Impact of bivaluridin and Genous stent in patients with acute myeloid leukemia undergoing emergency percutaneous coronary angioplasty for acute coronary syndrome

Leukemia (2012) **26,** 2300–2301; doi:10.1038/leu.2012.93

Hematological disorders are considered risk factors for acute and late complications in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI). In particular, thrombocytopenia (TP) is associated with a higher risk for bleeding in patients with ACS treated with antithrombotic therapies[1] and has been shown to be a predictor of in-hospital mortality in patients undergoing PCI.[1] In acute myeloid leukemia (AML), replacement of normal bone marrow with leukemic cells causes anemia, TP, and abnormal white blood cells count. Therefore, these patients represent a challenge for clinicians if PCI strategy for ACS is required. Several trials demonstrated that, in patients with acquired TP, the incidence of bleedings is reduced with bivalirudin treatment, a thrombin-specific anticoagulant, as compared with heparin plus glycoprotein (GP) IIb/IIIa inhibitor use.[1,2] Moreover, patients undergoing PCI with stent deployment require a mandatory dual antiplatelet therapy (DAT) to prevent the risk of stent thrombosis, myocardial infarction and death.[3,4] Accordingly, PCI guidelines indicate the DAT course ranging from 2–4 weeks after plain-old balloon angioplasty, 4–6 weeks after bare-metal stent or up to 6–12 months after drug-eluting stent.[5] Here, we report the case of a patient with severe AML who developed chest pain as a result of ACS-non-ST elevation myocardial infarction (NSTEMI).

A 69-year-old male patient was admitted to our coronary care unit with chest pain and ST depression on ECG in V1-V4 leads, history was notable for hypertension, dyslipidemia and smoking habitus. Blood pressure was 80/50 mm Hg and heart rate was110 bpm. At echocardiographic examination, left ventricle appeared mildly dilated and ipokinetic with ejection fraction (EF) of 35%. Regional abnormalities were described; in particular, ipokinesia of the interventricular septum and the apex and akinesia of the inferior wall. Serum levels of troponin I were increased(3.5 ng/ml). Haemochrome revealed anemia (Hb: 9.9 g/dl, RBC: $2.89 \times 10^6/\mu l$), low white blood cells count (WBC: $1.33 \times 10^3/\mu l$) and TP ($93 \times 10^3/\mu l$) leading to a strong suspect of leukemia. A pharmacological therapy with ASA 100 mg/die, clopidogrel 300 mg loading dose, carvedilol 6.25 mg, rosuvastatin 20 mg/die, spironolacton 25 mg/die and lisinopril 10 mg/die was administered. Owing to the persistence of angina and the hemodynamic instability, the patient underwent emergency coronary angiography. The CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA Guidelines) bleeding score predicted a risk of in-hospital major bleeding of 8.4%, corresponding to a moderate risk, with a 6.9% risk of death.[6] Coronary angiography was performed from the right femoral approach through a six French sheat and

