Neurological toxicities among children patients during treatment for acute lymphoblastic leukemia and occurrence of neuropsychological late effects after the treatment

Powikłania neurologiczne u dzieci z ostrą białaczką limfoblastyczną w trakcie leczenia a występowanie następstw neuropsychologicznych po jego zakończeniu

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Abstract

Due to chemotherapeutical agents used in ALL treatment protocols, the neurological toxicity can be observed. In a group of 1855 children with ALL treated according to the ALL-IC 2002 protocol, 250 (13.5%) cases of neurological (both central and peripheral) toxicities occurred. As a pilot study, only patients from the Lublin center entered the study. A battery of neuropsychological tests were administered in 3 studied groups: 1. Survivors with treatment-related acute neurological toxicities history – clinical (CG); 2. Patients during treatment – prospective clinical (PCG), and 3. Matched healthy controls (CtrG). The aim of our study was to evaluate the connection between the occurrence of neurological toxicities during treatment for ALL and neuropsychological late effects in children after treatment completion. We found a lower IQ level in both clinical groups as compared to healthy controls. In CG patients we found more specific neuropsychological difficulties than in PCG and controls. In 2 from 4 CG patients we diagnosed dyslexia-like disorders. Our findings need further research based on CG patients from other pediatric onco/hematology wards.

Streszczenie

Chemioterapeutyki stosowane w leczeniu ostrej białaczki limfoblastycznej u dzieci (ALL) mogą prowadzić do wystąpienia powikłań neurologicznych (centralnych i obwodowych). W grupie 1855 dzieci z ALL leczonych w Polsce protokołem ALL-IC 2002 u 250 (13,5%) doszło do ich wystąpienia. Celem badania była ocena związku między występowaniem powikłań neurologicznych a funkcjonowaniem neuropsychologicznym dzieci wyleczonych z ALL. Jako pilotaż przeprowadzono badania pacjentów z jednego ośrodka (Lublin). Opracowano baterię testów neuropsychologicznych, którymi przebadano 3 grupy: 1) dzieci wyleczone z ALL, u których w trakcie leczenia doszło do powikłań – grupa kliniczna (CG); 2) pacjenci w trakcie leczenia – grupa kliniczna prospektywna (PCG), 3) dzieci zdrowe dobrane wg wieku i płci (CtrG). W porównaniu ze zdrowymi dziećmi w obu grupach klinicznych stwierdzono obniżenie IQ. U dzieci wyleczonych z ALL, u których wystąpiły komplikacje neurologiczne, stwierdzono więcej specyficznych trudności neuropsychologicznych niż w pozostałych grupach. Dwoje z czworga dzieci z tej grupy miało zaburzenia o typie dysleksji. Uzyskane wyniki wymagają rozszerzenia o pacjentów leczonych w innych ośrodkach.

Key words: children with acute lymphoblastic leukemia (ALL), neurological toxicity, neuropsychological late effects.
Słowa kluczowe: dzieci z ostrą białaczką limfoblastyczną (ALL), powikłania neurologiczne, następstwa neuropsychologiczne.

Introduction

Survival rates in childhood acute lymphoblastic leukemia (ALL) have improved for the last decades. Nowadays, the event-free survival rates after treatment of childhood ALL are 80% [1]. Due to chemotherapeutical agents and prophylactic cranial radiotherapy used in treatment protocols, neurological toxicity can be observed. The neurological complications in ALL can be divided into two broad categories: infiltration of the CNS by leukemic cells (primary involvement) and complications due to disease *per se* and/or therapy (secondary manifestations) [2]. The most common neurological complications involve acute alteration in consciousness, seizures, leukoencephalopathy, cerebral infarctions, paralysis, neuropathy, and ototoxicity [3]. The incidence of neurological complications in ALL varies between 3% and 13% depending on different studies [4]. These complications have an impact on patients' quality of life and cognitive functioning. For this reason, the goal of current ALL treatment is to minimize adverse neurological and neuropsychological late effects. Patients are stratified for treatment, and almost 80% received chemotherapy only [5]. However, the risk of neurocognitive late effects in survivors of childhood ALL treated with chemotherapy only is still probable [6, 7]. In longitudinal studies on long-term neurocognitive outcome after treatment with chemotherapy alone, a decline in global IQ is reported [8, 9]. In those groups of children, findings on cognitive functioning are of average academic attainment and normal cognitive development. Declines are found in visual-motor integration, verbal fluency and arithmetic skills [6, 7, 10, 11]. Risk factors for poor neurocognitive outcome after chemotherapy-only CNS-directed treatment are younger age and female gender [6, 12]. In our study, we evaluated the connection between the occurrence of neurological toxicities during treatment for ALL and neuropsychological late effects in children after treatment completion.

