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Prognostic factors of ALK-negative anaplastic large cell lymphoma: A single Institution Experience

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Dear Editor

Anaplastic large cell lymphoma (ALCL) was recognised as a subgroup of tumors which is defined as a neoplastic proliferation of lymphoid cells, with bizarre morphologic features, that are anaplastic in appearance, have a propensity to grow cohesively, invade lymph node sinuses and consistently express the CD30. Revisions of the fourth Edition of the WHO Classification (2016), have classified anaplastic lymphoma kinase (ALK)-ALCL as a definitive and recognized entity [1]. Our aim was to study the most relevant prognostic factors that impact the clinical course of ALK-ALCL.

This study is retrospective carried out over an 18-year period (1999–2016) and conducted at our Pathology Department (Salah Azaiz Institute, Tunisia). Based on the criteria of the 2016 WHO classification, 52 cases were systematically reviewed. A total of consecutive 34 patients with ALK-ALCL were included. Immunohistochemistry study was performed to determine the phenotype of tumor cells. Clinical information for each patient including the age, the gender and the Ann Arbor stage was abstracted from the medical records. Additional data recorded including the performance status (PS), the level of LDH, extranodal involvement and medullary invasion were obtained. The International Prognostic Index (IPI) was used to stratify patients within the various disease entities. Treatment outcome was determined by overall survival (OS). IBM SPSS 16 software was used for the statistical analyses. Statistical tests used were Log Rank test, the method of Kaplan and Meier and chi-square test. P values less than 0.05 were considered significant.

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Authors' contributions

Raoudha Doghri: general supervision

Linda Bel HadjKacem: Redaction the manuscript

Lamia Charfi: pathological diagnosis

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Nadia Boujelbene: revision of the manuscript

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Characteristics of ALK– ALCL are summarized in table 1. In contrast to increased age, gender, IPI score, LDH rate, lymphoma's phenotype and extranodal sites except medullar involvement, Advanced *Ann Arbor stage* and *medullar involvement* were significant poor prognostic factors ($p=0.004$ and $p=0.000$ respectively)(Table 1).

ALK–ALCL occurs generally in patients with a peak incidence in adults (40–60 years) with preponderance of male [1–2]. ALK– ALCLs are characterized by unfavourable clinical features (high age and advanced stage at diagnosis, high risk IPI features) and a poor prognosis which is reported to be better than peripheral T-cell Lymphoma, Not Otherwise Specified, and to be worse than ALK+ALCL [4,5,7]. In our study, the OS was 48.5% and this is comparable with prior estimates (30–49%) [2–4]. Most patients presented with advanced disease (stage III and IV), were all aged more than 50 years, suggesting that ALK –ALCL with advanced stage occur frequently in adults more than children and young adults. Bone marrow involvement are considered as a prognostic factor either in our study ($p=0.000$) or in the literature review [3,5–6].

ALK–ALCL was always CD30-, more frequently cytotoxic marker positive and EMA positive, and was less likely to express various T-cell markers (CD2, CD3, CD4, CD43) [3].

Other prognostic factors have been reported in the literature including the expression of proteins involved in the regulation of apoptosis and of CD56 [4] and other genetic rearrangements [1] without a real consensus.

In summary, the most important prognostic factor according to the experience of our institution is *medullar involvement* and *Ann Arbor stage*.

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TABLE 1
Characteristics of ALK– ALCL

Univariate analysis of the overall survival time in ALK–ALCL

Characteristics	number	Percentage %	P
Age			<i>0.330</i>
<16	8	23.52	
16–60	18	52.96	
>60	8	23.52	
SEX			<i>0.259</i>
Male	22	64.7	
Female	12	35.3	
LDH			
Elevated	23	67.64	<i>0.282</i>
Normal	11	32.36	
Extranodal Site			<i>0.730</i>
Yes	8	23.52	
NO	12	35.5	
Medullar involvement	6	17.66	0.000
Missing	8	23.52	
Ann Arbor Stage			0.004
I–II	4	11.84	
II–IV	24	70.5	
Missing	6	17.66	
IPI Score			<i>0.394</i>
0–2	25	73.5	
3	0		
Missing	9	26.5	
Phenotype			<i>0.880</i>
T	18	52.96	
Null	15	44.11	
Missing	1	2.93	