

Lifethreatening Complications in a Patient with Perioperative Drug Eluting Stent Thrombosis: Case Report

Perioperatif İlaç Salımlı Stent Trombozlu Bir Hastada Hayatı Tehdit Edici Komplikasyonlar

Chryssoula STAIKOU,^a
Antonios VEZAKIS,^b
Matthaios STAMELOS^a

Departments of
^a1st Anaesthesiology,
^b2nd Surgery,
Athens University Faculty of Medicine,
Aretaieion Hospital, Athens

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Yazışma Adresi/Correspondence:
Chryssoula STAIKOU
Athens University Faculty of Medicine,
Aretaieion Hospital,
Department of 1st Anaesthesiology,
Athens,
YUNANİSTAN/GREECE
c_staikou@yahoo.gr

ABSTRACT Patients with coronary stents represent a challenge for the involved physicians, especially regarding the management of their antiplatelet therapy. We present the perioperative complications of a patient with Drug Eluting Stent whose dual antiplatelet therapy was discontinued preoperatively. The patient had discontinued both aspirin and clopidogrel 7 days before her scheduled semi-elective laparoscopic cholecystectomy. Postoperatively the patient developed substernal pain with aVL, V2-V6 ST elevations and was transferred to the Interventional Cardiology Unit where the stent was replaced and dual antiplatelet therapy was restarted. Stent thrombosis resulted in anterior myocardial infarction followed by lifethreatening arrhythmias, cardiogenic shock and cardiac conduction abnormalities. The patient received amiodarone which induced and respiratory insufficiency. Finally, the patient was discharged home after 39 days of hospitalization. The risks/benefits of perioperative dual antiplatelet therapy modifications and the existing guidelines are also discussed.

Key Words: Aspirin; drug-eluting stents; clopidogrel; embolism and thrombosis; complications; perioperative care

ÖZET Koroner stentli hastalar, özellikle antitrombosit tedavi alanlar doktorlar için zor bir gruba oluşturmaktadırlar. Bu yazıda operasyon öncesi dual antitrombosit tedavisi kesilen, ilaç salımlı stenti olan bir hastanın perioperatif komplikasyonlarını bildiriyoruz. Hasta, semi-elektif laparoskopik kolesistektomi planlanmasından 7 gün önce aspirin ve klopidogrelden oluşan dual tedavisini kesti. Operasyon sonrası aVL, V2-V6 ST elevasyonları ve substernal ağrıları olan hasta Girişimsel Kardiyoloji birimine transfer edildi, burada stenti çıkarılıp dual antitrombosit tedaviye yeniden başlandı. Stent trombozu anterior miyokard infarktüsüne yol açtı, onu takiben de ölümcül aritmiler, kardiyojenik şok ve ileti anormallikleri oluştu.

Anahtar Kelimeler: Aspirin; ilaç salımlı stentler; klopidogrel; emboli ve trombozis; komplikasyonlar; perioperatif bakım

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The perioperative management of patients with coronary stents may be quite challenging for the involved physicians, and may pose a question regarding the risks and benefits associated with modifications of the dual antiplatelet therapy (DAT) these patients receive. We present the sequale of postoperative complications that occurred in a surgical patient with Drug Eluting Stent (DES) whose DAT was discontinued preoperatively. The patient gave a written informed consent regarding the presentation of her case.

CASE REPORT

A 71-year-old female patient (58 kg, 155 cm) was scheduled for laparoscopic cholecystectomy due to recurrent episodes of cholecystitis. The patient's medical history included coronary artery disease with effort-induced angina, arterial hypertension, hyperlipidaemia and paroxysmal atrial fibrillation after acute emotional stress. Two months preoperatively, she had undergone percutaneous transluminal coronary angioplasty in two significant stenoses (90%) in the proximal and middle third of the Left Anterior Descending Coronary Artery (LAD) and had a DES placed in the proximal segment of LAD. Preoperative electrocardiogram revealed a sinus rhythm of 58 beats/min, while echocardiography showed an ejection fraction (EF)³60%. The remainder of her physical and laboratory preoperative examinations were unremarkable. Her surgical history included appendectomy, caesarean section and lower limb orthopedic surgery. Following DES placement, she was put on aspirin 100 mg/day and clopidogrel 75 mg/day; the rest of her pharmacological treatment consisted of irbesartan/hydrochlorothiazide 150/12.5 mg/day, atorvastatin 20 mg/day, pentaprazole 80 mg/day and ciprofloxacin 1 g/day for the cholecystitis. At admission, she had discontinued both aspirin and clopidogrel for a week in order to minimize the risk of surgical bleeding and was receiving enoxaparin 12000 IU/day, according to her cardiologist's instructions. An urgent meeting was called, where the surgeon, the anaesthesiologist and the cardiologist extensively informed the patient about the risks and the possible management options. After discussing the critical situation, especially regarding the high risk of perioperative stent thrombosis, the decision was to proceed promptly with the surgery, since symptoms of cholecystitis persisted, and recommence DAT as soon as possible. The Department of Interventional Cardiology would be standby for any emergency intervention needed.