Material and methods

Study design and data collection

The study was carried out among children treated for ALL according to the ALL-IC 2002 protocol, who suffered from neurological (both central and peripheral) toxicities during treatment. For the study, the inter-hospital (n = 14) database was used which gathers data on children treated for ALL in 2002–2009 according to the ALL-IC protocol. In the group of 1855 children with ALL, 250 cases of neurological toxicities occurred (13.5%). The number of neurological late effects cases was very diverse and varied from 0 to 38% of all treated patients with ALL (Table 1).

Due to the attempt to evaluate the connection between the occurrence of neurological toxicities during treatment for ALL and neuropsychological late effects it was decided to do a pilot research among the patients from Lublin. The method of selecting patients for the study is shown in Figure 1. Among 158 patients with ALL, 15 (9.5%) suffered from neurological toxicities. 6 out of those died, 2 patients were excluded from the study (mental handicap, poor knowledge of Polish) and 2 patients were excluded because of age over 20 years old. In the end, 4 patients entered the study.

For the research reasons three study groups were created: clinical group (CG) – 4 patients after the completion of treatment for ALL; prospective

Table 1. Distribution of the occurrence of neurological toxicities within hospital centers
Tabela 1. *Rozkład występowania powikłań neurologicznych wg ośrodków*

Center	Number of neurological complication cases	Number of patients with ALL	%
Białystok	33	91	36.3
Bydgoszcz	36	113	31.9
Chorzów	16	85	18.8
Gdańsk	20	131	15.3
Katowice	0	63	0.0
Kielce	5	54	9.3
Kraków	16	232	6.9
Lublin	15	158	9.5
Łódź	21	131	16.0
Poznań	4	185	2.2
Szczecin	27	70	38.6
Warszawa	10	264	3.8
Wrocław	37	186	19.9
Zabrze	10	92	10.9
Together	250	1855	13.5

ALL – acute lymphoblastic leukemia

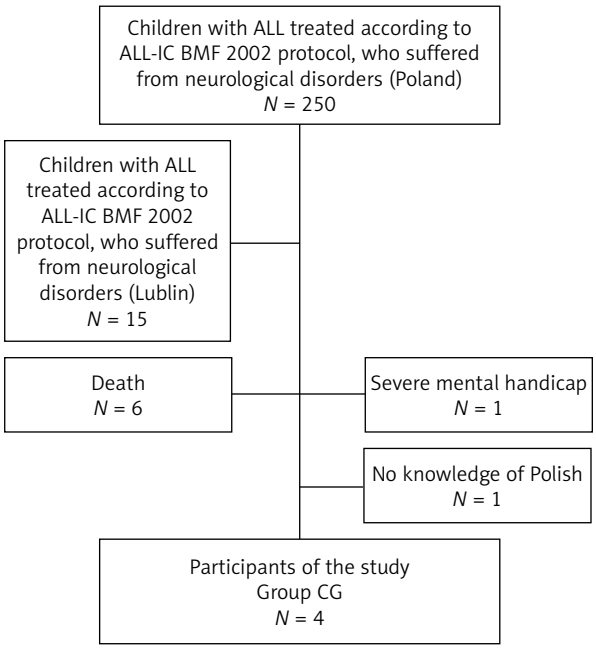

Figure 1. Inclusion criteria into the study group of patients after the completion of treatment for acute lymphoblastic leukemia (ALL) – clinical group (CG)
Rycina 1. *Kryteria włączające dzieci do grupy klinicznej pacjentów po zakończonym leczeniu ALL (CG)*

clinical group (PCG) – 4 patients during treatment for ALL (I protocol ALL-IC) and control group (CtrG) – 4 healthy children selected depending on age and gender.