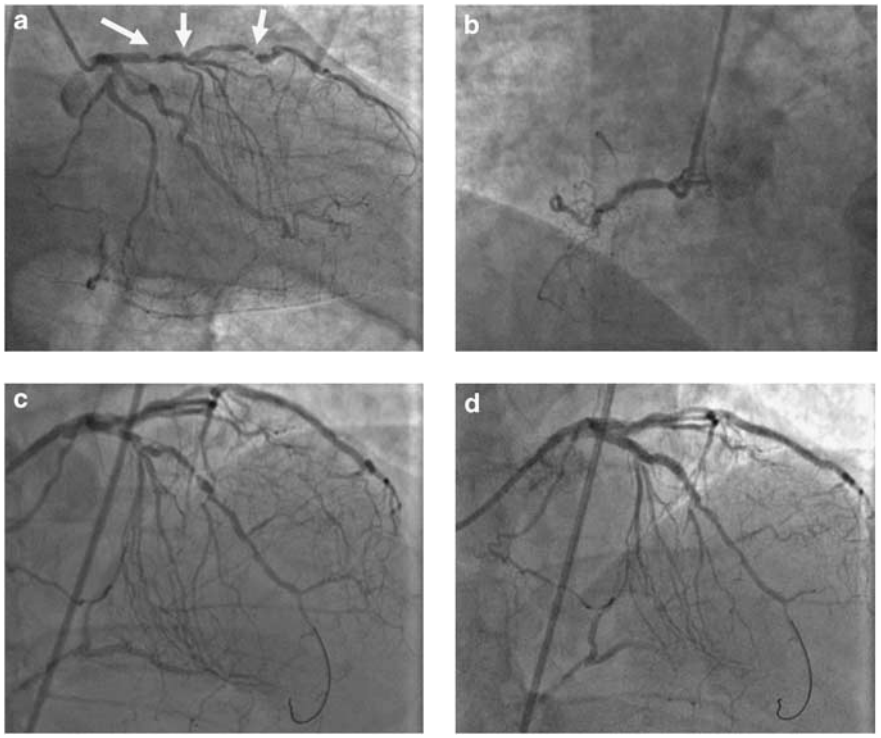

Figure 1. (**a**) Coronary angiography of left anterior coronary artery (LAD) and left circumflex. Showing multiple severe stenosis on the LAD and collateralization for the right coronary artery (RCA). Arrows indicate the stenosis treated by PCI and stenting. (**b**) Coronary angiography showing the total chronic occlusion of the RCA. (**c**) LAD after crossing lesions with guidewire. (**d**) LAD after PCI and stenting.

Accepted article preview online 2 April 2012; advance online publication, 24 April 2012

showed a severe coronary artery disease, with multiple critical stenoses on the proximal and middle segment of left anterior descending coronary artery (LAD), and a chronic total occlusion of right coronary artery (Figures 1a and b). According to clinical and instrumental data, we decided to perform a PCI on LAD. Before PCI, a loading dose of Bivalirudin (0.75 mg/kg) was administered followed by an infusion of 1.75 mg/Kg/h up to 2 h after procedure. Then, a Launcher EBU guiding catheter (Medtronic, Minneapolis, MN, USA) was advanced to the LAD, and, after predilation with balloon catheter, a Genous-R-stent 3.0×33 mm (OrbusNeich, Fourt Lauderdale, FL, USA) was deployed, at 8.0 atm for 30 s,in the proximal-medium portion of LAD. Finally, a non compliant balloon catheter (3.0×15 mm) was used to post dilate the stent with good angiographic result (Figures 1c and d), ST resolution and stopping of chest pain. Hemostasis of femoral artery was obtained by Angioseal 6F. After PCI hematological advice has been requested and bone marrow aspiration was consistent with AML secondary to myelodisplastic syndrome, supporting our initial suspect. The echocardiographic examination, performed 5 days after PCI, showed improved left ventricular global function (EF 48%), and restored kinesis of the interventricular septum and apex. Thus, 15 days after PCI plus stenting, patient stopped DAT and started chemotherapy according to hematological advice. At 30 days follow-up, no cardiovascular event or bleeding complication was reported and the patient was discharged after completing the first cycle of chemotherapy. According to guidelines on myocardial revascularization, unfractionated heparin (UFH) plus GP IIb/IIIa inhibitor therapy is the optimal pharmacological strategy for high-risk patients with NSTEMI undergoing PCI.[5] However,this strategy is associated with several complications such as heparin-induced TP and increased risk of bleedings.[7] Bivalirudin alone, compared with heparin plus GPIIb/IIIa inhibitors, has been proved to be safe and effective in high-risk patients undergoing PCI. The Genous stent is a bio-engineered coronary stent coated with Anti-hCD34-specific antibodies that, capturing to the luminal stent struts circulating endothelial progenitor cells CD-34+ from the peripheral blood, accelerates vascular healing, thus, allowing a short DAT, particularly useful in patients with contra-indication or impossibility to a long term DAT (undeferrable surgery, oncological diseases, allergy or/and intolerance to ASA and/or Thienopyridine, high bleeding risk).[8] In the reported case, we adopted strategy of PCI with bivaluridin, as pharmacological therapy, and stenting with the Genous stent obtaining a good procedural and clinical success in the absence of bleedings. Finally, the use of Genous stent, allowing the early DAT discontinuation after PCI, gave to the patients the chance to start the required therapy for AML. We have recently reported that, in patients with contraindications to long-term DAT due to severe comorbidities, allergy and/or intolerance to antiplatelet therapies or major surgery requirements early after PCI, the use of Genous stent is a safe and effective strategy allowing early DAT discontinuation, 2 weeks, after PCI. Moreover, we reported the use of pro-healing stent as a safe and effective strategy in patients with severe hemophilia undergoing PCI for NSTEMI.[8–10]

