Cardiopulmonary Bypass for A Patient with Systemic Mastocytosis

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Abstract

A patient with systemic mastocytosis was seen in our practice for coronary revascularization. Systemic mastocytosis is a disease characterized by proliferation of mast cells which, under stress, are likely to release vasoactive substances. Coronary artery bypass grafting, utilizing cardiopulmonary bypass with moderate hypothermia, resulted in no clinical problems attributable to this rare pathology. Steps to lessen or eliminate stresses likely to precipitate problems associated with histamine release are discussed.

Introduction

Systemic mastocytosis (SM) is a relatively uncommon disease with features that can have serious consequences during general anesthesia. SM is a disease of mast cell proliferation. Mast cells are connective tissue cells whose specific physiologic function remains unknown. These cells are capable of producing cytoplasmic granules which contain histamine and heparin. Small quantities of hyaluronic acid and serotonin may also be present, as well as prostaglandin D. The name “mast cell” is derived from the German “mastzellen,” or “well fed cell,” coined by Paul Ehrlich in 1877, because of the large number of these granules in the cell.

Mastocytosis falls into two clinical forms. The benign or juvenile form, sometimes called urticaria pigmentosa, is seen in infancy or early childhood and is generally limited to mast cell infiltration of the skin. The malignant or adult form of SM is more severe and involves widespread involvement of other organs, particularly the reticuloendothelial system.

The clinical feature of SM with which the perfusionist should be concerned is the degranulation of mast cells releasing histamine, heparin, and prostaglandin D. This release may be triggered by pharmacological, physical or psychological stimuli. Curare and morphine trigger histamine release, and so may many other compounds. Heat and cold may also lead to histamine release. Care should be taken not to administer cold intravascular solutions, especially blood. Electrocautery pads must have adequate electrolyte jelly to prevent burns. The patient should be kept calm.

Liver and gut involvement are commonly seen in SM. In severe cases there may be significant depression of clotting factors synthesized by the liver. Combined with a potential for the release of unknown quantities of heparin it may be difficult to interpret the dose-response relationship to exogenous heparin used to ensure adequate anticoagulation before and during cardiopulmonary bypass (CPB). A patient with SM may have increased metabolic or excretory mechanisms for dealing with the excess heparin found in this disease. Consequently, the use of a dose-response curve and frequent determination of the activated clotting time (ACT) is crucial for the management of anticoagulation. Allergic reactions may also be encountered when giving protamine sulphate to reverse the effects of heparin.
Case Report

A 51-year old white male initially came to our attention as a candidate for cardiac surgery. He had a history of substernal chest pain radiating into his neck and left arm leading to a diagnosis of coronary artery disease. He also presented with a thirty year history of symptoms of SM, including recurring multiple macular eruptions over his entire body and generalized “bone pain” described by the patient as arthritis and back pain. The patient denied prior episodes of syncope, nausea, or diarrhea. In 1974 a positive skin biopsy confirmed SM (more than five mast cells in a high power field).

In the days preceding his surgery we sought to determine what drug sensitivities, if any, he might have as a result of his SM. Small intradermal aliquots of butorphanol (0.2 mg) and dopamine (0.04 mg) resulted in no reddening or swelling. Fentanyl (0.005 mg), pancuronium (0.2 mg), protamine (1.0 mg), nitroprusside (1.0 mg), isoproterenol (0.02 mg), dobutamine (25 micrograms), atropine (0.08 mg), and diazepam (0.1 mg) elicited either very mild or questionable reactions. Because we definitely foresaw its use, protamine was subsequently tested intravenously (10 mg). No reaction was elicited. The patient had been receiving the antihistamine, diphenhydramine, prophylactically for years obviating the need to test this drug.

On the evening before surgery the patient received chlorpheniramine (9 mg) and diphenhydramine (25 mg) orally. On the morning of his surgery the patient received cimetidine (300 mg) orally, diphenhydramine (50 mg) intramuscularly and methylprednisolone (100 mg) intramuscularly.

His ACT was 144 seconds, which is in our range of normal. Systemic heparinization was achieved with 370 units/Kg. which brought his ACT to 638 seconds. Additional heparin, however, was needed frequently during CPB to maintain the ACT above 480 seconds. This additional need for heparin was notably greater than average, for our practice. He required approximately 5,000 units of heparin every thirty minutes during CPB. This need doubled during the rewarming period. No allergic reaction was seen using the calculated protamine dose to return the patient’s ACT to its baseline level.

Moderate hypothermia (25°C measured in the nasopharynx) was reached after eighteen minutes of cooling with ice water. Four cross clamp periods of 10 to 12 minutes each allowed the three distal anastamoses and one of the proximal anastamoses to be made, the final proximal anastamosis being made with partial cross clamping of the aorta. Total pump time was two hours and twenty minutes. Vasoactive drugs were not required during CPB since the patient’s blood pressure (measured at the radial artery) remained between 55-85 mmHg at flow rates ranging from 1.6-2.5 L/M²/min. The patient weighed 95 Kg. with a body surface area of 2.03 M². Rewarming to 38°C required 43 minutes with a water to blood temperature gradient not exceeding eight degrees centigrade. This relatively slower rewarming phase was accomplished unevenly. Lactated Ringers was used for volume replacement during CPB. The pump was primed with lactated Ringers solution and 100 cc of 25 percent albumin and 100 meq of sodium bicarbonate which is our normal protocol. No blood was used during CPB since the patient’s hematocrit never fell below 25 percent. After CPB the patient did receive two units of packed red cells which had been rewarmed to 37°C. This addition was for the purpose of raising the patient’s hematocrit to 30 percent. Again, no problems were seen.

Conclusion

We found that cardiac surgery, using CPB, may be performed successfully on a patient with SM, but special care should be exercised to avoid histamine release as well as the other potential problems which have been reported to appear in patients with this disease. Antihistamines may be used prophylactically, but they may occasionally provoke the release of histamine.1 Cromolyn sodium, discovered in 1965 and used to treat asthma, is a drug which may possibly stabilize the mast cell before it can fragment. However, the mechanism by which it operates is not clear.2 Cromolyn sodium is still classified as an experimental drug for use in patients with SM and as such was unavailable for our use with this patient at our hospital.

This patient recovered from surgery for coronary artery bypass grafting and was released from the hospital without complications attributable to SM.

References