The study took place from September to December 2013 among children treated in the Department of Pediatric Hematology, Oncology and Transplantation in Lublin.

Characteristics of the studied group

Four children entered the CG group (3 girls and 1 boy). Their average age at the moment of study was 11.1 years old (between 8.6 and 14.4). The average age at the time of diagnosis was 2.11 years old (between 1.7 and 4.3), the average age at the completion of treatment was 6 years old (between 4.1 and 9.4), while the period of time since diagnosis until the moment of study varied between 4.2 and 10.1 years (average 7.9) and since the completion of the treatment – between 1.10 and 6.10 years (average 4.9). Within all these patients the treatment was completed and every one of them undergoes only control examinations at the hematological clinic at the University Pediatric Hospital in Lublin. Table 2 shows types of neurological toxicities found in studied patients.

The control group (CtrG) was represented by 4 children at the age between 8.8 and 13.5 years old (M = 10.7) selected according to the method of pair selection, so that the age, distribution of gender were possibly close to the clinical group (CG). The inclusion criteria were absence of somatic diseases or psychic disorders as well as diagnosis of dyslexia among two older children (due to the diagnosis of dyslexia among children from the CG group).

Due to the plan of prospective research, a prospective clinical group was created (PCG) including 3 patients (2 girls and 1 boy) currently hospitalized at the Department of Pediatric Hematology, Oncology and Transplantation in Lublin, during treatment for ALL according to ALL-IC BFM 2009 protocol. The average age of studied children was 10.0 years old (between 8.1 and 12.11) (Table 3).

Battery of neuropsychological tests

In the study, certain methods were used to evaluate neuropsychological and intellectual functioning of patients, regarding functions often described as sensitive to disorders caused by cancer treatment such as: *attention, motor-vision coordination, and op-*

Table 2. Neurological toxicities during treatment
Tabela 2. *Powikłania neurologiczne w trakcie leczenia*

Patient/sex	ALL Stage	Neurological toxicities	Treatment period	Treatment	Duration
L.H./girl	ALL IRG, CNS involvement	Descent of the eyelid Squinting left eyeball Limping on the left lower limb	Protocol I 35th day, delay in CHT 5 days	Luminal 2 x 15 mg	1 month
B.K./boy	ALL SRG	Abnormal EEG Peripheral neurotoxicity, III stage	Protocol I	Clonazepam 2 x 0.25 mg Rehabilitation	3 months 1 month
B.A./girl	ALL SRG, Bone involvement	Limping on left lower limb Set foot to the inside	Protocol I, 0–15th days	Pyralgin	2 weeks
P.K. /girl	ALL IRG	Neutropenia Inflammatory infiltration of the face& neck Septic shock Coma, Seizures Paralysis	Protocol I, 27th day	Luminal, Meronem, Vanco, Vorikonazol	2 months

ALL – acute lymphoblastic leukemia

Table 3. Characteristics of clinical and demographic variables in studied groups
Tabela 3. *Charakterystyka zmiennych klinicznych i demograficznych w badanych grupach*

Variables		Clinical group (*N* = 4)			Control group (*N* = 4)			Prospective clinical group (*N* = 3)		
		M	min.	max.	M	min.	max.	M	min.	max.
Current age		11.1	8.6	14.4	10.7	8.8	13.5	10.0	8.1	12.11
Age at the time of diagnosis		2.11	1.7	4.3	–	–	–	9.8	7.10	12.11
Age at the completion of treatment		6	4.1	9.4	–	–	–	–	–	–
Time since diagnosis		7.9	4.2	10.1	–	–	–	0.4	0.1	0.7
Time since the completion of treatment		4.9	1.10	6.10	–	–	–	–	–	–
Variables		**N**		**%**	**N**		**%**	**N**		**%**
Gender	female	3		75	3		75	2		67
	male	1		25	1		25	1		33
Diagnosis of dyslexia		2		50	2		50	–		–

