progressively increased (Figure 1) and the ecography was normal. Viral A, B and C HV markers were all negative. Liver biopsy was not considered because of the compromized hemostasis and the age of the patient. At 2 months, he was admitted because of another arterial embolism. Calcium heparin was initiated, while liver tests became progressively normal. On the seventh day, with defervescence in the thrombotic phenomena, he was released under calcium heparin, followed by low molecular heparin, which was sustained indefinitely, without recrudescence of the liver's enzymatic parameters.

The fast defervescence on the liver tests and the absence of other causative factors confirm the cause-effect relationship between the drug and the cholestasis, though we did not consider re-challenge for ethical reasons. Likewise, it is worth noting the low response to warfarin if we consider that recurrence was not avoided. This leads us to speculate that there is a metabolic resistance to the drug on a hepatic level, which would explain both phenomena observed in this patient. Although we have been able to find other reports about warfarin-related hepatitis,[4-6] we have not found similar complications after the treatment with acenocoumarin. We think that, in spite of the apparent scarcity of this drug-related hepatitis, this possibility should be taken into account because of the frequency of the anticoagulant treatment.

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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), were studied during outpatient therapy for a certain length of time during acute episodes.

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 artefactually 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 (BeringWerke AG, Germany). The fibrinolytic system was investigated detecting plasma levels of plasminogen activator inhibitor (PAI-1) activity and fibrin degradation product (FbDP) with a chromogenic substrate-based assay and an immunoturbidimetric assay, respectively, according to manufacturer instructions (Boehringer Mannheim, Germany). Since infectious disease and sepsis, which are common occurrences in AIDS patients, may predispose thromboembolic complications,[4,5] 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,[6] 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.[2]

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.

	HIV- infected patients (n=22)	*Healthy controls (n=20)*	*p*
F 1+2	1.30 (0.68-2.45)*	0.90 (0.40-1.27)	p<0.0002
AT III (%)	103.60 (68.00-142.00)	104.00 (86.00-112.00)	n.s.
protein C(%)	74.41 (26.10-132.20)	99.15 (80.00-117.60)	p<0.0003
FbDp (mg/mL)	1.21 (0.28-2.40)*	0.29 (0.10-0.48)	p<0.001
PAI-1 (AU/mL)	10.41 (7.00-21.00)	4.50 (1.00-9.00)	p<0.0001

**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.).[8] 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[9,10] 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.[4]

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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

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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