The patient received general anaesthesia under haemodynamic monitoring consisting of a 5-lead electrocardiogram and invasive blood pressure

measurement. In order to maintain haemodynamic stability, agents with a favourable cardiovascular profile, such as etomidate 20 mg, fentanyl 150 µg and rocuronium 45 mg were used for induction of anaesthesia and tracheal intubation. Sevoflurane at 1.5-2% end-tidal concentration in an oxygen/air mixture (FiO₂: 0.5) was used for maintenance of anaesthesia, since it offers both cardiovascular stability and easy dosage titration. Fentanyl 150 µg in incremental doses was used for intraoperative analgesia and rocuronium 10 mg in repeated doses was administered for neuromuscular blockade. The patient remained haemodynamically stable throughout the procedure: her arterial blood pressure fluctuated between 112/67 and 163/86 mmHg and her heart rate between 63 and 82 beats/min. Paracetamol 1 gr and morphine 3 mg intravenously were given for postoperative analgesia. The surgery lasted 110 minutes and was uneventful. The neuromuscular blockade was successfully reversed with sugammadex 120 mg and the patient emerged smoothly from anaesthesia. During the immediate postoperative period she remained calm, pain-free and haemodynamically stable. Two hours postoperatively, the patient developed substernal pain with aVL and V₂-V₆ ST elevations indicative of anterior wall myocardial infarction (MI), and was promptly transferred to the Interventional Cardiology Unit. Emergency angiography revealed an in-stent total occlusion which was unlogged by performance of balloon angioplasty followed by stent placement. DAT was immediately restarted with a loading dose of clopidogrel 600 mg and aspirin 300 mg. A few hours after the intervention the patient developed two episodes of ventricular fibrillation which responded to defibrillation. Following these episodes, a new right bundle branch block and an episode of atrial flutter occurred, the later being successfully treated with electrical cardioversion. The patient received antiarrhythmic treatment with amiodarone 300 mg intravenously over 20 min (15 mg/min) as a loading dose, followed by 1 mg/min infusion for 6 hours and 0.5 mg/min maintenance infusion for 42 hours. The patient remained for 48 hours in severe cardiovascular instability under dopamine and noradrenaline. Over the next days the patient's car-

diac function improved but she developed a complete atrio-ventricular block which required insertion of a temporary pacemaker. Echocardiography showed significant myocardial wall hypokinesia resulting in an EF of 30%. Amiodarone was restarted in a dose of 200 mg/day per os and two weeks later the patient was discharged home in a good clinical condition, with an EF of 35%. Nine days later, she was readmitted to hospital due to dyspnea and severe hypoxaemia which required endotracheal intubation. A pulmonary artery catheterization showed no signs of pulmonary embolism or heart failure. A computerised tomography (CT scan) revealed bilateral reticular opacities, subpleural micronodular areas with local septal thickening and also tissue of lipoid density. The clinical and radiographic findings were compatible with subacute amiodarone-related pneumonitis. Amiodarone was discontinued and methyl-prednisolone 125 mg/day was started. The patient's condition improved over the following week and she was extubated, while corticosteroid was gradually tapered. Thereafter, her course was uneventful and was discharged home after a total of 39 days of hospitalisation.

DISCUSSION

Dual antiplatelet therapy, consisting of aspirin and clopidogrel, is administered for 6-12 months after DES placement.^{1,2} Elective surgery should be postponed until completion of therapy,^{1,2} since discontinuation of DAT is considered the most important risk factor for late stent thrombosis occurring 31 days-1 year after its placement.³ The risk of stent thrombosis is further increased perioperatively due to the stress response to surgical trauma and subsequent hypercoagulability.³

