandIMFunder blastic crisis stage n= 24
Febrile Neutropenia	Abs. Numb.	51	42	-	18	31	-
	%	35	30	-	15	25	-
mucositis	Abs. Numb.	44	42	-	31	25	12
	%	30	30	-	25	20	50
pneumonia	Abs. Numb.	19	21	70	43	19	18
	%	13	15	39	35	15	75
Herpeticinfection	Abs. Numb.	9	8	33	6	14	-
	%	6	6	18	5	11	-
Infections of the higher respiratory ways	Abs. Numb.	7	7	18	12	25	4
	%	5	5	10	10	20	5
intestinal damage	Abs. Numb.	7	7	-	5	5	4
	%	5	5	-	4	4	5
Urinary Tract Infection	Abs. Numb.	3	3	-	4	4	-
	%	2	2	-	3	3	-
abscesses and phlegmons	Abs. Numb.	3	3	11	3	-	-
	%	2	2	6,3	2	-	-
sepsis	Abs. Numb.	3	5	2	1	-	-
	%	2	3	1,3	1	-	-

Oncological aspects of toxic goiter thyroid gland

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According to the literature the frequency of thyroid cancer with a combination of toxic forms of goiter has been steadily increasing (3, 4, 5) and ranges from 2,1 to 5,7%.Toxic adenomais the most dangerous in this respect amongtoxic forms of goiter (3,5). The main causes of cancer growth against the background of toxic goiter are the overall growth of cancer pathology, long thyrostatic therapy of hyperthyroidism, improvement of diagnostics, etc. Against the background of toxic goiter the multicentric growth of carcinomas is observed in 21,3-22, % of cases.

In the presence of thyroid cancer it is marked persistent severe course with a high propensity for recurrence of hyperthyroidism and insufficient effect of conservative therapy (1,2).