Case Report

Glucose-6-Phosphate Dehydrogenase (G6PDH) Deficiency in a Patient with ST-Segment Elevation Acute Myocardial Infarction Successfully Treated by Simple Thrombectomy

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We report the case of an 82-year-old Sardinian woman affected by “favism” (i.e. intolerance to fava beans) with chest pain associated with persistent massive ST elevation in V2-V6 leads, admitted to our department after transfer from a rural hospital without catheterization facilities.

On immediate transfer to the catheterization laboratory for primary percutaneous intervention (PCI), coronary angiogram showed proximal left anterior descending (LAD) thrombotic occlusion.

In consideration of her history of glucose-6 phosphate dehydrogenase deficiency and “loss of consciousness” at a young age after taking aspirin, which contraindicated aspirin therapy, we treated this patient using a new, two-step strategy, with an emergency minimalist intervention using manual thrombectomy and intracoronary glycoprotein IIb/IIIa (GP IIb/IIIa) inhibition with abciximab. Subsequent angiography control confirmed the persistence of Thrombolysis in Myocardial Infarction Trial (TIMI) grade 3 flow and the presence of an intermediate proximal LAD coronary lesion, which was not treated, also due to the persisting contraindication to aspirin.

In our opinion, minimalist intervention with a thrombectomy device (especially in patients characterized by a high intracoronary thrombus burden) and/or with the use of a small balloon or gentle dilation, sustained by maximized antithrombotic therapy may represent an interesting and rational approach, allowing interventionalists to postpone stenting in the setting of primary PCI in special cases.


Key words; Favism, Myocardial infarction, Manual thrombectomy

Introduction

Patients contraindicated for aspirin because of hypersensitivity or active gastric bleeding pose a challenge for percutaneous intervention (PCI), especially in the emergency setting. We report a case of ST-segment elevation acute myocardial infarction (STEMI) caused by thrombotic proximal left anterior descending (LAD) occlusion in a patient with glucose-6-phosphate dehydrogenase deficiency (G6PDH) and three episodes of “loss of consciousness” at a young age after taking aspirin, which contraindicated its use. We successfully treated this patient using a two-step strategy, with an emergency minimalist intervention using manual thrombectomy and intracoronary glycoprotein IIb/IIIa (GP IIb/IIIa) inhibition with abciximab. This case shows that an aggressive, thrombectomy-only strategy may be sufficient to restore flow in an emergency, and recanalization may be sustained by a maximized antithrombotic regimen (abciximab, clopidogrel and heparin) allowing interventionalists to postpone stenting in the setting of primary PCI in special cases.

Case Presentation

A 82-year-old hypercholesterolemic Sardinian woman with chest pain of one-hour duration, associated with persistent massive ST elevation in V2-V6 leads, was admitted to our department after transfer
from a rural hospital without catheterization facilities. On admission to the rural hospital (3 a.m.), the patient reported a history of “favism” (i.e. intolerance to fava beans) and three episodes of “loss of consciousness” at a young age after assumption of aspirin.

On arrival at our department (4 a.m.) she was still complaining of typical chest pain, and was diaphoretic with blood pressure of 100/50 mmHg. Killip class was III and she was immediately transferred to the catheterization laboratory for primary percutaneous intervention (PCI). Coronary angiogram showed proximal left anterior descending (LAD) thrombotic occlusion (Fig. 1A). After crossing the lesion with a flexible-tip 0.014” diameter wire (BMW Universal, Abbott, Temecula, USA), facilitated by the use of a second, anchoring wire placed in the first diagonal (Fig. 1B), a thrombus score of 4 was revealed, and manual thrombectomy was performed using the DIVER CE MAX system (Invatec-Medtronic, Roncadelle, Italy). After removing the wire from the first diagonal, multiple, slow passages of the thrombectomy catheter were performed, and a large amount of fresh thrombus was removed. Restoration of Thrombolysis in Myocardial Infarction Trial (TIMI) grade 3 flow was obtained, and a weight-adjusted abciximab bolus plus nitroprusside 400 mcg were administered intracoronarily. As hyperemic flow was observed and residual stenosis was not deemed to be angiographically significant, no stent was implanted. (Fig. 2A, 2B) Myocardial blush grade was 3 at the end of the procedure, and >70% ST resolution in the lead with the maximum ST elevation was observed at 90 minutes.

