Editorial comment
Hemophilia and percutaneous coronary interventions

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Among the congenital defects of blood coagulation, hemophilia A (deficiency of factor VIII) or B (deficiency of factor IX) have an incidence of 1 of 5000 live male births and 1 of 30 000 live male births[1], respectively. The severity of coagulation impairment is usually rated as mild (> 5%), moderate (1-5%) or severe (< 1%) on the basis of factor deficiency, with a different degree of hemorrhagic risk.

It is well accepted that patients with coagulation defects have a reduced incidence of coronary artery disease and fatal ischemic events[2,3], probably due to a protective effect of the impaired coagulation against the classical pathogenetic mechanisms of the acute coronary syndromes. Nevertheless, hemophilia does not preclude the presence of coronary artery disease[4-6] and the low incidence of cardiovascular events could be related to the rarity of hemophilia itself and the reduced life span.

Due to the progress and the improvement in substitution therapy (purified or recombinant factors), leading to a lower incidence of severe hemorrhagic complications and to an increased life expectancy, patients with hemophilia can survive and develop a symptomatic coronary artery disease. Thus, it is possible that these patients are submitted to invasive procedures and/or therapies.

The report of Bovenzi et al.[7] describes the case of a young male affected by severe hemophilia B suffering from an acute coronary syndrome, submitted to coronary angiography and percutaneous coronary intervention, with stent deployment and subsequent administration of abciximab for the acute thrombotic occlusion of the stent.

Up today, only 4 cases of coronary percutaneous angioplasty (with a different degree of severity in the coagulation impairment) and only 2 with coronary stenting are reported in patients with hemophilia, but none has been treated with intravenous inhibitors of platelet glycoprotein IIb/IIIa[8-11].

In the experience of Bovenzi et al.[7], the patient, without antithrombotic pre-treatment (aspirin or other antiplatelet drugs, heparin) was administered purified plasma factor IX 30 min before the procedure, and received a dose (5000 IU) of unfractionated heparin in the catheterization laboratory. Immediately after stent deployment, the authors observed the thrombotic occlusion of the vessel and abciximab was promptly administered, followed by complete recanalization of the coronary artery, without any clinically relevant bleeding.

This case is very interesting, because it is opening a window looking on an unexplored clinical field for the cardiologists; and more question are arising from this experience.

• How to define the severity of coagulation impairment in order to plan an effective invasive procedure with a safe and correct therapeutic choice? Moreover, some patients could have more than one associated coagulation defect, and we have to search for detecting it before the procedure.

• How to treat patients with hemophilia before the percutaneous intervention? In these patients no aspirin, tienopyridine and heparin are administered, differing from the usual clinical practice[11].

- Could it have been the cause of early thrombotic occlusion of the vessel?
- When we have to administer the substitu-

tion therapy? Immediately before or some days before the procedure? In the 4 cases published, both strategies are reported[8-11].
- Which dose, how and how long (boluses or continuous infusion) we have to administer the substitutive therapy after the procedure?
- How and when we have to monitor the effects of the substitution therapy?

This patient has been treated 30 min before the procedure, with a dose of purified plasma factor of 30 IU/kg (lesser than usually adopted before major surgery) in order to reduce the hemorrhagic risk due to the arterial puncture, and showed a very early thrombotic stent occlusion successfully treated with the abciximab infusion and without hemorrhagic complications. In previous experiences the dose of the replacement therapy varied, depending on the therapeutic strategies and the duration of administration[8-11]. A control of the level of the replaced factors before the procedure has been reported.
- Can we reduce the risk of potentially prothrombotic effects of the substitution therapy by anticipating the administration and pre-treating safely the patient with the usual antithrombotic (antiplatelet and heparin) therapy[12]? It is described a prothrombotic effect with the use of substitution therapy[13], leading to myocardial infarction in some cases[14,15], due to different causes (pivotal role of factor IX in the coagulation cascade, impurity of the substitutive factor, administration of prothrombin complex concentrate promoting the clot formation).
• How to treat the patient during the invasive procedure?
- Can we use in all cases unfractionated heparin, and platelet glycoprotein IIb/IIIa inhibitors if necessary? Intravenous heparin has been administered in the reported cases, but never were the platelet glycoprotein IIb/IIIa inhibitors, that are increasing the hemorrhagic risk in patients without coagulation defects[16] and are contraindicated in patients with hemorrhagic diathesis.
- How long can we continue the infusion of the antithrombotic drugs? And which doses are safely tolerated? It is well known that the half-life of the factor IX substitutive therapy is about 18 hours, and the hemorrhagic risk increases again and reaches a dangerous level after this time.
• How to treat patients after the procedure? It is well known that after coronary stenting a double oral antiplatelet therapy is mandatory for 4 weeks, in order to prevent thrombotic occlusion[17]. Probably, in cases with mild to moderate deficiency of factor IX the usual therapy could be started with caution; in more severe cases, can the derangement of coagulation pattern protect patients from thrombotic occlusion, even without the suggested therapy?

Among the 2 previously reported cases, only one patient received aspirin and ticlopidine, without hemorrhagic complication[10].

Unfortunately, most of these questions are, up today, without answers. Because of the low number of patients with hemophilia and the lower number of these submitted to coronary angiography, percutaneous coronary interventions or coronary artery bypass grafting, it is very difficult to plan a trial in order to answer the questions asked before.

Nevertheless, it will be very useful to collect data about the occurrence of clinical manifestations of coronary artery disease in hemophilic patients, the use of invasive diagnostic or therapeutic procedures, and the clinical follow-up.

We think that hematologists and cardiologists should meet each other in order to define a common data set, organize a registry of these cases, and discuss about several questions regarding the optimal clinical management of these patients.

The new therapeutic opportunities have lengthened the life expectancy of some critically ill patients, and cardiologists must be ready to treat these cases. A widening of our clinical field of interest is exciting and mandatory.

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