Should Patients With Atherosclerosis or Peripheral Vascular Disease Be Stratified for Factor V Leiden?

To the Editor:

We read with interest the article of Rosendaal et al relating to the association between factor V Leiden and myocardial infarction in young women. We were impressed by the association between smoking and the manifestation of factor V Leiden in thrombosis/atherosclerosis and the high prevalence of the heterozygote gene state in the group. We recently found a similarly high prevalence of factor V Leiden in peripheral vascular disease patients.

Thirty-eight peripheral vascular disease patients who had undergone infrainguinal vein graft bypass were studied to determine the relationship between vein graft stenosis and hyperhomocysteinaemia (mean age, 66.8 years). Twelve patients were current smokers and 21 were past smokers, confirmed by carbon monoxide measurement. A strong association between hyperhomocysteinaemia and vein graft stenosis was found, especially in men. In these patients and seven others who underwent infrapopliteal bypass grafting with prosthetic material we performed a detailed hematological analysis including activated protein C resistance (APCR). We were surprised to find 6 of 33 patients (24%) not taking Warfarin had APCR. To better define this population, polymerase chain reaction (PCR) for factor V Leiden was performed on all 45 patients and it revealed 6 patients with APCR to be factor V Leiden—positive. PCR showed that 1 patient on Warfarin therapy and 1 patient without APCR were factor V Leiden—positive. The prevalence of factor V Leiden in this cohort was 18% (8 of 45), compared with a locally determined prevalence of 3.5%—similar to published United Kingdom prevalences. Of the 8 patients with factor V Leiden, 1 patient was homozygous. There was no difference in the prevalence of hyperhomocysteinaemia in patients with (5 of 8) or without (17 of 38) factor V Leiden; however, the one homozygous factor V Leiden patient had the highest homocysteine level that we measured at 45 μmol/L. He had no history of deep venous thrombosis. Of the 8 patients with factor V Leiden, all except 1 were past or present smokers.

We would suggest that there is an association between hyperhomocysteinaemia, factor V Leiden, smoking, and atherosclerosis as well as deep venous thrombosis but that the interaction between cause and effect is not clear. The exciting possibility of predicting not only thrombotic risk but the risk of atherosclerosis in patients with recognized risk factors might exist if the manifestation of these genetic factors and their relationship with environmental factors was better understood. We believe that the opportunity to risk stratify all patients with atherosclerosis with respect not only to recognized risk factors such as smoking but also systemic factors such as factor V Leiden now exists and would allow a more accurate assessment of the need for therapeutic intervention.

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REFERENCES

Epstein-Barr Virus Lytic Infection in Lymphocytes and the Persistence of the Virus

To the Editor:

In their interesting report, Prang et al showed the presence of peripheral blood mononuclear lymphocytes (PBMC) positive for Epstein-Barr virus (EBV) lytic proteins. This is in agreement with the updated theory of EBV persistence. However, this is not the first paper reporting lymphocytes expressing EBV lytic proteins in vivo.

It used to be believed that epithelial cells are responsible for the primary infection and the persistence of EBV. EBV lytic infection in epithelial cells is differentiation-associated and virus released there infects lymphocytes later on. The first report proposing a different view for the role of EBV-infected lymphocytes in the persistence of the virus was published in 1988. Later in 1990, Rickinson proposed a new model which shows how lymphocytes can contribute to the persistence of the virus through expansion at the germinal center, and also to the transmission of the virus to distant epithelial cells by spontaneous lytic infection. Rickinson’s model still emphasizes the role of epithelium in the primary infection of EBV. In 1994, Niedobitek and Young proposed that both primary EBV infection and the persistence of the virus are mediated by lymphocytes. How can mucosal lymphocytes become infected by EBV without the help of epithelial cells if the epithelium is not damaged? The presence of intraepithelial lymphocytes may provide an explanation. I have previously shown the presence of EBV-infected intra-epithelial lymphocytes in the nasopharyngeal mucosa of EBV seropositive people who had no EBV-associated disease or malignancy and the
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