Diagnosing anaplastic large cell lymphoma: A challenging case

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Abbreviations: ALCL: Anaplastic Large Cell Lymphoma.

Clinical Image

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]. 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 pathological population (May-Grünewald-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