erative memory. Due to unavailability (in Poland) of normalized methods of neuropsychological evaluation to assess those functions among children under 11 years old it was decided to use the methods aimed at older children with the consideration of their limits. Potential development possibilities of the children included in the study enabled using those methods and the comparison to the control group limits the influence of other factors, e.g. the age. Eventually, the choice of tests included following methods: Wechsler's Intelligence Scale for Children (WISC-R), Attention test (D2), Diagnosis of Brain (DUM), Wisconsin Card Sorting Test (WCST) and experimental version of Comprehensive Trail-Making Test (CTMT sample A-C, trail 1-5).

Wechsler's Intelligence Scale for Children

Wechsler's Intelligence Scale for Children is used to measure intellectual factors, meaning overall competence or the abilities of understanding the world and effective functioning. It can be used among children between 6 and 16 years old. It consists of six verbal tests and six non-verbal tests. It is possible to state the IQ for Full Scale, Verbal or Non-Verbal Scale as well as comparison of individual intellectual abilities with norms for an adequate age group of the studied child [13].

Attention test

The test enables the evaluation of attention ability, multitasking as well as the rate and accuracy of perception. The task is to cross as many letters 'd' as possible within 20 seconds following criteria included in the key, from 14 lines of 47 letters 'd' and 'p' with one, two, three or four lines. The results are stated on the basis of the velocity (number of seen symbols) or accuracy (number of errors) of the task [14].

Diagnostics of Brain Damage

Diagnostics of Brain Damage is aimed to evaluate the functioning of memory during learning the figurative material. The task is to remember a series of figures shown in the pictures and later to recreate them using five wooden sticks. The task is completed when the studied person creates correctly all figures, if not – they have six attempts. The results may be analyzed regarding criteria of learning, number of recreated figures, the factor of instability, as well as analysis of errors: perseveration, rotation, mirroring and fabrication [15].

Wisconsin Card Sorting Test

The method aims to evaluate the operative memory and executive functions, meaning supervising, controlling and directing the cognitive activity of a person. The Polish normalization was taken on a group of people between 21 and 79 years old, however, the authors of the original test accept the possibility of evaluating children and adolescents (in the USA the test is used for children above 6.6 years old). The studied person is shown 4 exemplar cards presenting different patterns, which are matched with other cards for the following criteria: color, shape or number of elements. It requires keeping in memory direct information on the current criteria, probable choices and execution of the task. The criteria change during the task without informing the patient. In evaluation of results, the following factors are taken into consideration: number of perseverative errors (*prefrontal area dysfunction*), number of

nonperseverative errors (*attention functions*) and number of correctly matched categories (*effectiveness of thinking*) [16].

Experimental version of the Comprehensive Trail-Making Test

Experimental version of the Comprehensive Trail-Making Test (CTMT) is used to evaluate the psychomotor speed, vision-spatial operative memory and the ability to switch attention. The task in part A, consisting of 3 attempts, is to connect with a line numbers 1–25 in the correct order in possibly shortest time. The attempts vary in terms of occurrence and number of distractors. In part B the task is to connect in the right order points described with numbers (1–21) and words in possibly short time; in part C – to connect words and letters in order 1-A-2-B-3-C etc. The factor representing the level of functioning is described in seconds and the number of errors [17]. In the study the experimental version of this test was used, although in Poland the Color Test of Connecting Points for Adults (CTT) is available. The Polish version of CTMT at the moment of the study was adapted only for adults, however the American version accepts examination of children of at least 11 years old. American norms of CTMT for children above 11 years old – more than 30 T indicates serious weakness, 30–35 T – small or medium weakness, 36–42 T – below average, 43–57 – average, 58–64 – above average.

