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POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Clinical Pathology Characteristics of 221 Pediatric Anaplastic Large Cell Lymphoma-3 Years Follow up and Experience from China Net Childhood Lymphoma(CNCL)

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Objective: To investigate the clinical-pathology characteristics, risk factors, necessary for VBL maintenance therapy,through summarize the clinical data of 221 cases of pediatric Anaplastic Large Cell Lymphoma (ALCL), treated with CNCL-ALCL-2017 witch is modify from BFM-ALCL-99 (±vincristine maintenance therapy) in China Net Childhood Lymphoma (CNCL).
Methods: Data were collected on 221 children with ALCL enrolled from CNCL at time between April 2017 to March 2023, including: numbers of cases enrolled in each single center, gender and age at the time of initial diagnosis, the first initial symptom, a delay diagnosis, the misdiagnosis disease , the site of involvement, the level of blood uric acid, the level of blood lactate dehydrogenase, the bone marrow and CNS status, tumor complication, complicated with HLH, staging and treatment subgroups, pathological subtypes, CD3 expression in tumor tissue, bone marrow and peripheral blood ALK gene expression at initial diagnosis (qPCR + FISH), and treatment outcomes, treatment strategy(vincristine maintenance or not), time from initial diagnose to relapse, second-line treatment regimen after relapse, and treatment outcomes after relapsed. Statistical analysis was conducted using SPSS 21.0 software.
Results: 221 cases were from 22 hospitals in China. Male = 144 cases, female = 71 cases, age range from 1-16 years (median age 8.9 years), duration from initial symptoms onset to diagnosis was 0.3-11 months (median time 1.0 months), delayed diagnosis was present in 51(23%) children (45 children were misdiagnosed with infectious diseases). Pathological subtypes

were: common sub type = 150(67.8%), small cell sub type = 19(8.5%), histiocytic variant subtype = 9(4%), ALK negative subtype = 12(5.4%).others = 31(14%). CD3 expression in tumor: negative = 119, positive = 91. ALK positive by qPCR in peripheral blood at the time of the initial diagnosis = 77, ALK positive by qPCR in bone marrow = 78, bulky disease= 21, mediastinal invasion = 84, CNS invasion = 17, skin invasion = 32. tumor related HLH = 25, normal LDH level at initial diagnosis = 133, 1-fold elevated = 45, 2-3-fold elevated = 39, 4-fold elevated = 2, >4-fold elevated = 2, stage I = 5, stage II = 24, stage III = 70, stage IV = 120 , leukemic stage = 2 . Grouping: group A = 1, group B = 21, group C = 191, group D = 8. Vincristine maintenance = 121. Median follow-up time was 35.4 months (0.5-74.9 months), OS at 3 years = 95.1±1.5% (95% CI = 90%-97.3%, Fig. 1), EFS at 3 years = 84.7±4.5% (95% CI = 79%-89.9%, Fig. 2), and there were a total of 23 patients with events, median time was7 months. There were 10 patients died, 5 of them quit to the treatment, median time was 5 months, and 13 patients who had an event but still alive after second line treatment. Univariate results of the 3 years EFS are detailed in Table 1, with statistically significant including (<0.05): tumor related HLH before treatment, LDH levels higher than 4 times normal and MDD positive at the beginning of the disease, and treated without VBL. The event patients are 23 cases ,the detailed in Table 2, which showed that the earlier the event occurs, the higher the mortality rate.

Conclusion: Pediatric ALCL in China is mostly found in school-age boys, and it is easy to be diagnosed as infectious diseases at the time of initial diagnosis due to high fever and elevated CRP. 87% of patients were diagnosed as late stage or high-risk group. The application of the CNCL-ALCL-2017 protocol showed a 3-year OS 84.7% and 3-year EFS 95.1%, indicating that the efficacy was significantly better than that of various centers before the multi center cooperation. The overall survival time is significantly better than the event free survival time, indicating that most patients with progression and recurrence still have a chance of re remission after second line treatment. Adverse prognostic factors include a significant increase in LDH levels at initial diagnosis, initial onset of HLH, positive MDD before treatment, and no use of vinblastine maintenance therapy. Recurrent children: The median recurrence time is 7 months, and the prognosis of early progression and recurrence is worse than that of late recurrence.

Key words: Anaplastic large cell lymphoma, Pediatric, Clinical-pathology features, Prognosis

Disclosures No relevant conflicts of interest to declare.

Figure 1, OS at 3 years in 221 children with ALCL

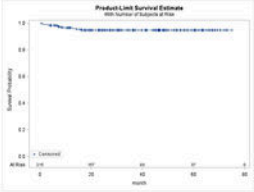


Figure 2, EFS of 221 children with ALCL at 3 years

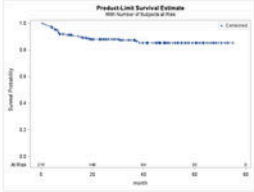
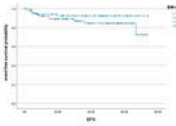


Table 1. results of univariate analysis of 221 cases of childhood mesenchymal large cell lymphoma

