Immunosuppression due to MACOP-B does not seem to cure the antiphospholipid syndrome

Sir,

Antiphospholipid antibodies (APA) are a heterogeneous group of immunoglobulins directed against negatively charged phospholipid, protein-phospholipid complexes, or plasma glycoproteins such as β-2-glycoprotein I and include anticardiolipin (ACA) and lupus anticoagulant (LAC) antibodies.

The presence of these antibodies has been associated with the clinical features of the so-called *antiphospholipid syndrome* (APS), which includes arterial and venous thrombosis, recurrent fetal loss, and thrombocytopenia.[1] Prospective studies published by Schved *et al.*[2] and Finazzi *et al.*,[3,4] have shown that hematologic malignancies can develop during follow-up of patients with APA.

A 36-year old woman with known APS was admitted to our department because of evidence of asymptomatic mediastinal widening and pleural effusion.

Needle biopsy with CT scan of the bulky mediastinal mass disclosed a diffuse large B-cell lymphoma. Staging failed to show other lymphoma localization. Laboratory data were normal except for ESR 38, LAD 674 U/L, copper 25.5 mmol/L, while Coombs' test and antinuclear antibodies diffuse type (titer 1/320) were positive.

The results of coagulation tests, kaolin clotting time (KCT), lupus anticoagulant Russell's venom viper time (RVVT), platelet neutralization procedures (PNP) and neutralization with hexagonal phase phosphatidylethanolamine test (PE) are shown in Table 1. The patient was treated with MACOP-B followed by mantle field radiotherapy (39.6 Gy in 22 fractions) obtaining a complete remission. Previously altered laboratory data normalized except for the antinuclear antibodies (positive at the same titer) and coagulation tests (KCT, RVVT, PNP,PE).

An association between APA and hematologic malignancies has been described rarely, even though a prospective Italian study[3] revealed that the principal cause of mortality and morbidity in patients with idiopathic APA is lymphoproliferative diseases emphasizing that the incidence of non-Hodgkin's lymphoma (NHL) in this category of patients is greater than expected for subjects in the Western world.

In a cross-sectional study by Stasi *et al.*[5] and in some case reports,[6,7] complete remission was associated with the disappearance of APA.

In our case no relapse has been documented despite 60 months of follow-up, while the RVVT test is still abnormal and PNP, PE, KCT and the antinuclear antibodies are still positive. Despite the fact that 12 weeks of therapy with chemotherapeutic and immunosuppressive agents has eradicated the lymphoma, the lymphoid subset producing APA[8] is evidently still present. We could, therefore, suppose that the lymphoproliferative disease does not originate from the same lymphoid subset producing APA even though, likely, from the same immune dysregulation causing the APS. This last possibility could explain the different responsiveness to the therapy. Nevertheless, if APA is a risk factor for lymphoproliferative disease, our patient should be at greater risk of relapse.

Larger studies are necessary to confirm the risk of evolution to hematologic malignancies in patients positive for APA and to clarify the prognostic value of persistent positivity for APA in patients treated for lymphoproliferative disorders.

Table 1. Coagulation tests before and after polychemotherapy.

Test	*Before polyCT*	*After polyCT*	*Normal values*
APTT	48 sec	60 sec (on warfarin)	30-40 sec
APTT diluted	141 sec	128 sec	32-43 sec
KCT	165 sec	163 sec	60-110 sec
PNP and PE	positive	positive	negative
APA	5 UPL/mL	7.3 UPL/mL	<5 UPL/mL
ACA-IgG	32 UGPL	33 UGPL	<5 UGPL/mL
ACA-IgM	negative	negative	<5 UPL/mL

CT = chemotherapy.

