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Letter to the Editor

Acute Myocardial Infarction Associated With the Prothrombin G20210A Mutation

To the Editor:

The prothrombin G20210A mutation is associated with an increased risk of venous thrombosis (1), but whether the mutation is also associated with premature artery disease and acute myocardial infarction (AMI) remains unclear. Some authors (2–5) do not find the prothrombin G20210A mutation to constitute a major risk factor, but others (6–9) suggest that it is associated with an increased risk of myocardial infarction and, more importantly, the risk substantially increases when one of the major cardiovascular risk factors (smoking, hypertension, diabetes mellitus, hyperlipidemia, or obesity) is also present, especially in AMI patients younger than 45 (7,8).

Here we report on two unrelated patients with AMI who were found to be heterozygous for the prothrombin G20210A mutation. The first patient was a 39-year-old white woman with no family history of coronary heart disease or venous thrombotic events. The patient had been hypertensive for 6 years and was under antihypertensive treatment with Norvas (amlodipine) 5 mg/day and Tenso-Stop (fosinopril) 20 mg twice/day. In addition, she was a heavy smoker (more than 20 cigarettes/day). She was neither diabetic, hyperlipemic, nor obese and was not taking oral contraceptives. She was admitted to the hospital with acute chest pain of 2 hours' duration that radiated out into the left arm and the neck. This together with a creatine phosphokinase level of 1,431 U/L and creatine phosphokinase-MB level of 185 U/L led to the patient being admitted into the Intensive Care Unit. The electrocardiogram showed a sinus rhythm with normal atrioventricular and intraventricular conduction, poor expression of the R wave between the VI and V3 derivations, and depression of the ST segment through VI and V4. The echocardiogram showed normal left ventricular function without thrombus in the left ventricular cavity. The final diagnosis was myocardial infarction without Q wave, located in the anterior ventricular wall.

The second patient was a 42-year-old white man whose father had died of an ischemic cardiac disease. The patient smoked more than 20 cigarettes/day but had no other cardiovascular risk factors and practiced sports regularly. The patient was admitted to the Intensive Care Unit with precordial pain of ischemic characteristics lasting several hours. The electrocardiogram indicated an anterior myocardial infarction with no Q wave and with anterior subepicardial ischemia. The coronariographic study showed one coronary lesion (descending anterior coronary artery) with good collateral circulation. The decision made at that moment was to apply conservative therapy. A later coronariographic evaluation showed that three coronary vessels were affected, and a coronary artery bypass was performed in four locations.

Six months after the acute episode, both patients were referred to our Thrombosis and Hemostasis Unit for a thrombophilia study, and in both patients the only abnormal finding was the presence of the prothrombin G20210A mutation. A family screening was performed in both cases. In the family of the first patient, the defect was also detected in her mother and her son, whereas in the family of the second patient, two of his sons were also carriers of the anomaly. One of them had had an episode of deep vein thrombosis at the age of 18 after 2 weeks of bed rest because of pulmonary tuberculosis.

In a population-based control study among women ages 18 to 44 years, the risk of myocardial infarction associated with carriership of the prothrombin G20210A mutation was 4.1%, with 5.1% of the patients and 1.3% of the controls being carriers of the prothrombin G20210A mutation. The risk increased sixfold when associated with other cardiovascular risk factors (7). Arruda et al. (8) obtained similar results in a study in which the prevalence of the prothrombin G20210A mutation was found to be 3% among 220 patients with myocardial infarction and 0.7% in 295 subjects from the general population. The mutation carriers (n = 7; 2 were male, 5 were female) included 3 of 63 patients (4.7%) in the premature AMI group and 4 of 157 patients (2.5%) in the nonpremature group. All seven carriers had, in addition, one or more cardiovascular risk factors.

Recently, Doggen et al. (9) also reported increased prevalence of the prothrombin G20210A allele in AMI male patients younger than 70 years. Of the 560 men with a first MI, 1.8% were found to be heterozygous carriers of the mutation, whereas 1.2% of the 646 healthy male subjects carried the mutation. The risk of MI in the presence of the prothrombin G20210A genotype increased by 50%. This risk rose substantially when one of the major cardiovascular risk factors was also present, with odds ratios varying between 3 and 6.

The two patients that we report on here, in whom AMI is associated with the prothrombin G20210A mutation, are less than 45 years of age and have one or more cardiovascular risk factors—smoking in the case of the

first patient, and smoking and hypertension in our second patient. This finding is consistent with previous studies (7–9) that highlight the synergy between cardiovascular risk factors and the prothrombin G20210A mutation for developing AMI. The interaction between atherosclerosis risk factors and genetic hemostatic defects seems to be especially relevant in young populations. Given the high prevalence of this novel genetic mutation in southern Europe (10), prevention or treatment of cardiovascular risk factors needs to be strengthened, and specific studies on this genetic mutation in young patients with AMI are recommended.

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REFERENCES

1. Poort SR, Rosendaal FR, Reitsma PH, et al. A common genetic variation in the 3′-untranslated region of the prothrombin gene is associated with elevated plasma prothrombin levels and an increase in venous thrombosis. *Blood* 1996;88:3698.
2. Corral J, González-Conejero R, Lozano ML, et al. The venous thrombosis risk factor 20210 A allele of the prothrombin gene is not a major risk factor for arterial thrombotic disease. *Br J Haematol* 1997;99:304.
3. Vargas M, Soto I, Pinto CR, et al. The prothrombin 20210 A allele and the factor V Leiden are associated with venous thrombosis but not with early coronary artery disease. *Blood Coagul Fibrinolysis* 1999;10:39.
4. Eikelboom JW, Baker RI, Parsons R, et al. No association between the 20210G/A prothrombin gene mutation and premature coronary artery disease. *Thromb Haemost* 1998;80:878.
5. Croft SA, Daly ME, Steeds RP, et al. The prothrombin 20210 A allele and its association with myocardial infarction. *Thromb Haemost* 1999;81:861.
6. Watzke HH, Schüttrumpf J, Graf S, et al. Increased prevalence of a polymorphism in the gene coding for human prothrombin in patients with coronary heart disease. *Thromb Res* 1997;87:521.
7. Rosendaal FR, Siscovick DS, Schwartz SM, et al. A common prothrombin variant (20210 G to A) increases the risk of myocardial infarction in young women. *Blood* 1997;90:1747.
8. Arruda VR, Siquiera LH, Chiaparini LC, et al. Prevalence of the prothrombin gene variant 20210G/A among patients with myocardial infarction. *Cardiovasc Res* 1998;37:42.
9. Doggen CJM, Manger Cats V, Bertina RM, et al. Interaction of coagulation defects and cardiovascular risk factors. Increased risk of myocardial infarction associated with factor V Leiden or prothrombin 20210 A. *Circulation* 1998;97:1037.
10. Rosendaal FR, Doggen CJM, Zivelin A, et al. Geographic distribution of the 20210 G to A prothrombin variant. *Thromb Haemost* 1998;79:706.