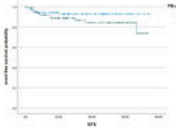
considerations	3 years EFS	P-value
Pathological type		0.65
common type n=150	81.1±3.9%	
Small cell type n=19	89.5±3.7%	
Histiocytic variant n=9	87.5±3.7%	
ALK negative n=12	81.8±5.6%	
CD3 expression		0.14
Negative n=119	82.2±2.7%	
Positive n=91	85.7±4.2%	
Peripheral blood of ALK expression by qPCR detection		0.05
Negative n=89	92.9±2.8%	
Positive n=77	75.1±6.8%	
Bone marrow of ALK gene expression by qPCR detection		0.07
Negative n=83	92.3±3%	
Positive n=78	72.4±1.9%	
Peripheral blood of ALK gene by FISH detection		0.06
Negative n=75	95.8±2.4%	
Positive n=31	77.3±2.6%	
Bone marrow of ALK gene by FISH detection		0.09
Negative n=76	93.4±3.4%	
Positive n=36	85.8±5.9%	
giant tumor		0.8
None n=200	84.2±5.3%	
With n=21	84.8±4.1%	

considerations	3 years EFS	P-value
Mediastinal invasion		0.58
None n=137	88.8±2.9%	
With n=84	66.5±3.4%	
Central nervous system violations		0.42
None n=204	83.3±5.3%	
With n=17	94.1±5.7%	
Complicated with HLH at the beginning of the disease		0.018
None n=196	85.3±5.9%	
With n=25	71.4±4.2%	
clinical staging		0.64
I n=5	100%	
II n=26	76.2±17.4%	
III n=116	86.7±3.4%	
IV n=74	89±4%	
LDH level		0.02
Normal n=133	84.9±7.2%	
1-fold elevated n=45	92.9±4%	
2-fold elevated n=39	76.7±7.5%	
3-4fold elevated n=2	50±3.5%	
> 4-fold elevation n=2	50±3.4%	
Therapeutic grouping		0.56
Group A n=1	100%	
Group B n=21	100%	
Group C n=191	81.4±6.1%	
Group D n=8	87.5±11.7%	
Treated with VBL		0.03
Y n=121	92±2.6%	
N n=100	67.3±15.4%	

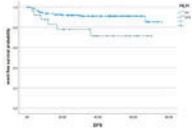
3years-EFS stratified by ALK gene detected by PBq-PCR



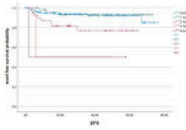
3years-EFS stratified by ALK gene detected by BM-q-PCR



3years-EFS stratified by complication of HLH



3 years-EFS stratified by LDH levels



3 years-EFS stratified by usage of VBL

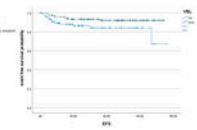


Table 2 Details of 23 evets patients

serial number	Event Type	EFS (months)	OS (months)	Florine/antibody therapy	is or isn't dead
1	Death from CNS progression on treatment	5	6	not have	dead
2	VELBL then progressed after 1 month of maintenance, and the original disease progressed and died 6 months after second-line treatment.	8	15	VBL (primary diagnosis)PD-1 (post relapse)	dead
3	Always positive for ALK by PCR, CNS relapse during maintenance	15	70	VBL (primary diagnosis)Erlotinib (after relapse)	survive (a serious accident)
4	Death from tumor complications due to progression of primary disease during treatment	7	7	not have	dead
5	Tumor Progress in Therapy	7	67	VBL (post relapse)Crizotinib (after relapse)	survive (a serious accident)
6	Comprehensive tumor progression in maintenance therapy	9	64	VBL (primary diagnosis)Erlotinib (after relapse)	survive (a serious accident)
7	Progress in treatment Abandonment of treatment	2	3	not have	dead
8	Central nervous system relapse during maintenance	18	60	VBL (primary diagnosis)Erlotinib (after relapse)	survive (a serious accident)
9	Progression on therapy, death from tumor progression despite second-line therapy	4	10	VBL (initial diagnosis + post relapse)Crizotinib, erlotinib (sequential application after relapse)	dead
10	Death from tumor complications	1	1	All are applications	dead
11	Poor response to early treatment, poor tumor retraction, CNS relapse	15	26	VBL (primary + relapse)Crizotinib (initial diagnosis)Erlotinib (relapse)	survive (a serious accident)
12	Tumor recurrence with elevated bone marrow ALK gene	12	44	VBL (post relapse)Ceritinib, Loratinib (sequential application after relapse)allogeneic hematopoietic stem cell transplantation	survive (a serious accident)
13	Progress in treatment	5	32	second-line chemotherapy	an unauthorized visit
14	Progress in maintenance therapy	36	60	VBL (first diagnosis, recurrence should be applied)Crizotinib (after relapse)	survive (a serious accident)
15	Death from tumor progression	3	3	not have	dead
16	Death from tumor progression after transplantation	6	12	not haveallogeneic hematopoietic stem cell transplantation	dead
17	Progress in treatment	3	30	not havesecond-line chemotherapy	survive (a serious accident)
18	Relapse off medication (ALK reversion)	30	30	None (2023.7 recurrence)	survive (a serious accident)
19	Progress in treatment (tumor foci)	5	27	VBL (primary diagnosis)ALK antibody (post-progression)	survive (a serious accident)
20	Deaths progressing in treatment	9	9	not have	dead
21	Relapse (ALK transitions)	20	27	VBL (none)Crizotinib maintenance (after relapse)	survive (a serious accident)
22	early relapse	7	21.9	VBL (none)Crizotinib (after relapse)	survive (a serious accident)
23	recur (of a disease)	5	17	VBL (none at first diagnosis)Erlotinib, Loratinib, Allogeneic Stem Cell Transplantation	dead

Figure 1

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