

# Life-threatening protamine allergic reaction in a patient with extra-adrenal pheochromocytoma undergoing off-pump coronary artery bypass grafting

The Editor,

Coronary artery bypass grafting (CABG) in patients with pheochromocytoma is rare and challenging for anesthesiologist.<sup>[1]</sup> To the best of our knowledge, severe protamine allergic reaction has never been reported in patient with pheochromocytoma undergoing CABG.

## CASE REPORT

A 59-year-old male was admitted with severe acute chest pain on and off at rest for 3 days. He gave a history of episodes of uneasiness and slight headache with raised blood pressure (BP). He gave a history of diagnosis of hypertension for 4 years back and episode of transient ischemic attack for 3 years back. On further evaluation, his 24 h urine sample had increased vanillylmandelic acid and noradrenaline levels. Ultrasonography, computed tomography (CT), and magnetic resonance imaging scan could not locate the tumor. Radioactive tracer study could not be carried out as the patient had financial constraints.

At the time of admission, his BP was 210/100 mmHg. He was on tablet telmisartan 80 mg OD, hydrochlorothiazide 40 mg OD, clonidine 0.1 mg OD, lorazepam 0.5 mg HS, aspirin 75 mg OD, and atorvastatin 20 mg HS. His cardiac enzyme markers were within normal range, but coronary angiogram revealed triple vessel coronary artery disease. Tablet aspirin was stopped, and injection heparin 5000 U QID intravenous (IV) and tablet phenoxybenzamine 10 mg QID were added. Other vital parameters and

physical examinations were unremarkable. Echocardiography revealed hypokinetic basal inferior wall, trace mitral, and tricuspid regurgitation with 50% ejection fraction. After obtaining informed risk consent, surgery was planned 3 days after admission.

Tablet telmisartan was stopped 24 h before surgery. He was given tablet alprazolam 0.5 mg and pantoprazole 40 mg orally in the night before and on the morning of surgery. Patient (weight 56 kg) was premedicated with 1 mg injection (injection) midazolam and 50 microgram (mcg) fentanyl. A 16 G IV cannula, 20 G radial artery cannula, triple lumen central venous pressure (CVP), and pulmonary artery catheter were placed before induction. Before induction heart rate (HR) was 67/min, systemic BP was 151/84 mmHg, pulmonary artery pressure (PAP) was 22/9 mmHg, and CVP was 3 mmHg. Anesthesia was induced with 1000 mcg injection fentanyl, 2 mg injection midazolam, 100 mg injection thiopentone, and endotracheal intubation was facilitated with 50 mg injection rocuronium. During tracheal intubation, there was a transient rise in BP. Anesthesia was maintained with bolus of 2 mg of injection vecuronium and continuous infusion of injection fentanyl 2 mcg/kg/min, midazolam 0.3 mcg/kg/min, vecuronium 1 mcg/kg/min, and air and oxygen (3 L) with isoflurane 1%. One hour after induction and 30 min before grafting, CVP (0 mmHg) and PAP (21/6 mmHg) gradually decreased. Additional fluids were given to raise CVP to 3 mmHg and maintained at the same level. Mean arterial pressure (MAP) was ranging from 74 to 106 mmHg during this period and maintained with

minimal inotropic support. Injection heparin was given before releasing distal end of the left internal mammary artery to achieve activated clotting time (ACT) >300 s. Off-pump coronary artery bypass (OPCAB) grafting was possible with moderate inotropic support of injection adrenaline 0.6 mcg/kg/min and injection noradrenaline 0.6 mcg/kg/min. During this period, MAP was 70–75 mmHg and mean PAP was 15–18 mmHg. At the end of grafting, MAP was 78 mmHg and mean PAP was 14 mmHg. Injection protamine 300 mg IV was given over 15 min after test dose. 5 min after protamine was given BP gradually started to fall with rise in PAP, which was not responding to the inotropes and vasopressors. Right ventricle became distended and left ventricular contractility decreased. Injection adrenaline 1 + 1 mg was given IV stat, but there was no response. At mean BP 45 mmHg and mean PAP 29 mmHg, patient was connected to cardiopulmonary bypass (CPB) with 4 L/min flows without cardioplegia on emergency basis after 3 min following IV injection of 225 mg of heparin. Intra-aortic balloon pump (IABP) support was started after inserting IABP balloon (34 cc) through femoral arterial access and continued during CPB. Injection milrinone 0.375 mcg/kg/min was also started. CPB support was continued for 1 h, and it was possible to gradually wean off from CPB over next half an hour. No protamine was given for reversal of heparin. Adequate fluids and blood components were given. Coagulation monitoring was guided by ACT and thromboelastography. In immediate postoperative period mean BP was 76 mmHg, mean PAP 18 mmHg cardiac output 4.90 L/min, cardiac index 3.20 L/min/m<sup>2</sup>, stroke volume 46.7 ml/beat, and systemic vascular resistance 979 dynes-s/cm<sup>5</sup>. In first 10 h, there was 800 ml blood in mediastinal and pleural drains. Trachea was extubated after 16 h from transfer in CTVS Intensive Care Unit. Inotropic support was gradually tapered, and IABP balloon was removed on the 2<sup>nd</sup> postoperative day (POD). Tablet metoprolol 25 mg BD and tablet diltiazem 30 mg TDS were started to maintain patency for radial artery graft. On the 3<sup>rd</sup> POD, mean BP was consistently between 110 and 125 mmHg. Tablet phenoxybenzamine 10 mg TDS was added. Patient was mobilized on the 4<sup>th</sup> POD.

## DISCUSSION

Anesthetic management of surgery with undiagnosed pheochromocytoma can be a nightmare because precipitated hypertensive crisis can lead to myocardial

infarction, arrhythmia, heart failure, and/or cerebrovascular hemorrhage. High index of suspicion in uncontrolled and resistant hypertension is needed to diagnose pheochromocytoma. In a diagnosed patient, preoperative control of BP is usually achieved with alpha blockade by phenoxybenzamine and beta blockers can be added if required to control HR and arrhythmia but should be started only after adequate alpha blockade is achieved.<sup>[2]</sup>

CPB can precipitate hypertensive crisis and tachyarrhythmias in these patients. OPCAB has been reported with the advantage of avoiding these complications in these patients.<sup>[1]</sup>

Systemic hypotension and pulmonary hypertension during 30 min after administration of IV protamine for reversal of heparin anticoagulation has been shown to be associated with adverse events and even mortality in CABG surgery.<sup>[3]</sup> Neutral Protamine Hagedorn (NPH) insulin use, fish allergy, and a history of nonprotamine medication allergy are independent risk factors for adverse events after CPB on the administration of protamine.<sup>[4]</sup>

Management of this patient was proceeding as planned until protamine was administered. This reported case of OPCAB with pheochromocytoma who had life-threatening protamine allergic reaction was managed successfully with CPB, IABP, and pharmacological support.

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## Conflicts of interest

There are no conflicts of interest.

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