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New technology and changing parameters of leukapheresis for blood cell transplantation

Sir,

Clinical investigators have recently developed an innovative technique of leukapheresis (LK) for blood cell transplantation (BCT) referred to as AutoPBSC System. This technique offers the following advantages: a) better collection efficiency of CD34+ hematopoietic progenitor cells; b) reduced collection of platelets; c) higher quality of LK components in terms of reduced contamination by granulocytes, platelets, and erythrocytes; d) reduced LK volume; and e) automation.[1] These advantages prompted us to evaluate the effectiveness of the AutoPBSC System and to extend classic parameters for starting LK, i.e., CD34+ cells $\geq 20/\mu L$ and platelets $\geq 30\times10^3/\mu L$,[2] also to poor-mobilizer and/or thrombocytopenic patients, i. e., with CD34+ cells $\leq 20/\mu L$ and/or platelets $\leq 30\times10^3/\mu L$, respectively. We confirm the advantages of the AutoPBSC System and demonstrate that efficient LK can successfully be performed also in these categories of patients.

Ninety-six leukaphereses were carried out in 65 consecutive patients undergoing BCT for treatment of poor prognosis malignancies (13 multiple myeloma, 12 breast cancer, 8 Ewing's sarcoma family of tumors, 9 non-Hodgkin's lymphoma, 7 Hodgkin's disease, 6 ovarian cancer, 3 rhabdomyosarcoma, 3 desmoplastic small cell tumor, 1 Wilms' tumor, 2 non-small cell lung cancer, 1 yolk sac tumor). The LK procedure implied processing 2.5-fold the individual's blood volume and adaptation of the AutoPBSC software default and harvest frequency as described by Ravagnani *et al*.[1] At the time of LK, the mean CD34+ cell count per µL was 106, the median 53, and the range 3-626; mean platelet count was 104×10^3 µL, median 92×10^3, range $15\text{-}456\times10^3$.

As detailed in Figure 1, the collection target of CD34+ cells $\geq 5\times10^6$ in a single LK was achieved in 100% (48/48) of procedures when the initial CD34+ cells $\geq 50/\mu L$ and 21% (10/48) when CD34+ cells $\leq 50/\mu L$. Single LK in poor-mobilizer patients (n = 17) with CD34+ cell counts $>10/\mu L$ and $\leq 20/\mu L$ (n=14) and $\leq 10/\mu L$ (n=15) yielded mean 2.1×10^6, median 1.8, range $0.7\text{-}3.7\times10^6$ and mean 1.7×10^6 CD34+ cells/kg, median 1.7, range $0.8\text{-}3.4\times10^6$, respectively; in

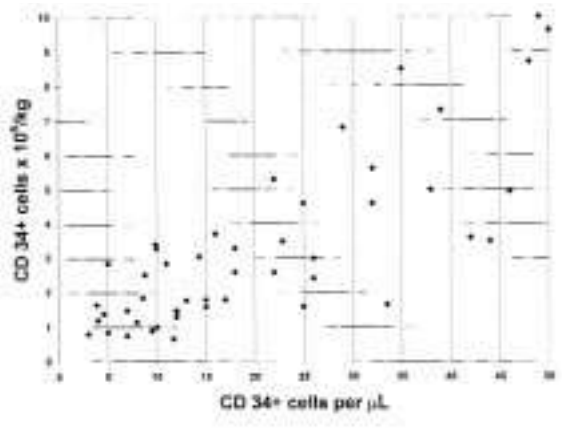

Figure 1. Yields of CD34+ progenitor cells by single LK versus CD34+ cell counts. Data shown are limited to the 48 procedures with CD34+ cells $\leq 50/\mu L$ (total LK=96).

thrombocytopenic patients (n = 7) a single LK yielded mean 3.9×10^6 CD34+ cells/kg, median 2.6, range $0.8\text{-}14.6\times10^6$; and in thrombocytopenic and poor-mobilizer patients (n = 5) it yielded mean 1.9×10^6 CD34+ cells/kg, median 1.8, range $0.8\text{-}3.1\times10^6$. Although platelet depletion in thrombocytopenic patients was negligible, a prophylactic platelet transfusion was given after LK to 3 patients.

Results of a single leukapheresis presented here compare favorably with those previously attained with other techniques[1,2] and confirm for the first time the advantages of the AutoPBSC System in poor-mobilizer and thrombocytopenic patients as well, thus facilitating the clinical application of blood cell transplantation.

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