During the recovery phase, the patient was treated with low-molecular heparin and clopidogrel and did not complain of other episodes of chest pain. On the seventh day of the hospital stay, after hematological consultation which confirmed the absolute contraindication to aspirin, she underwent repeat coronary angiography, which revealed the persistence of TIMI 3 flow and the presence of proximal LAD intermediate stenosis (Fig. 3A, 3B). Measurement of transstenotic pressure immediately after high-dose intracoronary adenosine administration (200 mcg) showed a fractional flow reserve (FFR) of 0.81.

The patient was subsequently discharged from hospital under chronic treatment with clopidogrel and weight-adjusted enoxaparin for 1 month. At the 2-year follow-up, the patient was alive and free from chest pain and major cardiovascular events.

Results and Discussion

We report a case of STEMI, caused by thrombotic proximal LAD occlusion in a patient with glucose-6-phosphate dehydrogenase deficiency (G6PDH), also called “favism”, the most common enzymopathy in humans. The prevalence of G6PDH deficiency is high in some regions, with an incidence of over 1% reported in the Mediterranean area (par-
particularly in Sardinia) and in the Middle East, India, Indochina, Southern China, and Central Africa.

This distribution is similar to that of the thalassaemias and is thought to be due to the selective advantage conferred from these phenotypes against endemic malaria infection in the past.

G6PDH has a sex-linked inheritance, characterized by a widely heterogeneous group of mutations which leads to a reduction of enzyme activity in red blood cells. This deficiency is associated with hemolytic crisis caused by oxidative stress, such as oxidant drugs, fava beans or systemic infections. In particular, several drugs, including 8-aminoquinoline, antimalarials, sulfanilamide, acetalilid, and some sulfones, are known to be hemolytic in such patients. Moreover, several drugs that have been shown to have a minor effect on red cell survival, such as aspirin, when given in large doses or in particularly sensitive patients, or when associated with other oxidant agents, can cause hemolytic crisis.

The association between aspirin intake and hemolytic episodes in patients with G6PDH has been reported on several occasions and in the majority of patients a severe hemolytic process had occurred after the ingestion of small therapeutic doses not exceeding 2 g/day. Interestingly, in a small series of 40 cases of hemolytic crisis reported in a population of glucose-6-phosphate dehydrogenase deficiency patients, registered in Algeria, ingestion of aspirin, even at a low dosage (≤400 mg), preceded the crisis in 5% of cases.

Individual variations in drug catabolism may result in a high level of metabolites that are responsible for hemolysis, making the prediction of hemolytic episodes after drug administration even more difficult in individual patients. Damage to red blood cells is thought to be mediated by hydrogen peroxide, either directly or by way of the formation of reactive oxygen species. Glutathione removes hydrogen peroxide through the glutathione peroxidase reaction until the newly formed oxidized glutathione is removed by glutathione reductase. The latter reaction, requiring continual reduction of NADP to NADPH, is dependent on the G6PD reaction and fails in red cells deficient in this enzyme.

The effects of aspirin and its metabolites on reduced glutathione (GSH), methemoglobin (MHB) and MHB reduction have been the object of several studies. Ziu et al. tested aspirin metabolites at various concentrations in vitro (sodium salts of salicylic acid (Na-SA), salicylic acid (Na-SU) and gentisic acid (Na-GA)), and showed that Na-GA decreased GSH levels appreciably, while only a slight