Statistical analysis

Due to a small number of patients in each group ($N = 4$) it was impossible to use statistic comparison analyses. Therefore, it was decided to use SPSS, ver. 20 to analyze the results. Average results for every group were taken into consideration, as well as standard deviation and the results of individual factors. This analysis is preliminary, on its basis it is only possible to point out a tendency occurring in the groups.

Results

The results show a serious ambiguity in terms of intellectual and cognitive functioning of children treated for ALL in the past (CG).

Table 4 presents the results of WISC-R among studied patients after treatment for ALL (CG) and during treatment (PCG) in comparison with the control group of healthy patients (CtrG). In the WISC-R Scale, after the completion of treatment the patients gained average results lower than the average results of both healthy patients and those during treatment.

The CG group of patients is inhomogeneous in terms of all factors. Within the results in this group, it can be distinguished that one girl (9.7 years old) had multiple difficulties in the field of different functions. The global level of her intellectual ability is below average. All the factors were observed to be lower – the Verbal Comprehension Index (VCI), the Perceptual Organization Index (POI), and the Freedom from Distractibility Index (FDI). Due to inharmonious development of individual functions, an analysis of results profile was done. Certain deficiencies were observed within abstract thinking, ability of spatial visualization, generalization and comparison. The results showed much limited common knowledge and direct auditory memory, as well as serious difficulties in mathematical operations. However, the results showed at least an average level (adequate to the age of a child) of social intelligence, ability to define words and the range of vocabulary, ability of perceptive organization and visual analysis, as well as visual-motor learning.

Table 5 shows the comparison of results of neuropsychological methods gained in studied groups.

Table 4. Comparison of results of Wechsler's Intelligence Scale for Children among studied patients
Tabela 4. *Porównanie wyników uzyskanych w Skali Inteligencji WISC-R przez badane dzieci*

Factor	Clinical group				Control group				Prospective clinical group			
	M	SD	min.	max.	M	SD	min.	max.	M	SD	min.	max.
FIQ	106.25	20.85	80	124	125	6.58	117	133	123	8.89	113	130
VIQ	101	18.83	77	117	116.25	10.34	104	128	121.33	13.42	106	131
PIQ	111.25	18.82	88	128	130	1.41	128	131	120.67	6.43	116	128
VCI	10.625	2.59	7.5	13.5	13.43	1.45	11.5	15	13.67	2.02	11.5	15.5
POI	11.25	3.41	7	14.25	14.56	0.43	14	15	13	1.09	12.25	14.25
FDI	10.16	3.45	6.33	14.66	11.085	0.918	10	12	12.11	1.17	11	13.33

In the experimental version of CTMT, the patients after treatment for ALL got much worse results than healthy children and patients during treatment. It was observed on the basis of average results in time for all 5 attempts together as well as overall result T-score (for 5 attempts).

The results of the CG group indicate disorders within visual-spatial operative memory, continuity of attention (attempts 1–3), shifting of attention (attempts 4–5), difficulties with visual searching and deficiencies in complex mechanisms of cognitive control, or lower psychomotor pace. In this group of patients a big diversity of results was stated (average results for 5 attempts between 38.2 and 177.8). The deficiencies can be stated not only by comparing the results with the norms for children above 11 years old, but also on the basis of considerable lower results in comparison with the results of children from the PCG group. The results of two children from the CG group (two girls, 8.8 and 9.7 years old) indicate severe lowering of functioning in studied terms. Among other patients in CG and PCG groups, as well as healthy children the functioning in studied terms was stated within norms (at least below average).

The comparison of average results and percentage ranges in D2 test indicates no considerable differences between the groups, however, the detailed analysis of individual results points out to certain regularity. In the CG group, in comparison with the norms for the adequate age of patients, attention disorders were found in two patients. The girl, diagnosed with deficiencies in several functions, shows a very low level of overall perception abilities, due to both pace and accuracy of studied material. However, the results of a boy, 11.11 years old indicate a high speed of perception and at the same time low accuracy, impulsiveness and superficiality in studying the material. In PCG and CtrG groups, in two girls (12.11 and 13.5 years old) disorders in attention were observed, including high impulsiveness, low accuracy of analysis, while a girl of 9.8 years old from the CtrG group showed a lowered pace of work with high accuracy of perception (indicating cognitive style, not attention disorders).

