



Case Report

Recurrent Cardiac Events Driven by Prothrombotic Burden in a Patient Undergoing Lipoprotein Apheresis for High Lp(a) Levels

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ABSTRACT

Introduction: Lipoprotein (a) [Lp(a)] is a marker for cardiovascular disease, involved in pathogenesis and progression of atherosclerosis. In selected high-risk patients, lipoprotein-apheresis could optimize secondary prevention and improve prognosis.

Aim: We presented the case of a 49-year-old man with high lipoprotein (a) levels and recurrent cardiac adverse events, despite maximal pharmacological therapy.

Case report: Four years before the admission at our Centre, he presented an anterior STEMI, treated with angioplasty and implantation of a drug eluting stent on left anterior descending artery, at the age of 47 years, in September 2012; one month later, the patients presented a new episode of angina, and exams showed a critical stenosis in the right coronary artery, treated by angioplasty and implantation of drug eluting stent. Because of high Lp(a) plasma levels, patient was subsequently on regularly 7-10 day lipoprotein apheresis.

Results and discussion: A thrombophilic screening was performed, showing the simultaneous presence of heterozygous V Leiden mutation and prothrombin G20210A mutation. He referred to our Centre in order to optimize therapy; we performed an endothelial function assessment showing a severe dysfunctional pattern.

Because of these findings, we prescribed dual antiplatelet therapy, and we added omega-3 fatty acids and association with nicotinic acid/laropiprant. According with current guidelines, considering the high risk of bleeding, we preferred not to administer anticoagulant therapy. At 6-month and 1-year follow up the patient continued lipoprotein apheresis and was asymptomatic for other cardiovascular events.

Conclusions: The assessment for the eventual presence of thrombophilia might become a useful tool in clinical practice for high-risk selected patients.

INTRODUCTION

Lipoprotein (a) [Lp(a)] is considered a marker for cardiovascular disease and it is involved in pathogenesis and progression of atherosclerosis [1]. Several evidences showed that elevated Lp(a) levels were a risk factor for a variety of atherosclerotic and thrombotic disorders [2]; in particular, high Lp(a) levels were associated to an increased risk of myocardial infarction and [3,4]. A meta-analysis by Sofi et al., showed the relationship between Lp(a) and venous thrombosis [5]. Therefore, in selected high-risk patients, lipoprotein-apheresis could be added to standard therapy to optimize secondary prevention and improve prognosis [6,7].

Aim

The aim of this study was to evaluate the usefulness of a thrombophilic screening



in a high risk patients presenting recurrent cardiac adverse events, despite maximal pharmacological therapy and the onset of lipoprotein apheresis treatment.

CASE REPORT

We presented the case of a 49-year-old man with high lipoprotein (a) levels and recurrent cardiac adverse events, despite maximal pharmacological therapy, admitted to the Transfusional-Apheretic Centre (SIMT), USL3 and Pistoia Hospital. The patient gave his informed consent; this study respects the Helsinki declaration.

Cardiovascular risk assessment

He suffered from hypertension at an early age and, at the time of the onset of lipoprotein apheretic therapy, he presented good blood pressure control with ramipril and carvedilol. Because of elevated levels of LDL-c and triglycerides he assumed therapy with rosuvastatin 40 mg per day. He was also overweight (BMI=26.2); he was not diabetic and he did never smoke. In the Table 1 we described the lipid profile before and after the onset of statin therapy.

Five years before he underwent to ultrasound assessment for atherosclerosis at common carotid and femoral arteries, evidencing the presence of a non-occlusive peripheral atherosclerosis; therefore, he started therapy with aspirin at 100 mg/day, according to current guidelines [8].

As for family history of heart disease, his father died after a fatal heart attack at the age of 44 years, while his brother, at the age of 45 years of age, had suffered from an ischemic stroke without neurological sequelae.

Description of cardiac events

In the September 2012, at the age of 47 y.o., the patient had the first cardiac thrombotic event, on aspirin and statin therapy; in particular, he suffered from an anterior STEMI treated with angioplasty and implantation of a drug eluting stent on left anterior descending artery. During the hospitalization, the patient did not show complications. However, one month after discharge, the patient presented a new episode of angina; further investigations showed the presence of a critical stenosis in the right coronary artery, subsequently treated by angioplasty and implantation of drug eluting stent. This lesion was not previously detected.

