Predictors of the development of infectious complications during post cytostatic cytopenia in patients with acute leukemia

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Objective

Patients with hematological malignancies undergoing chemotherapy (CT) have high incidence of infections which profile is affected by various factors including neutropenia. The initial stages of the disease (screening and induction therapy) are very often accompanied by the development of infections complications in adult patients with acute leukemia. The aim of our study was to determine in patients with newly diagnosed acute myeloid leukemias (AML) and acute lymphoblastic leukemias (ALL) of the possible influence of clinical and laboratory parameters at the screening stage on the development of infectious complications during post-cytostatic cytopenia.

Methods

The prospective study (2021) included 49 adult patients diagnosed with acute leukemia who received the induction stage of therapy: 33 patients with AML, 2 patients with a mixed-cell variant with myeloid predominance, 6 patients with AML with changes associated with myelodysplasia, 8 patients with ALL. In the study sample, 30 patients received an induction course of polychemotherapy with high doses ("7+3", FLAG-Ida, Hyper-CVAD/HMA), 19 received courses with standard doses of chemotherapy drugs ("7+3", CALGB, ALL-2009). The paired Student's t-test and Pearson's goodness-of-fit test (chi-square) were used to compare qualitative traits. The Mann–Whitney U-test was used to compare quantitative traits. The study of the relationship of the influence of screening factors on the development of an infectious complication during the period of cytopenia was studied by the Spearman's rank correlation coefficient. Differences were considered statistically significant if the probability of an error-free prediction was 95% ($p \leq 0,05$).

Table 1. - Clinical and laboratory parameters of patients with acute leukemia distributed depending on the presence of infectious complications during post-cytostatic cytopenia.

Indicator	Infection in cytopenia	Non infection in cytopenia	Statistical significance of differences
Male, abs. (%)	22 (45)	9 (18,4)	$\chi2$= 21,97; p= 0,69
Age, Me [Q_{25}-Q_{75}]	38 [34-50]	40 [29-44]	U= 257,5; p= 0,58
Diagnosis, abs. (%):			
- AML	20 (66,7)	13 (68,4)	$\chi2$= 0,191; p= 0,979
- ALL	5 (16,7)	3 (15,8)	
- mixed cell AL-variant	1 (3,3)	1 (5,3)	
- AML with changes associated with myelodysplasia	4 (13,3)	2 (10,5)	
Infection in screening, abs. (%):			
- yes	19 (63,3)	4 (21,1)	U= 164,5; p= 0,0138
- no	11 (36,7)	15 (78,9)	
Number of hospitalizations, abs. (%):			
- primary	15 (50)	12 (63,2)	U= 247,5; p= 0,448
- repeated	15 (50)	7 (36,8)	
Temperature in screening, abs. (%):			
- yes	16 (53,3)	3 (15,8)	U= 178,0; p= 0,0289
- no	14 (46,7)	16 (84,2)	
Microbiological examination of material from the posterior pharyngeal wall, abs. (%):			
- etiologically significant microflora	13 (43,3)	1 (5,3)	U= 176,5; p= 0,0267
- non etiologically significant microflora	17 (56,7)	18 (94,7)	
Microbiological examination of material from the anus, abs. (%):			
- etiologically significant microflora	14 (46,7)	1 (5,3)	U= 167,0; p= 0,0159
- non etiologically significant microflora	16 (53,3)	18 (94,7)	
C-reactive protein, Me [Q_{25}-Q_{75}]	40,65 [6,6-87,0]	12,8 [1,8-37,9]	t= 1,196; p= 0,238
Leukocytes, Me [Q_{25}-Q_{75}]	23,7 [6,1-59,8]	19,8 [8,0-63,4]	t= 0,52; p= 0,605
Blasts in blood (%), Me [Q_{25}-Q_{75}]	52,0 [26,0-77,0]	45,0 [15,0-76,0]	t=0,553; p=0,583
Neutrophils, Me [Q_{25}-Q_{75}]	1,44 [0,38-3,39]	1,52 [0,93-3,69]	t= 0,785; p= 0,436
Neutrophils (%), Me [Q_{25}-Q_{75}]	8,5 [4,0-15,0]	7,0 [3,0-15,0]	t= 0,129; p= 0,898
Lymphocytes, Me [Q_{25}-Q_{75}]	2,57 [1,53-6,18]	3,2 [1,9-5,6]	t= 0,54; p=0,591
Lymphocytes (%), Me [Q_{25}-Q_{75}]	14,5 [9,0-27,0]	18,0 [13,0-33,0]	t= 0,516; p= 0,608
Haemoglobin, Me [Q_{25}-Q_{75}]	93 [82-108]	103 [95-120]	t= 1,373; p= 0,176
Platelets, Me [Q_{25}-Q_{75}]	50,5 [27-94]	66 [26-136]	t= 1,404; p=0,167
Blasts in bone marrow (%), Me [Q_{25}-Q_{75}]	70,25 [46,7-79,3]	63 [50-79]	t= 0,057; p= 0,954
Total Protein, Me [Q_{25}-Q_{75}]	69,35 [62,6-77,0]	73,7 [68,7-78,6]	t= 1,509; p= 0,138
IgG in screening, Me [Q_{25}-Q_{75}]	9,99 [8,43-12,7]	11,56 [10,23-14,04]	t= 0,785; p= 0,436
IgM in screening, Me [Q_{25}-Q_{75}]	1,11 [0,88-1,77]	1,29 [0,72-1,71]	t= 0,379; p=0,706
IgA in screening, Me [Q_{25}-Q_{75}]	2,47 [1,65-2,99]	2,46 [1,8-3,14]	t= 0,032; p=0,974
Chemotherapy, abs. (%):			
- high doses	17 (56,7)	13 (68,4)	U= 251,5; p= 0,498
- standard doses	13 (43,3)	6 (31,6)	