The execution of DUM test in all measures was weaker among CG patients than among healthy children or patients from the PCG group. On average, the biggest amount of figures was set by healthy children – 37, a bit less among PCG patients – 36, the smallest number of figures was set by CG patients – 26. The children of the CG group made on average more perseverative errors, rotations and fabrications than the other two groups. This indicates a lowered pace of learning on visually perceived material and lower level of attention, as well as deficiencies in short-term memory. In two patients from the CG group, severe deficiencies in terms of direct visual memory and learning abilities were stated (girl 9.7 years old and boy 11.11 years old). In PCG and CtrG groups, two girls (9.1 and 13.5 years old) showed slight lowering in direct visual memory.

The execution of the WCST test was in all factors weaker among CG patients than among healthy children, however similar to the results of the PCG group (except the number of attempts and number of correct answers; these results were better in the PCG group).

The patients treated for ALL (both CG and PCG groups) needed more attempts to solve the test than healthy children. They made also more errors, both perseverative and non-perseverative. Also, within the thinking term, all patients with ALL got worse results than healthy patients. However, patients of the CG group needed less time to pass the first category than children from PCG and CtrG groups. The errors they made later and perseverations may indicate low flexibility of cognitive processes. A girl from the CG group, showing multiple disorders in cognitive functioning, managed to solve correctly only two categories, while all healthy patients solved all 6 categories and within the PCG group there was one girl (8.1 years old) who solved only 5 categories. The girl with multiple deficiencies from the CG group got considerably lower results in all factors in comparison to both healthy patients and those treated for ALL. It was stated that she solved three times less categories than other studied children from all the groups. She gave twice as much perseverative answers, made twice as much errors and over twice as much perseverative errors, while giving twice less term answers (consistent with criteria). Her results indicate considerable disorders in terms of executive functions and formulating logical concepts. She had strong difficulties in context analysis, showed deficiencies in planning and controlling, but also adjusting to changing conditions (stiffness and schematic action). Comparing her results with average raw results of Heaton's studies (1981) for $N = 459$ [16], 2002 of average age 11.64, the results of the girl were lowered by 2 aberrations from average in terms of the number of attempts, number of errors and number of term answers. However, in terms of the number of perseverative answers, perseverative errors and number of solved categories, her results were lower by 3 aberrations from average.

Among children during treatment for ALL (PCG) only the results of one girl (8.1 years old) were deviated from the average of healthy pa-

Table 5. Comparison of results of neuropsychological tests
Tabela 5. *Porównanie wyników uzyskanych w testach neuropsychologicznych przez badane dzieci*

Tests		Clinical group				Control group				Prospective clinical group			
		M	SD	min.	max.	M	SD	min.	max.	M	SD	min.	max.
CTMT	Av. time of 5 attempts	99.65	61.91	38.2	177.8	55.55	11.95	33	83	57.07	22.29	24	106
	CI T-score	30.75	13.94	18	48	41.25	4.99	37	48	44	16.46	34	63
D2	WZ	368.5	129.93	232	530	330.25	81.06	267	442	382	156.21	282	562
	% range WZ	67.98	38.49	15.9	97.1	66.08	25.11	34.5	90.3	74.9	27.16	46	99.9
	% B	5.3	3.91	2	10.3	6.3	2.56	4.4	10	6.23	5.7	2	12.8
	ZK	136.5	53.97	84	212	119	17.11	105	142	135.33	32.93	112	173
DUM	Number of attempts	5.5	1	4	6	5.5	1	4	6	4.67	2.31	2	6
	Result	26.25	19.01	4	49	37	4.97	33	44	36.33	14.64	23	52
	% range	30.25	34.53	<4.8	77.3	49.85	26.69	18.2	80	52.2	39.91	16.7	95.4
	Pe	2.75	1.71	1	5	0.5	1	0	2	1	1	0	2
	Ro	3.25	3.2	0	6	2	1.83	0	4	0	0	0	0
	Od	1.75	2.36	0	5	1.25	2.5	0	5	2	3.46	0	6
	Zm	6	10.03	0	21	1.25	2.5	0	5	0	0	0	0
WCST	Number of attempts	106	23.15	86	128	94.25	10.31	84	105	119	8.54	111	128
	Correct answers	67	10.86	54	79	73.5	7.23	65	80	80.33	9.07	72	90
	Errors (%)	34.25	17.82	16	58	21.5	2.08	19	24	32	11.27	19	39
	Pers. answers (%)	22	16.79	7	46	15	2.16	12	17	20	11	9	31
	Pers. errors (%)	19.75	14.73	7	41	11.925	2.05	10.7	15	17.33	8.02	9	25
	Non-pers. errors (%)	13.25	6.44	7	21	9.85	1.65	8	12	14.63	5.73	9.9	21
	Term answers (%)	57	22.58	28	79	71.375	2.49	69.5	75	59	15.62	49	77
	1st category	12	1.41	11	14	14	4.76	11	21	17.67	6.11	11	23
	Number of categories	5	2	2	6	6	0	6	6	5.67	0.58	5	6

