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Unusual Life-Threatening Protamine Reaction in a Patient after Off Pump CABG - A Case Report

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Abstract

Immunologic reactions to protamine sulphate during cardiac surgery are very rare. The frequency and outcome of such adverse reaction is unclear. Clotting of distal anastomosis sites and proximal site (in aorta) is very rare. We report a case of unusual life-threatening reaction to protamine that occurred in a non-diabetic patient following the uneventful off pump coronary artery bypass grafting operation.

Keywords: Coronary Artery Bypass Graft (CABG) surgery; Protamine sulphate; Clot, Anastomosis site

Introduction

Protamine sulfate is a standard therapy for reversing heparin anticoagulation during coronary artery bypass graft (CABG) surgery. However, the safety of protamine has been questioned because of adverse reactions ranging from minor haemodynamic instability to fatal cardiovascular collapse. Although catastrophic events are rare, major adverse response related to protamine administration occur during 2.6% of cardiac surgical procedure. These "Protamine reactions" are highly associated with adverse post-operative outcome and are exaggerated in patient with impaired myocardial function.

Case Report

A 54-year-old male with history of thigh abscess drain 2 weeks back and non-Diabetes Mellitus (DM) with no allergy anemia, no history of previous surgery had unstable angina pectoris, his all blood reports (bleeding time, clotting time, prothrombin time, fasting blood sugar, HbA1C (Glycosylated Hemoglobin), platelet count, total leukocyte count, hemoglobin, etc.) are within normal limits.

Coronary angiography revealed triple vessel disease pre-operatively. Echocardiography shown normal left ventricular ejection fraction with no valvular dysfunction. An elective Coronary Artery Bypass Grafting (CABG) operation planned. After median sternotomy, left internal mammery artery and saphenous venous vein prepared. Then off pump coronary artery bypass grafting (CABG) was successfully done. The grafts were *in situ* Left internal mammery artery (LIMA) (2.5 m) with good flow to mid left anterior descending (LAD) (1.5 m) done. Then reverse saphanous venous graft (RSVG) grafted into-obtuse marginal (OM2) (2.0) sequential to distal right coronary artery (2.2 mm) proximal reverse saphanous venous graft (RSVG) to aorta done by partial aortic clamp. During distal right coronary artery (dRCA) grafting the blood loss was little higher as the shunt was not properly placed. So, some arrhythmatic changes occurred but grafting was finished without haemodynamic disturbance.

Heparin was reversed by half dose of slow IV injection of protamine sulphate. While sternal weiring done suddenly patient heart got arrested after ECG changes and bradycardia. Heparinisation done immediately. Sternum re-open, internal massage given by the same time cannulation of aorta and single two stage venous cannulation done through RAA and patient on CPB. Cross clamp of aorta done. Antegrade cardioplegia given and heart arrested in diastole.

So, in doubt we opened left anterior descending (LAD) and clot found in the graft so, redo left anterior descending (LAD) artery grafting done, also RSVG piggy back to right posterior descending artery (Rpda) anaestomasis done. Rewarming started cross clamp off. Gradual weaning from cardio pulmonary bypass done. Blood pressure and heart rate came to normal with minimal inotropic support protamine started haemostatis done. Sternum closed.

Again, arrhythmia noticed in monitor during closure of sub cutaneous layer and sternum reopened. We found proximal RSVG blocked. Redo proximal anastomosis followed by redo distal RCA done and clot removed after heparisation. We closed the sternum without protamine with high activated clotting time. Sternal wound closed in layer and patient was shifted to ICU. Then patient drained approximately 1200 ml with 3 hrs and haemoglobin decreased, we reopened the patient in Operation Theatre. Haemostatis done, little protamine given 20% of total dose. Patient improved next day and extubated. After 3 days we shifted the patient to the ward. Finally discharged after 8 days from hospital and at present the patient is doing well, He is also coming for regular checkup.

Discussion

We know protamine reactions are unusual and are often unpredictable, although they have been noted with greater frequency in patients taking NPH insulin (risk may be increased 30 to 50 folds) those with fish or medication allergies, those with previous protamine exposure and those who have hard vasectomies. Awareness of the possibility of their development and a prompt response if a reaction is noted are essential because protamine reactions are associated with increased perioperative mortality. The incidence of adverse reaction has been reported as varying from 0.06% to 10.6%.