Results

Among total study subjects, 30 patients experienced infectious episodes during cytopenia. According to the results of the study, the presence in patients with a newly diagnosed AML and ALL at the screening stage of such phenomena as a temperature reaction (U= 178,0; p= 0,0289), the presence of an infectious process during the attack of the disease (U= 164,5; p= 0,0138), the results of microbiological studies of the material from the posterior pharyngeal wall (U= 176,5; p= 0,0267) or anus (U= 167,0; p= 0,0159) with the presence of etiologically significant microflora (Escherichia coli, Acinetobacter baumannii, Klebsiella pneumoniae spp, Candida spp) are statistically significant predictors of the development of infectious complications during post-cytostatic cytopenia. These results are confirmed by a quantitative assessment of the statistical analysis of the relationship between the phenomena by the Spearman's rank correlation coefficient. At the same time, there was no statistically significant effect of the input parameters of peripheral blood and bone marrow of patients (p >0,05).

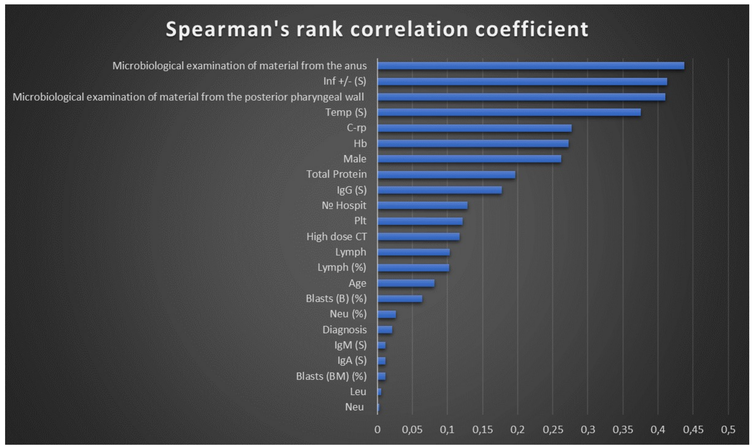

Figure 1. - Results of Spearman's rank correlation analysis of predictors of the development of infectious complications during post-cytostatic cytopenia in patients with primary acute leukemia

Conclusions

The presence in patients with newly diagnosed AML and ALL during the period of the disease attack of such factors as an infectious process, temperature reaction, the result of a microbiological study of material from the posterior pharyngeal wall or anus with an etiologically significant microflora can be predictors of the development of infectious processes in the period of post cytostatic cytopenia, and how as a result, they form a high-risk group of patients for the development of infectious complications.

Key words

Acute leukemia, infectious complications, post cytostatic cytopenia