A case-tailored decision is recommended in urgent and semi-elective procedures, as in our patient, and the risk of stent thrombosis versus the risk of surgical bleeding should be carefully evaluated.^{1,4} According to guidelines, in surgical interventions with low and moderate risk of bleeding, as in the case we present, the surgeon should be encouraged to operate on DAT.^{1,2} Especially during the first weeks after stent

placement, when the risk of thrombosis is high, it is suggested that -if needed- clopidogrel should be replaced by short lived reversible antiplatelet drugs, such as the glycoprotein IIb-IIIa inhibitors eptifibatide and tirofiban, with or without heparine.¹⁻⁴ Our patient received enoxaparine for "bridging" therapy, which failed to prevent stent thrombosis. Even though substitution of aspirin or thienopyridines with heparines represents a common practice,¹ these agents are not the "bridging" therapy of choice in patients with DES.^{1,2,4} Heparines are mainly antithrombotic drugs with minimal antiplatelet action,^{1,4} while aspirin and clopidogrel inhibit platelet aggregation via cyclooxygenase inhibition and antagonism of the adenosine diphosphate receptor P2Y₁₂, respectively.^{1,4}

In surgical procedures with high risk of bleeding, clopidogrel may be discontinued 5 days prior to surgery, while aspirin should be maintained perioperatively.^{1,2} If the risk of surgical bleeding is potentially catastrophic, as in intracranial procedures, both clopidogrel and aspirin should be discontinued 5 days preoperatively.^{2,4} In all cases, DAT should be recommenced as soon as possible postoperatively, thus in less than 24h, if possible.¹

The incidence of cardiovascular complications in patients with coronary stents undergoing non-cardiac surgery range from 0.6% to 45%.⁴ The incidence of MI and mortality ranges from 25 to 65% and 45 to 75%, respectively.³ In our patient, stent thrombosis resulted in an extensive anterior wall acute MI with significant impairment of cardiac contractility and lifethreatening arrhythmias. The patient received amiodarone which induced severe pneumonitis with subsequent respiratory insufficiency. Amiodarone has been associated with a 5% risk of pulmonary toxicity,⁵ which may present as acute or subacute/chronic pneumonitis with mortality rates between 9 and 50%.⁵ Risk factors include advanced age, co-existing lung pathology, dosage and duration of treatment.⁵ Even though treatment of 6-12 months duration and doses > 500 mg/day are associated with an increased risk of pulmonary

toxicity, this serious adverse effect may develop even within a few days of therapy onset and at quite low doses, such as 200 mg/day.⁵ In our patient, toxicity developed subacutely, in less than 1 month of treatment with a dose of 200 mg/day.

In patients with coronary stents, perioperative management plan is usually not an easy, straight-forward choice. They should be fully informed about the severity of their condition, perioperative risks, benefits and uncertainties of each treatment option. Also, an early preoperative multidisciplinary approach by the specialists involved in the perioperative care, thus the cardiologist, anaesthesiologist, haematologist and surgeon, is mandatory. The existing guidelines, even though considered to be recommendations and not rules, are based on evidence and can help the physician to choose the optimal therapeutic strategy for the individual patient.² In our patient, the involved physicians discussed the case management a week after DAT discontinuation. This delay significantly influenced and increased the difficulty of decision making. A multidisciplinary approach early before the

scheduled surgery might have resulted in a different plan, especially regarding the DAT management and timing of surgery.

Perioperative vigilance for early recognition of myocardial ischaemia/infarction is of vital importance. When stent thrombosis is suspected, prompt transfer to an Interventional Cardiology Unit for assessment and emergency catheterisation is required. Time is critical, since mortality increases from 4.3% at 90 minutes to more than 25% if a delay of more 120 minutes occurs.⁴ In the case we present, close cooperation with the cardiac catheterisation laboratory and prompt intervention was lifesaving for the patient.

In the case we present, discontinuation of DAT was associated with major perioperative cardiac complications. In surgical patients with coronary stents an early multidisciplinary approach is of paramount importance, and existing guidelines should be considered by the involved physicians.^{1,4} Dual antiplatelet therapy or at least aspirin should be continued perioperatively in cases with acceptable risk of surgical bleeding.

REFERENCES

1. Abualsaud AO, Eisenberg MJ. Perioperative management of patients with drug-eluting stents. *JACC Cardiovasc Interv* 2010;3(2): 131-42.
2. Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS); European Association for Percutaneous Cardiovascular Interventions (EAPCI), Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T, et al. Guidelines on myocardial revascularization. *Eur Heart J* 2010;31(20):2501-55.
3. Popescu WM. Perioperative management of the patient with a coronary stent. *Curr Opin Anaesthesiol* 2010;23(1):109-15.
4. Barash P, Akhtar S. Coronary stents: factors contributing to perioperative major adverse cardiovascular events. *Br J Anaesth* 2010; 105(Suppl 1):i3-15.
5. Papiris SA, Triantafyllidou C, Kolilekas L, Markoulaki D, Manali ED. Amiodarone: review of pulmonary effects and toxicity. *Drug Saf* 2010;33(7):539-58.