With great interest we read the report of Winkelmann et al. [1]. The authors suppose that the increased ploidization of the megakaryocytes observed in patients with metastatic tumors is due to the mitogenic or growth factor with thrombopoietin-like activity produced by the tumor itself. We wish to provide some additional evidence in favor of this hypothesis. Thrombopoiesis-stimulating factor or thrombopoietin (TPO) and megakaryocyte colony-stimulating factor (MEG-CSF) have been detected in plasma or serum [2, 3] and urine [4, 5] of patients with disturbed thrombopoiesis. In the experiment was used the urine of a 76-year-old white male who was 71 years old when prostatic adenocarcinoma and polycythemia vera (PV) were recognized. The diagnosis of adenocarcinoma was confirmed during the histological studies of biopsy specimens and the current-day criteria of the Polycthyemia Vera Study Group [6] for the diagnosis of PV were fulfilled. The patient was treated with diethylstilbestrol but no significant improvement was achieved. As a treatment of his hematologic disorder the patient received two courses of 32P and his hematocrit fell to normal levels, but platelet counts remained high and ranged from 400 × 10^9/l to 1,200 × 10^9/l. At the moment of study he did not receive any active treatment and his peripheric blood count showed Hb 142 g/l, Ht 40, platelets 500 × 10^9/l, WBC 9.4 × 10^9/l. The serum of this patient, tested for TPO in a mouse bioassay system by measuring the incorporation of 75Se-sele-nomethionine (75SeM) into platelets of assay mice after the method of Penington [7] with slight modification [8], revealed elevated TPO levels (131% of control, p < 0.02). This suggested the existence of high levels of TPO in urine too. Urinary extracts were prepared from the urine of the patient and pooled urines of 3 healthy donors using the method described by Espada and Gutnisky [9].

This method has been developed for the concentration of erythropoietin (EPO), but physicochemical characteristics of TPO and EPO are similar [10], so both are present in urinary preparations. In the case described here urinary EPO did not contribute to the

<table>
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<tr>
<th>Dose of urinary extract injection, mg</th>
<th>Percent incorporation of 75SeM into platelets, p</th>
<th>control patient</th>
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</thead>
<tbody>
<tr>
<td>2.5</td>
<td>0.121 ± 0.013 (6)</td>
<td>0.184 ± 0.007 (6)</td>
</tr>
<tr>
<td>5</td>
<td>0.141 ± 0.017 (7)</td>
<td>0.201 ± 0.120 (6)</td>
</tr>
</tbody>
</table>
Number of animals in parentheses. Values are means ± SE.

TPO activity since the patient had normal level of hemoglobin. The determination of TPO activity in these urinary preparations was performed according to the method mentioned above [7, 8]. The urinary TPO activity of the patient was significantly higher (p < 0.002 and p < 0.05 respectively) than that of normal donors at both doses studied (2.5 and 5 mg) (table 1).

The increased TPO activity in the serum and urine of this patient cannot be attributed to PV, since the levels of normal hematopoietic stimulating factors (EPO, TPO, MEG-CSF) are not augmented in this myeloproliferative disease [2, 11], which results from clonal proliferation of a pluripotential hematopoietic stem cell [12]. On the other hand, there is some evidence that thrombocytosis observed in some cases of metastatic carcinomas is accompanied by increased levels of TPO-like factor(s) [2, 13]. So the most logical is to suggest, in agreement with the hypothesis of Winkelmann et al. [1], that the TPO-like activity observed in the serum and urine of this patient is due to the capacity of prostatic adenocarcinoma to realize an autonomous production of this factor(s).

References


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