Role of the Intrinsic Coagulation Pathway in Atherogenesis Assessed in Hemophilic Apolipoprotein E Knockout Mice


Objective—The contribution of thrombosis and coagulation in atherogenesis is largely unknown. We investigated the contribution of the coagulation intrinsic factor VIII (FVIII)–dependent pathway in atherogenesis.

Methods and Results—Apolipoprotein E and FVIII double–deficient mice (E°/FVIII°) were generated. Aortic root lesions were analyzed in 14-week-old and 22-week-old female mice maintained for 8 or 16 weeks, respectively, on a normal chow diet or a hypercholesterolemic diet.

Conclusion—Despite a higher plasma total cholesterol concentration compared with E° mice, E°/FVIII° mice developed dramatically less early-stage atherosclerotic lesions. Whereas early lesions in E° mice contained abundant fibrin(ogen) deposits on which few platelets adhered, lesions in E°/FVIII° were almost devoid of fibrin(ogen), and no platelets could be detected. The genotype effect on development and composition of lesions tended to decrease with time. This study demonstrates that the activation of the intrinsic pathway of coagulation is potently proatherogenic at the early stage of atherogenesis. (Arterioscler Thromb Vasc Biol. 2005;25:e123-e126.)

Key Words: atherosclerosis ■ hemophilia ■ mouse ■ knockout

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