Hemophagocytic syndrome in patients with acute myeloid leukemia undergoing intensive chemotherapy

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Supplementary data

Methods

Endpoints

The primary endpoint of the study was overall survival. For each participant, the length of follow-up corresponds to the period between the date of diagnosis and July 1, 2012 or the date of death if the patient died during the study period. The response to treatment was evaluated after full hematological recovery (e.g, when neutrophils and platelet counts were > 1 G/L and > 100 G/L to document complete responses), or at day 35 in cases of prolonged aplasia, and defined according to the international consensus criteria as complete response (CR) or complete response with incomplete blood count recovery (CRi).[15] Early death was defined as death from any cause occurring between the start of chemotherapy and the response assessment. Resistant disease, death in aplasia and relapses were defined according to Cheson criteria.[15] The duration of neutropenia was defined as the number of days between d1 of chemotherapy and the first day with neutrophils higher than 0.5 G/L or death for those who died with less than 0.5 G/L.

Statistical analysis

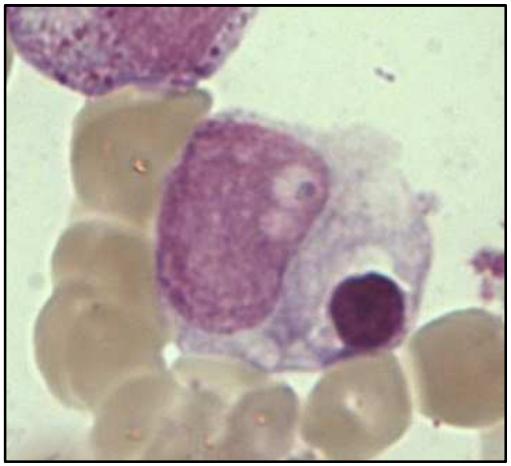
Statistical analysis was performed on STATA statistical software, release 11.2 (STATA Corporation, College station, TX, USA). We described patients' characteristics using number and frequency for qualitative data and number, median and Inter-Quartile Range (IQR) for quantitative data. Qualitative variables were compared between groups (HLH+, HLH-/HemoPh+ and HLH-/HemoPh- patients) using the χ^2-test (or Fisher's exact test in the case of small expected numbers). Student's *t*-test was used to compare the distribution of quantitative data (or Mann-Whitney's test when distribution departed from normality or when

homoscedasticity was rejected). Differences in survival functions were tested using the Log-Rank test. The independent impact of HLH on overall survival was assessed using a Cox model adjusted for age, secondary AML, white blood cell count, cytogenetics, performance status and consolidation treatment by autologous or allogeneic stem cell transplantation (SCT). HLH+ patients first become at risk of HLH+ mortality at the date of HLH+ diagnosis and patients treated with autologous or allogeneic SCT first become at risk of SCT mortality at the date of SCT. Since the linearity hypothesis was not fully respected for WBC, this continuous co-factor was transformed into ordered data: $\leq$ 50 G/L and > 50 G/L. The proportional-hazard assumption was tested for each covariate by the “log-log” plot method curves ((-ln{-ln(survival)}), for each category of nominal covariate, versus ln(analysis time)). None of the assumptions could be rejected. Interactions between HLH and the independent covariates were tested in the survival model (none were significant). All reported p-values were two-sided and the significance threshold was < 0.05.

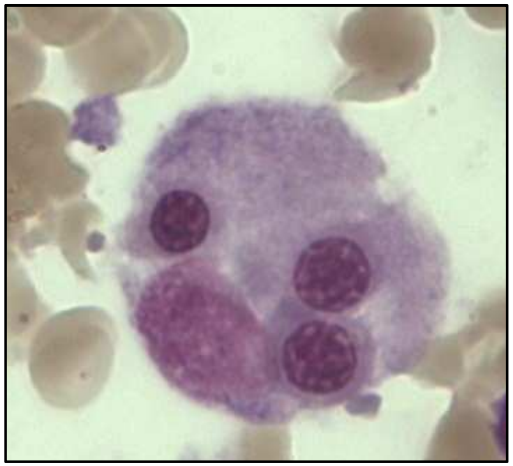
Supplementary figure.

Light microscopic representative images of May–Grünwald–Giemsa (MGG) stained bone marrow smear showing macrophages containing hematopoietic cells in their cytoplasm (x100). A, B, C. Erythroblast. D. Platelets.

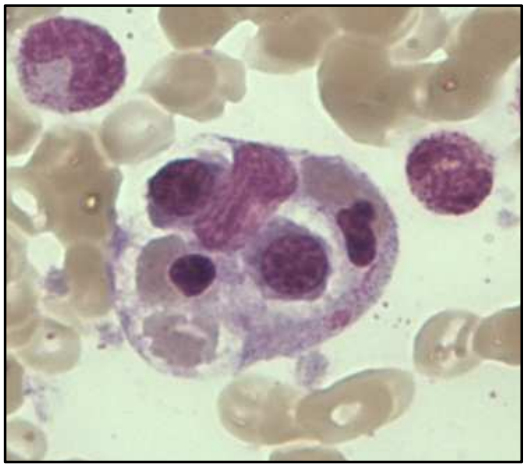
A



B



C



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