Thrombophilic condition in HIV-infected patients

Sir,

Various hemostatic disorders associated with hypercoagulable conditions have been reported in HIV infection, even in the absence of clinically apparent thrombosis and showing no correlation to the stage of the disease.\(^1\)\(^2\) To further investigate whether HIV infection was associated with an ongoing prothrombotic state, twenty-two consecutive HIV-infected patients, classified as having AIDS (10 M, 12 F, aged 35 ± 10; mean ± SD), none of the patients had laboratory or clinical evidence of hepatopathy or renal failure. None had a history of smoking, drug abuse, diabetes, obesity, or previous thrombotic events. The control group consisted of twenty age- and sex-matched HIV-negative healthy individuals (9 M, 11 F, aged 30 ± 4, mean ± SD). None of the patients had laboratory or clinical evidence of hepatopathy or renal failure. None had a history of thrombosis or had received anticoagulant therapy. Since the analysis of the molecular markers of hemostatic parameters can lead to artifically elevated results,\(^3\) blood collection and handling were carried out under strictly standardized conditions. The activation of the coagulation system was studied measuring plasma concentrations of the prothrombin fragment 1+2 (F1+2) using ELISA (Bering Werke AG, Germany). The fibrinolytic system was investigated detecting plasma levels of plasminogen activator inhibitor (PAI-1) activity and fibrin degradation products (FbDP) with a chromogenic substrate-based assay and an immunoturbidimetric assay, respectively, according to the manufacturer instructions (Boehringer Mannheim, Germany). Since infectious disease and sepsis, which are common occurrences in AIDS patients, may predispose thromboembolic complications,\(^6\) plasma levels of antithrombin III and protein C activities were also evaluated using chromogenic substrate-based assays, according to the manufacturer instructions (Boehringer Mannheim, Germany). Data were compared by the Mann-Whitney U test. The Spearman rank test was used to evaluate the correlation between parameters. A p value < 0.05 was considered to be statistically significant. Our results, as reported in Table 1, suggest that HIV-infection is characterized by hemostatic disorders, such as elevated plasma levels of F1+2, FbDP and PAI-1 activity, and lower plasma levels of protein C activity, usually considered as risk factors for thrombosis in the general population. In particular, F1+2, a sensitive marker of endogenous thrombin generation,\(^7\) and FbDP, an index of unopposed plasmin activity,\(^7\) were found to be significantly correlated in our group of patients, as previously reported in HIV infection.\(^8\)

Table 1. Plasma levels of prothrombin fragment 1+2 (F1+2), antithrombin III (AT III), protein C, fibrin degradation products (FbDP) and plasminogen activator inhibitor (PAI-1) in 22 HIV-infected patients and in 20 age- and sex-matched healthy individuals. Results are given as median with their range.

<table>
<thead>
<tr>
<th></th>
<th>HIV-infected patients (n=22)</th>
<th>Healthy controls (n=20)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1+2 (µg/mL)</td>
<td>1.30 (0.68-2.45)*</td>
<td>0.90 (0.40-1.27)</td>
<td>&lt; 0.0002</td>
</tr>
<tr>
<td>AT III (%)</td>
<td>103.60 (68.00-142.00)</td>
<td>104.00 (86.00-112.00)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Protein C (%)</td>
<td>74.41 (26.10-132.20)</td>
<td>99.15 (80.00-117.60)</td>
<td>&lt; 0.0003</td>
</tr>
<tr>
<td>FbDP (mg/mL)</td>
<td>1.21 (0.28-2.40)*</td>
<td>0.29 (0.10-0.48)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PAI-1 (AU/mL)</td>
<td>10.41 (7.00-21.00)</td>
<td>4.50 (1.00-9.00)</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

\(^*\)Correlation between F1+2 and FbDP plasma levels: r = 0.43, p < 0.05.

On the other hand, it has been suggested that a lower protein C activity may affect thrombotic events when associated with other hypercoagulable conditions (thrombin generation, fibrinolytic shut-down, inflammation, etc.).\(^7\) The mechanism responsible for the enhancement of procoagulant properties and impairment of fibrinolytic capacities in HIV infection is still being studied. However, the loss of endothelial integrity due to HIV infection itself has been suggested as the cause\(^8\) and could explain the higher levels of PAI-1 activity we found in AIDS patients. In conclusion, our preliminary results show that HIV infection is associated with an on-going prothrombotic state. We think that this condition should be taken into account, especially when septic events occur as complications, since infectious agents and inflammation mediators have been shown to shift the coagulation-fibrinolysis equilibrium of endothelial cells towards fibrin formation.\(^7\)

References

Letters to the Editor

733
MEETING ANNOUNCEMENTS

First Announcement of the
EUROPEAN GROUP FOR BLOOD AND BONE MARROW TRANSPLANTATION
Working Party on BMT on Pediatric Diseases
Barcelona, May 7-9, 1998

Deadline for scientific contributions:
January 20, 1998

Further information is available
through the Administrative Secretariat:
MIZAR TRAVEL
Josep Irla i Bosch, 5 Entlo. 1*, 08034 Barcelona, Spain
Tel. +34.3.2801188; Fax. +34.3.2055799.
e-mail: mizar@chi.es

or through the Scientific Secretariat:
JUAN J. ORTEGA AND T. OLIVÉ,
Servicio de Hematologia, Hospital Materno Infantil,
Vall d’Hebron, Pas. Vall d’Hebron, 119-129,
08035 Barcelona, Spain
Fax. +34.3.4282171

PRELIMINARY PROGRAM

Thursday 7 – educational program
• HLA typing. Implications in outcome of unrelated BMT
• GVHD and GLV. Implications in GVHD prophylaxis regimens.
• Allogeneic hematopoietic progenitor cells from different sources. Biological and technical aspects.
• Peripheral blood progenitor cells for transplants in children.
• Umbilical cord blood for transplants in children.
• Indications and results of progenitor cell transplants in pediatric diseases: acute leukemias, myelodysplastic and myeloproliferative diseases, solid tumors, immunodeficiencies, congenital hemopathies and metabolic diseases.

Friday 8 – main sessions
• GVHD: prophylaxis and treatment.
• Progenitor cell transplants with alternative donors in children.
• Long-term survivors: late effects, sequelae, quality of life

Poster sessions

Saturday 9 – main session
• Immunological reconstitution and infectious complications in transplanted children

Protocol sessions

3. Narayan S. Preanalytical aspects of coagulation testing. Haema-
343-50.
4. Fera G, Semeraro N, De Mirto V, Schiraldi O. Disseminated intra-
40:49-56.
6. Bauer KA, Rosenberg RD. The pathophysiology of the prethrombot-
7. Bick RL. Disseminated intravascular coagulation and related syn-
8. Esmon CT. Inflammation and thrombosis: the impact of inflamma-
tion on the protein C anticolagulant pathway: Haematologica 1995;
80(Suppl. 2):49-56.
9. Re MC, Furlini G, Cenacchi G, Preda P, La Placa M. Human immun-
deficiency virus type 1 infection of endothelial cells in vitro.
10. Lafeuillade A, Alessi Mc, Poizot-Martin I, et al. Endothelial cell dys-

Correspondence: Dr. Rosita Trotti, IRRCS Istituto Neurologico Fonda-
zione, “C. Mondino”, via Palestro 3, 27100 Pavia, Italy. Tel. international +39.382.380268. Fax interna-
tional +39.382.380286.