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Diagnosing anaplastic large cell lymphoma: A challenging case

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Abbreviations: ALCL: Anaplastic Large Cell Lymphoma.

Clinical Image Description

A 61-year-old man with multiple comorbidities was hospitalized following urosepsis. Broad-spectrum antibiotic therapy was initiated. Blood testing on admission revealed high levels of lactate dehydrogenase and beta-2 microglobulin, along with an important neutrophilic leukocytosis (25,310/μL) that persisted over its hospitalization. A blood smear revealed no morphologic findings, but flow cytometry showcased the presence of that could not be completely characterized. A total body scan was performed, revealing multiple lymphadenopathies above and below the diaphragm that raised suspicion on a lymphoproliferative disease. The histologic samples obtained through endoscopically guided biopsies of the lesions were non-evaluable for pathological characterization. Meanwhile, the patient quickly developed multiorgan failure and was taken into intensive care ten days after admission.

A bone marrow aspirate was subsequently performed and finally provided diagnosis, showcasing the presence of a morphologically heterogeneous cellular population of various sizes which shared a basophilic cytoplasm and small and abundant vacuoles. Some of the cells had a hand mirror shape and others possessed a blastic morphology (panel A and B, x1000 magnification). Flow cytometry demonstrated the expression of CD30 (panel C) and granzyme along with various T-cell antigens (CD3c, CD2, CD4 and CD5), suggesting the diagnosis of Anaplastic Large Cell Lymphoma (ALCL). These findings were consistent with genetic studies, as fluorescent in situ hybridization revealed an *ALK* rearrangement (panel D, LSI ALK Dual Color Break Apart probe), further confirmed by molecular testing detecting a rare *RNF213:: ALK* fusion gene. Further examinations revealed a complex karyotype and TCR rearrangement analysis confirmed monoclonality. Despite our best efforts, the patient eventually passed away after multiorgan failure following septic shock.

ALK-positive ALCL usually presents in young male adults and can have a rapidly fatal evolution [1-3]. Diagnosis is based on lymph node histology with the detection of the so-called hallmark cells, of big size, exocentric horseshoe-shaped nucleus and pale eosinophilic paranuclear zone, but some variants can have a smaller size and leukemic expression [3]. The rare presence of extreme neutrophilia on diagnosis results from inadequate secretion of IL-17 by the malignant cells [3]. Flow cytometry commonly reveals CD30 positivity concomitant with cytotoxic molecules like perforin or granzyme B, as well as T-cell antigens within the tumor cells [3]. The presence or absence of an ALK rearrangement, defines two clinically and biologically different groups of distinct prognosis [2,3]. Nucleophosmin (NPM1) is *ALK*'s binding partner on 80% of *ALK*-positive *ALCLs*. In the remaining cases, *ALK* has been found to fuse with several other partners, including *RNF213*, which was detected in our patient. This rearrangement has been documented in a limited number of patients, and its impact on the prognosis of the disease remains unclear [4].

Despite histological studies remain as the gold standard, the hematologic characterization of the disease is crucial and proved to be diagnostic in our case.

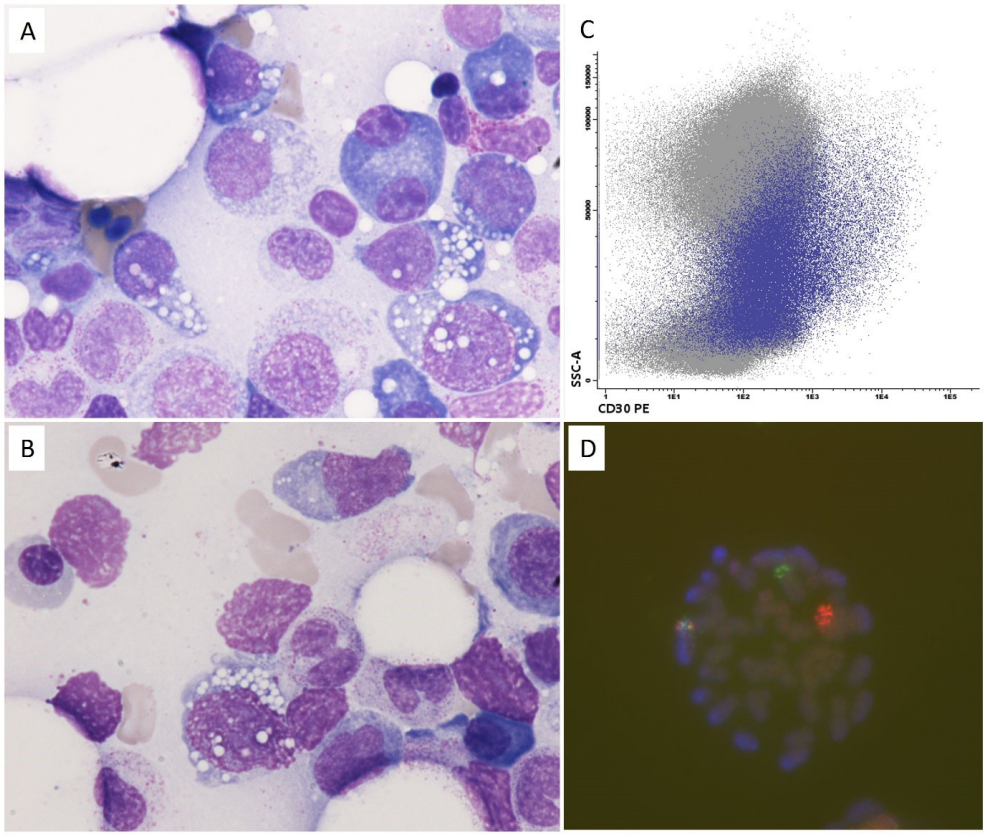

Figure 1: Medullary study at diagnosis. **A-B**: Morphological appearance of the pahological population (May-Grünwald-Giemsa stain, x1000 magnification). **C**: CD30 expression in the pathological population (blue) compared to the remaining nucleated cells (grey). **D**: FISH performed at diagnosis (Dual Color LSI break-apart probe targeting the *ALK* gene).

Declarations

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References

1. Alaggio R, Amador C, Anagnostopoulos I, Attygalle AD, Araujo IB de O, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. 2022; 36: 1720-48.

2. Campo E, Jaffe ES, Cook JR, Quintanilla-Martinez L, Swerdlow SH, et al. The International Consensus Classification of Mature Lymphoid Neoplasms: a report from the Clinical Advisory Committee. Blood. 2022; 140: 1229-53.

3. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised 4th edition. Lyon: International Agency for Research on Cancer. 2017: 413-421.

4. Van der Krogt JA et al. Anaplastic lymphoma kinase-positive anaplastic large cell lymphoma with the variant RNF213-, ATIC- and TPM3-ALK fusions is characterized by copy number gain of the rearranged ALK gene. Haematologica. 2017: 102(9): 1605–1616.

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