Further examinations found elevated Lp(a) plasma levels (90 mg/dL). Lp(a) levels were measured by an immune-nephelometric method (LPAX IMAGE Beckman Coulter); values ≥ 50 mg/dL were considered abnormal. Therefore, according to the American Society for Apheresis (ASFA) guidelines [9], from January 2013 the patient started lipoprotein apheresis treatment. The therapeutic program included a procedure every 7-10 days; lipoprotein apheresis was performed by the H.E.L.P. (Plasmat Futura, B.Braun, Melsungen, Germany) technique. The mean blood volume processed per each session was approximately 8000 ml of plasma. HELP technique was able to reduce LDL-c and Lp(a) by at least 70%. Patient suspended ramipril and this drug was replaced by an AT1 inhibitor for the risk of a bradykinine syndrome.

Despite the apheretic therapy, one month later the patient was symptomatic for angina at rest. A new echocardiogram showed normal chambers diameters and

Table 1: Lipid profile before and during statin therapy.

	Total -c	LDL-c	HDL-c	TG	VLDL-c
Before statin therapy	280	172	50	290	58
During statin therapy	165	93	52	100	20

Total cholesterol, total-c; LDL cholesterol, LDL-c; HDL cholesterol, HDL-c; triglycerides, TG; VLDL Cholesterol, VLDL-c
Data are expressed in mg/dL

ventricular function, without valve disease; a myocardial perfusion scintigraphy was positive for a defect of uptake in LAD territory. The next angiogram showed a new occlusion of the previously treated vessel, and the patient performed a coronary artery bypass graft.

RESULTS

Because of his cardiovascular risk and family history, a thrombophilic screening was performed; the examination showed the simultaneous presence of heterozygous V Leiden mutation and prothrombin G20210A mutation. Other tests, investigating the presence of antiphospholipid antibodies or lupus anticoagulant, were negative; levels of antithrombin, S protein and C protein were within normal range.

In order to optimize drug therapy and cardiovascular profile, the patient referred to our Centre for Vascular Function, Careggi Hospital. He underwent assessment of endothelial function by peripheral arterial tonometry (EndoPAT 2000™ device, Itamar Medical LTD Caesarea, Israel); the exam showed a severely dysfunctional vascular pattern (LnRHI=0.2, n.v. >0.4). Test assessing platelet function showed a platelet inhibition, according to current therapy with aspirin and clopidogrel.

Because of these findings, we optimized drug therapy in order to reduce cardiovascular risk and improve endothelial function. Therefore, we prescribed dual antiplatelet therapy, and we added omega-3 fatty acids and nicotinic acid/laropiprant. According with current guidelines, considering the high risk of bleeding, we preferred not to administer anticoagulant therapy. At 6-month and 1-year follow up the patient continued lipoprotein apheresis and was asymptomatic for new cardiovascular recurrences. According to results of HPS2-THRIVE Study [10], nicotinic acid/laropiprant had been withdrawn from the market in 2013, and patient suspended this therapy.

DISCUSSION

This case highlights the role of thrombophilia in influencing the therapeutic response and the risk of recurrent cardiovascular events. Current literature lacks provide evidence of causality between the presence of thrombophilia and cardiovascular events [11] and guidelines discourage the assessment of genetic testing for thrombophilia [12,13]; however, patients with a hereditary protein S, protein C or antithrombin deficiency had a high absolute risk for venous thromboembolism [14]. Moreover, hereditary thrombophilia was frequently reported in young patients [15] with acute coronary syndromes.

The presence of endothelial dysfunction is a well-known cardiovascular risk factor, associated with recurrent cardiac events and a poor prognosis [16,17].

Evidences showed that Lp(a) levels are positively associated with CAD events; moreover, pro-atherogenic, pro-thrombotic and anti-fibrinolytic activities of high Lp(a) levels, in addition to thrombophilic alterations, could facilitate the occurrence and progression of atherosclerotic damage and increase the risk of coronary events [18].

Several studies reported the role of lipoprotein apheresis in reducing the risk of recurrences in patients with coronary artery disease and high Lp(a) levels [19-21].

The assessment for the eventual presence of thrombophilia might become a useful tool to optimize cardiovascular risk stratification and therapy for high-risk selected patients [22].



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