Letters to the Editor

1778-9.


Malignant Lymphomas

Soluble syndecan-1 levels in different plasma cell dyscrasias and in different stages of multiple myeloma

We measured serum levels of syndecan-1 in patients with multiple myeloma (MM), solitary plasmacytoma and monoclonal gammopathy of undetermined significance (MGUS). We then studied serum syndecan-1 levels in MM patients stratified by the Durie-Salmon staging system and the correlation of syndecan-1 levels with well known independent prognostic factors of MM.

haematologica 2004; 89:370-371

We investigated 67 patients: 13 had monoclonal gammapathy of undetermined significance (MGUS), 4 had solitary plasmacytoma, and 50 had multiple myeloma (MM). All plasma cell dyscrasias were defined by the diagnostic criteria of the American Southwest Oncology Group (SWOG).1 For comparative analysis of patients the following data and parameters were registered: age, sex, percentage of plasma cells in the bone marrow, immunoglobulin (Ig) class, serum M-protein concentration, serum levels of β2-microglobulin, albumin, calcium, creatinine, total alkaline phosphatase, and C-reactive protein (CRP).

Patients were subdivided by the Durie-Salmon staging system.2 At the time of evaluation 35 patients with MM had already undergone some form of chemotherapy. The other group of 15 previously untreated MM patients were followed during their chemotherapy. The median follow-up period of the patients was 6 months. Seven patients received ICOMP (idarubicin, cyclophosphamide, vincristine, methylprednisone) therapy, and 8 patients received VAD (vincristine, doxorubicin, dexamethasone) therapy for 6 months. All patients were treated with bisphosphonates. Response to therapy was determined by the change in M-protein concentration and the ratio of bone marrow plasma cells 6 months after initiation of chemotherapy. Objective therapeutic response was defined as at least a 50% reduction of serum paraprotein concentration.

The serum concentration of soluble syndecan-1 in patients with MM was measured using a commercially available human syndecan-1 enzyme-linked immunosorbent assay (ELISA) kit (Diacalone Research, Besancon, France).

Results were considered statistically significant when the p value was less than 0.05. Comparisons between groups were performed using the Mann-Whitney U-test. Response to treatment was analyzed with multiple logistic regression techniques.

Table 1. Correlations between serum syndecan-1 and other variables.

<table>
<thead>
<tr>
<th>Serum creatinine</th>
<th>Serum β2-microglobulin</th>
<th>Plasma cell content (%) of bone marrow</th>
<th>Serum M-component</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>50</td>
<td>49</td>
<td>49</td>
</tr>
<tr>
<td>r</td>
<td>0.378</td>
<td>0.379</td>
<td>0.407</td>
</tr>
<tr>
<td>p</td>
<td>0.007</td>
<td>0.007</td>
<td>0.004</td>
</tr>
</tbody>
</table>

r: indicates correlation coefficient for syndecan-1 and the designated variable.

The median serum syndecan-1 value was less than 0.05. Comparisons between groups were performed using a semiquantitative method, syndecan-1 levels were elevated in the sera of 7 out of 20 myeloma patients. Higher serum levels of soluble syndecan-1 were associated with higher levels of serum β2-microglobulin and elevated plasma cell content in the bone marrow.8 Evaluation of data collected from 138 MM patients showed that the serum syndecan-1 concentration could serve as an independent prognostic parameter in addition to serum β2-microglobulin and WHO performance status.10 In our study, patients with MM showed a higher median level of serum syndecan-1 than did patients with MGUS or plasmacytoma. The differences between these groups were significant.

A comparison of serum syndecan-1 levels among the myeloma subgroups also revealed significant differences. A
correlation was found between the level of serum β2-microglobulin, monoclonal protein concentration or bone marrow plasma cell content. A significant decrease in median syndecan level was observed in patients responding to chemotherapy, whereas the median syndecan level did not change in non-responders. Our results indicate that there is a marked difference in the serum syndecan-1 levels in different forms of plasma cell dyscrasias. Moreover, the level of syndecan-1 is higher in patients with higher stage MM. Further evaluation of patients is needed to evaluate the role of syndecan-1 in the prognosis of MM.

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Multiple Myeloma

Oral idarubicin, dexamethasone and vincristine in the treatment of multiple myeloma: final analysis of a phase II trial

This prospective phase II study evaluated a regimen with vincristine, oral idarubicin and dexamethasone (VID) in 74 patients with multiple myeloma. A partial response was achieved in 57% (41/72) of patients with previously untreated disease and in 35% (16/46) with refractory diseases. VID chemotherapy is an effective and tolerable oral alternative in an outpatient setting for these patients.

The combination of a continuous infusion of doxorubicin and vincristine with high-dose oral dexamethasone (VAD) has become a standard treatment for patients with multiple myeloma but the necessary central venous line causes considerable complications. Therefore, oral alternatives would be preferable. We tested such an alternative (vincristine, idarubicin and dexamethasone) in 74 patients with multiple myeloma.

For this trial, the following inclusion criteria had to be fulfilled: (i) diagnosis of multiple myeloma according to the British Columbia Cancer Agency Criteria; (ii) at least stage II disease according to the staging system of Durie and Salmon, and (iii) refractory disease (i.e. unresponsive to previous therapy) or previously untreated disease.

Vincristine was administered as an intravenous bolus injection on day 1 (2 mg). Idarubicin was given as a capsule, 10 mg/m² per day p.o., on days 1–4 (total dose 40 mg/m² per course). Dose escalation (up to 13 mg/m²/d) and dose reduction (to 8 mg/m²/d) was possible. Dexamethasone was given at a dose of 40 mg p.o. on days 1–4, 9–12, and 17–20. Courses were repeated starting on day 29 to reach a total of 6–8 courses. An interim report of this trial was published in 1997.¹ Response was defined by European Group for Blood and Marrow Transplantation (EBMT) criteria. Seventy-six patients were registered, but two patients were excluded after registration: one had been previously treated with idarubicin and dexamethasone and one died from pre-existing pneumonia on day 3. The remaining 74 patients (Table 1) received a total of 322 courses of VID, and a median of 4 (interquartile range 3–6). Patients with refractory disease had been heavily pretreated (Table 1). Twenty-one patients (9/46 with refractory, 12/28 with previously untreated disease) received autologous stem cell transplants; their survival data were censored at the time of transplantation. Five patients died within two months of entering the study (early death, two from sepsis in neutropenia in the first course) and one patient was lost to follow-up after the first course. These patients were counted as failures in the efficacy evaluation. Complete informa-

Table 2. Serum syndecan-1 levels in myeloma patients receiving chemotherapy.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syndecan-1 ng/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responders n=41</td>
<td>258</td>
<td>106</td>
</tr>
<tr>
<td>Range</td>
<td>97.3-460</td>
<td>57.3-440</td>
</tr>
</tbody>
</table>

Non-responders n=4

|               |          |           |
| Syndecan-1 ng/mL |          |           |
| Median         | 327      | 361.7     |
| Range          | 245-466  | 251-486   |


References

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