Taken together, these data suggest that in high-risk patients, such as patients with AML and severe TP, a strategy based on bivalirudin and Genous stent is efficacious and safe in order to achieve both ischemic protection and bleeding risk reduction.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

G Galasso[1], T Niglio[1], S De Luca[1], C De Biase[1], V Parisi[1] and F Piscione[2]
[1]*Department of Clinical Medicine, Cardiovascular Science and Immunology, Federico II University of Naples, Naples, Italy and* [2]*Department of Medicine and Surgery, University of Salerno, Salerno, Italy*
E-mail: gengalas@unina.it

REFERENCES

1 Hakim DA, Dangas GD, Caixeta A, Nikolsky E, Lansky AJ, Moses JW *et al.* Impact of baseline thrombocytopenia on the early and late outcomes after ST-elevation myocardial infarction treated with primary angioplasty: analysis from the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial. *Am Heart J* 2011; **161**: 391–396.
2 De Luca G, Cassetti E, Verdoia M, Marino P. Bivalirudin as compared to unfractionated heparin among patients undergoing coronary angioplasty: A meta-analyis of randomised trials. *Thromb Haemost* 2009; **102**: 428–436.
3 Wilson SH, Fasseas P, Orford JL, Lennon RJ, Horlocker T, Charnoff NE *et al.* Clinical outcome of patients undergoing non-cardiac surgery in the two months following coronary stenting. *J Am Coll Cardiol* 2003; **42**: 234–240.
4 Airoldi F, Colombo A, Morici N, Latib A, Cosgrave J, Buellesfeld L *et al.* Incidence and predictors of drug-eluting stent thrombosis during and after discontinuation of thienopyridine treatment. *Circulation* 2007; **116**: 745–754.
5 Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T *et al.* Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* O2010; **31**: 2501–2555.
6 Subherwal S, Bach RG, Chen AY, Gage BF, Rao SV, Newby LK *et al.* Baseline risk of major bleeding in non-ST-segment-elevation myocardial infarction: the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA Guidelines) Bleeding Score. *Circulation* 2009; **119**: 1873–1882.
7 Chong BH, Isaacs A. Heparin-induced thrombocytopenia: what clinicians need to know. *Thromb Haemost* 2009; **101**: 279–283.
8 Piscione F, Cassese S, Galasso G, Cirillo P, Esposito G, Rapacciuolo A *et al.* A new approach to percutaneous coronary revascularization in patients requiring undeferrable non-cardiac surgery. *Int J Cardiol* 2011; **146**: 399–403.
9 Piscione F, Cassese S, Galasso G, Rapacciuolo A, De Rosa R, Piccolo R *et al.* Coronary stenting early before non-cardiac surgery: is the endothelial progenitor cell capturing coronary stent a solution? *Minerva Cardioangiol* 2010; **58**: 147–152.
10 Petrillo G, Cirillo P, Leosco D, Maresca F, Piscione F, Chiariello M. Percutaneous coronary intervention in a patient with acute non-ST-elevation myocardial infarction and haemophilia A: a 'genous' experience. *Haemophilia* 2011; **17**: e239–e247.