tients, in two categories – perseverative answers and perseverative errors. This may indicate a lower level of cognitive control and low flexibility of thinking. However, taking into consideration the fact that the results in other factors were within norms, it may be concluded that she showed only a small lowering in terms of executive functioning.

Discussion

The incidence of neurological complications in children treated for ALL in Poland according to the ALL-IC 2002 protocol is 13.5% and corresponds to average numbers stated in the literature [4]. The numbers of reported neurological toxicities in Polish pediatric onco/hematology centers varies between 0% and 38% depending on the center. A wide range in numbers of neurological incidences reported should be explained on a regional level. In Lublin, the number of acute neurological complications is 9.5%.

Both studied groups of children with ALL, clinical (CG) and prospective clinical (PCG) groups, were treated with chemotherapy only. The children after treatment and those during treatment show more disorders in cognitive functioning than healthy children. This is confirmed by the results of earlier studies [18–21]. Among patients who suffered from neurological

toxicities during treatment, high diversity in cognitive functioning was observed. Two children showed significant difficulties within attention keeping, operative memory and learning on material given. Similar difficulties within attention and disordered process of memorizing were stated also in other studies [8, 10]. Moreover, it is questionable if the dyslexic difficulties stated in our study among children after treatment (group CG) really picture this specific disorder. It should be reaffirmed by dyslexia-specific tests. Two children showing the toughest disorders in different matters were diagnosed within the first year of their lives, while the two other, who do not show significant disorders, at the age of 4. This is confirmed by studies presented in the literature concerning the dependence of younger age at the moment of diagnosis and latter disorders of cognitive processes [6, 7].

The girl, who showed several disorders in neuropsychological functioning, was also observed with multiple neurological toxicities. The occurrence of serious neurological toxicities during treatment may increase the risk of significant specific difficulties in cognitive functioning, particularly memory processes. However, this needs to be confirmed on a bigger group of patients and by longer studies [9].

All the difficulties in various aspects of cognitive functioning that were observed among patients with ALL indicate the necessity of providing corrective-compensational therapy of cognitive functions adjusted to the patient, with special attention paid to those patients who suffered from neurological toxicities [22].

A small sample group is an important limitation of our study, but it was set up as a pilot study. Further research is worth continuing. Especially the hypothesis on the dyslexia-like disorders as a result of ALL treatment complicated by neurological toxicities.

Conclusions

The aim of our study was to evaluate the connection between the occurrence of neurological toxicities during treatment for ALL and neuropsychological late effects in children after treatment completion. We found a lower IQ level in both clinical groups related to healthy controls. In CG patients we found more specific neuropsychological difficulties than in PCG and controls. In 2 from 4 CG patients we diagnosed dyslexia-like disorders. Our findings need further research based on CG patients from other pediatric onco/hematology wards.

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