Fig. 2. Angiography after multiple passages with the mechanical thrombectomy device. Angiography from the cranial left anterior oblique view (left panel) and enlarged detail of lesion site (right panel) revealing restoration of TIMI 3 flow after multiple, slow passages with the mechanical thrombectomy device, the DIVER CE system (Invatec Medtronic, Roncadelle, Italy) removing a large quantity of fresh thrombus.
lowering of the GSH level was observed with Na-SA and Na-SU. These effects of aspirin metabolites were more pronounced in G6PD-deficient erythrocytes as compared to G6PD-normal erythrocytes, thus highlighting the importance of G6PD in aspirin toxicity. Moreover, although Na-GA concentrations (<3.5 mg/100 mL) found in vivo after a therapeutic dose of aspirin administration seem unable to directly trigger hemolysis, aspirin and its metabolites reduce the tolerance to oxidative stress, as clearly demonstrated by Stockman et al. Thus, a genetic disease that is usually benign can sometimes become life threatening, depending on the intensity of the oxidative damage, the biochemical properties of the variant enzyme and the clinical condition of the patient. Our patient was thought to be particular sensitive to the oxidant stress-inducing action of aspirin, as confirmed by her clinical history.

Patients who are contraindicated for aspirin because of hypersensitivity or active gastric bleeding pose a challenge for PCI, especially in the emergency setting. Drug-eluting stents are contraindicated and, even if bare metal stents are used, which are thought to be less thrombogenic, no antithrombotic or antiplatelet monotherapy regimen is currently recommended. Additionally, there is some evidence that in the acute phase of STEMI, once flow is restored using minimalist intervention (such as a thrombectomy device and/or small balloon or dilation), immediate stenting can be safely avoided, especially in patients characterized by a high intracoronary thrombus burden. This strategy may be extremely useful in patients contraindicated for dual antiplatelet therapy, because incomplete therapy is the main cause of the risk of stent thrombosis. As in our case, a minimalist approach may be sufficient to restore flow in an emergency, and recanalization may be sustained by a maximized antithrombotic regimen (abciximab, clopidogrel and heparin) allowing the investigation of the contraindication to aspirin and/or to initiate a desensitization protocol before stent placement.

In our patient, the clinical success of thrombectomy allowed us to postpone stenting after consultation with an hematologist who, however, did not clear the patient for aspirin use, citing an official document of the Italian Health Authorities. Additionally, the unwillingness of the patient to take aspirin (she firmly refused), the persistent TIMI 3 flow with non-critical coronary stenosis and the possible catastrophic consequences of hemolytic crisis in the acute phase of STEMI or during dual antiplatelet therapy were other factors in deciding our strategy.

To the best of our knowledge, there is only one other report about STEMI in patients with favism, by Rigattieri et al. The incidence of cardiovascular disease in patients with favism seems to be low, and the cardiovascular protective role of this genetic alteration has been hypothesized. In the case reported by Rigattieri, however, there was no clear association between previous aspirin use and hemolytic crisis. Thrombectomy was not performed, and balloon dilatation of the right coronary artery (culprit lesion),
with restoration of TIMI 3 flow was preferred. A test of the tolerance to low-dose aspirin was then performed with a successful result; two sirolimus-eluting stents were then implanted at the ostium of the circumflex artery to complete for revascularization; however, the use of a classic balloon dilatation strategy exposes the patient to the risk of vessel dissection, which may lead to the need for bail-out stenting, with potentially severe consequences if aspirin cannot be administered.

In our opinion, the use of a two-step strategy, with an initial minimalist approach using manual thrombectomy, which has a very low risk of dissection and distal embolization in experienced hands, might allow the interventionalist to postpone stenting until conditions can be improved. A recent study by Isaaz et al. confirmed that this approach results in immediate and sustained recanalization, with a high rate of ST-segment resolution in about 80% of patients with STEMİ, a percentage close to that observed after stent implantation.

**Conclusions**

We report the rare case of a patient with favism and a real contraindication to aspirin, presenting with antero-lateral STEMI. We treated this patient using a two-step strategy, an emergency minimalist intervention using manual thrombectomy and intracoronary GP IIb/IIIa inhibition with abciximab. Subsequent angiography control confirmed the persistence of TIMI 3 flow and an intermediate proximal LAD coronary lesion, which was not treated, also due to the persistent contraindication to aspirin. In our opinion, a
minimalist intervention with a thrombectomy device (especially in patients characterized by a high intracoronary thrombus burden) and/or with the use of small balloon or gentle dilation, sustained by maximized antithrombotic therapy may represent an interesting and rational approach, allowing interventionalists to postpone stenting in the setting of primary PCI in special cases.

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