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Type 1

Systematic hypotension from rapid administration (entire neutralising close after CPB given within 3 minutes). This is caused by a histamine relate reduction in systemic and pulmonary vascular resistance. It can be avoided by infusing the protamine over a 10-15-minute period and should be reversible with alpha agent support (Figure 1).

Type 2

Anaphylactic reaction resulting in hypotension, tachycardia, bronchospasm, flushing and pulmonary edema (Figure 2).

Type 2A: Idiosyncratic IgE-or-IgG-mediated anaphylactic reaction. Release of histamine, leukotrienes and kinins produces a systemic capillary leak causing hypotension and pulmonary edema. This tends to occur within the first 10 minutes of administration.

Type 2B: Immediate nonimmunologic anaphylactoid reaction.

Type 2C: Delayed reactions, usually occurring 20 minutes or more after the protamine infusion has been started, probably related to complement activation and leukotriene release, producing wheezing, hypovolemia and non-cardiogenic pulmonary edema from pulmonary capillary leak.

Type 3

Catastrophic pulmonary vasoconstriction manifested by elevated pulmonary arterial pressure, systemic hypotension from peripheral vasodilatation, decrease left atrial pressure, RV dilatation and myocardial depression. This reaction tends to about 10-20 minutes after protamine infusion started (Figure 3).

The incidence of catastrophic reactions to protamine during cardiovascular surgery is reported 0.13%.

In our case, reported here that after giving protamine 80% of total dose, clotting of anastomosis site occur. Again, in second time reversal of heparin was given with lesser dose of protamine, but clotting of proximal and distal anastomosis site noticed and finally heparin reversal done only with 25% total dose of protamine given and ACT came to normal.

In our opinion in spite of normal blood report this type of reaction to protamine is very rare, it may be due to high blood loss during grafting (distal) so that body protects itself with high secretion of coagulant factors also may be due to thigh abscess drained two weeks back causing hyper coagulation stage?

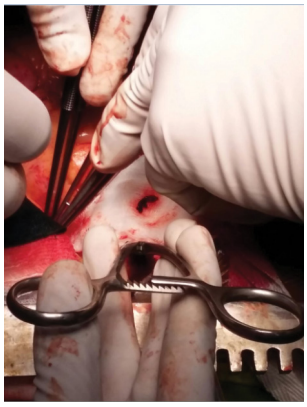

Figure 1: Intra operative picture showing clot removed from distal anastomosis site.

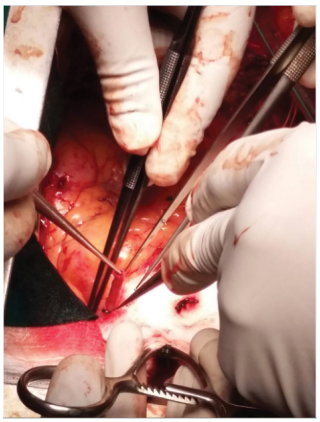

Figure 2: Intra operative picture showing clot removed from vein.

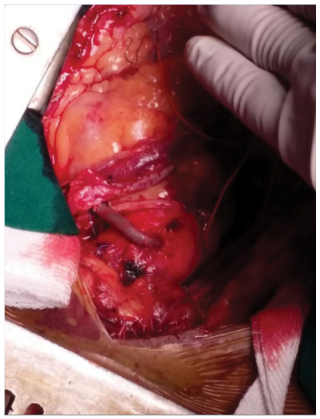

Figure 3: Intra operative picture showing clotting at the site of proximal reverse saphenous venous graft RSVG anastomosis.

So, chances of hyper coagulation and graft blockage can be prevented by lesser dose of protamine given to reversal heparinization. Additionally, when a severe adverse reaction to protamine is suspected or noticed, we postulate that heparin should not be reversed despite a greater risk of bleeding and subsequent re-exploration [1-4].

Avoiding rapid infusion of protamine sulphate and re-treating at risk patients with attest dose of 5-10 mg is recommended before administrating the full dose. Finally, some new drugs came to substitute the protamine for example platelet factor 4 (PF4) but not accepted or used by most of institute or hospital because of unavailability and high cost [5-8].

Conclusion

We present this case to emphasize the unusual life-threatening protamine reaction following off pump coronary artery bypass grafting. It can manifest early or late depending on the doses and duration of protamine administration. Hence, one should keep in mind beside usual reactions to protamine as it can be masked (unusual reaction to protamine) after chest closure. Untreated unusual life-threatening protamine reaction can lead to a significant mortality and morbidity. Hence, prompt diagnosis appropriate management of any protamine reaction are essential.

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