Letter to the Editor

Interim interleukin 6 levels correlate with progression-free survival in patients with classic Hodgkin’s disease: a pilot study

Dear Editor,

Hodgkin’s lymphoma (HL) is an uncommon neoplasm with an estimated number of 65,950 cases globally; its incidence varies significantly by age, sex, ethnicity, geographic location and socioeconomic status, being more frequent in young people. It is classified as either nodular lymphocyte predominant Hodgkin’s lymphoma (NHL-PH) or classical Hodgkin’s lymphoma (CHL).¹ The CHL accounts for 95% of all HL cases and can be further subdivided into four histological subtypes.²

The biology of HL depends on the interaction of the few pathognomonic, morphologically abnormal germinal B giant cells (Reed-Sternberg cells), with the surrounding reactive infiltrate composed of T-cells, histiocytes, eosinophils, and plasma cells. The ability of Reed-Sternberg cells to survive during negative selection in the germinal center depends, partially, on deregulated NFκB expression, closely related to the involvement of the Epstein-Barr Virus (EBV).³ The increase in NFκB transcription factor levels enhances the expression of several cytokines, including interleukin 6 (IL-6).⁴,⁵ As such, increased IL-6 levels at diagnosis may then be associated with a worse prognosis⁶ and with the presence of B symptoms and bulky disease.⁷

We evaluated all consecutive patients with CHL who were treated in the Department of Hematology at Hospital Mário Covas in Santo André, Brazil according to the WHO criteria to assess if IL-6 could relate to prognosis and should be studied as a prognostic marker, either at diagnosis or at mid-treatment evaluation (interim). Patients who were included from March 2012 to July 2015, were otherwise treated with the Doxorubicin, Bleomycin, Vinblastine and Dacarbazine (ABVD) regimen (Table 1). Two patients died during the study. The median follow-up was 23 months.

No significant correlations were observed between IL-6 levels, at either diagnosis or after treatment, with IPS, I-PET results or OS. Interestingly, the IL-6 levels at diagnosis were not correlated with the PFS. The interim IL-6 level significantly correlated with the PFS (p < 0.0001). Patients with IL-6 higher than 8.05 pg/mL after treatment had significantly lower PFS rates, compared to those with lower IL-6 levels (log rank p = 0.0149) (Figure 1). Two patients had iodine-124 positron emission tomography (I-PET) delayed to the 3rd cycle, due to logistic issues.

Table 1

<table>
<thead>
<tr>
<th>Patient features</th>
<th>n = 21</th>
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<tbody>
<tr>
<td>Male</td>
<td>9 (42.8%)</td>
</tr>
<tr>
<td>Median age (max–min)</td>
<td>28 (17–68)</td>
</tr>
<tr>
<td>&gt;50 years</td>
<td>3 (14.2%)</td>
</tr>
<tr>
<td>Stages III and IV</td>
<td>14 (66.7%)</td>
</tr>
<tr>
<td>Unfavorable prognosis</td>
<td>13 (61.9%)</td>
</tr>
<tr>
<td>Treatment first line (ABVD)</td>
<td>14 (66.7%)</td>
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The evaluation of response parameters at intermediary points in the CHL treatment, such as I-PET, seems to stratify patients into different prognostic subgroups for whom diverse therapeutic strategies can be considered.

To the best of our knowledge, our study is the first to show that lower IL-6 concentrations in the middle of treatment (Interim IL-6) correlated with a superior disease-free survival (DFS) in patients with CHL treated with chemotherapy. The small sample of patients precluded the use of multivariate analysis. Nevertheless, because we observed no significant associations between IL-6 after treatment and I-PET, it is possible that interim IL-6 could potentially add to I-PET for patient prognostic stratification after the start of therapy.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES


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