Anesthetic Considerations in Mastocytosis

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The serious complications associated with anesthesia administered to patients with pheochromocytoma and carcinoid syndrome have been amply documented in the anesthesia literature. Mastocytosis, an uncommon disease also frequently associated with the liberation of a potent vasoactive substance, histamine, has not to our knowledge received previous attention in the anesthesia literature. The salient features of this disease and a case report are presented.

Mastocytosis is characterized by an abnormal accumulation of mast cells which, along with the basophils of the blood, are the main sites of the body's histamine stores. When an increase in mast cells occurs in the skin, the condition is commonly known as "urticaria pigmentosa." It is estimated that systemic mastocytosis, the presence of pathologic infiltrations of mast cells in other than cutaneous tissue, occurs in approximately 10 per cent of all cases. Almost any organ may be involved, but those most commonly affected are bones, liver, spleen, lymph nodes, and peripheral blood. Occasionally, systemic involvement may be present without cutaneous lesions.

Pruritus, urticaria and flushing, the most common symptoms, occur in approximately 40 per cent of patients with mastocytosis. Less frequent but more serious manifestations of the generalized vascular disturbance are hypotension, tachycardia, syncope, and shock. The decrease of arterial blood pressure and cardiac output produced by histamine is attributed to vasodilatation and pooling of blood in the peripheral and splanchnic vascular beds. Headache, abdominal cramps, diarrhea, and vomiting may also occur during an attack. Rarely, high fever or grand-mal convulsions have been reported. Although the mast cell contains large stores of heparin, it is rarely released into the circulation, and a clinically-evident bleeding tendency is very unusual. The low (6 per cent) incidence of respiratory distress is not surprising, considering the relative insensitivity of normal human bronchial musculature to peripherally injected histamine.

In addition, abnormal accumulations of mast cells in the lung are rare in mastocytosis, and histamine released elsewhere in the body is markedly reduced in concentration by the time it reaches the bronchial musculature through tissue binding, dilution, and metabolism.

Symptoms can occur in patients with skin lesions, as well as in those with systemic disease. They may occur seemingly spontaneously or be triggered by such varied stimuli as mechanical irritation of the lesion, psychological stress, temperature change, alcohol, vomiting, exercise, and drugs, especially known histamine-releasers. Although symptoms have been correlated with histamine release, urinary histamine levels may be elevated even between attacks. Identical symptoms have been produced in normal individuals by injected histamine or by the administration of high doses of a potent histamine-releasing drug.

REPORT OF A CASE

In 1971, a 78-year-old man was admitted for surgical correction of a carpal-tunnel syndrome. In 1966, complaints of fatigue prompted a hemoglobin determination, which revealed mild anemia. Subsequent examination of bone marrow revealed mastocytosis. The patient denied having skin rashes, flushing, urticaria, and syncope. He had been having episodes of "chest tightness" and wheezing, which had responded to the chronic administration of an antihistamine. Penicillins had provoked similar episodes previously, but no other allergies were noted.

Physical examination revealed liver and spleen of normal size; no adenopathy, dermographism, or skin lesions were found. Abnormal laboratory findings included 50 per cent mast cells on sternal marrow puncture, hemoglobin 11–12 g/100 ml, and 12 per cent eosinophils on differential. Normal values obtained in studies made when the
patient was asymptomatic included blood histamine level, protamine titration, coagulogram, and chest x-ray.

The patient was premedicated with diazepam, 10 mg, injected intramuscularly an hour before induction of anesthesia. A regional perfusion block was performed with 50 ml of 0.5 per cent lidocaine in 0.9 per cent saline solution administered over a 2-3-minute period. During the injection, an erythematous flush over the entire arm below the tourniquet was noted. At the end of the injection, nummous erythematous wheals approximately 1-3 cm in diameter were also noted over the arm below the tourniquet. Transient pruritus was present before anesthesia was attained. Diphenhydramine (Benadryl), 50 mg, was injected through the scalp vein needle below the tourniquet and flushed through without obvious effect. The operation proceeded, and 10 minutes before termination additional diphenhydramine (50 mg) was given (systemically) intravenously to counteract the effects of any histamine released when the tourniquet was removed. By the end of the operation, which lasted one hour, the wheals had disappeared, and no systemic cutaneous manifestations or hypotension occurred when the tourniquet was released.

In the recovery room the patient's exposed fingers were redder and more swollen than would be expected from reactive hyperemia. Venous return was not impaired by the bandage, and the swelling was believed secondary to increased capillary permeability as a result of the previous histamine release, later manifested when circulation was restored.

Eight days postoperatively, intradermal testing with 0.02 ml of 0.5 per cent and 1 per cent lidocaine with preservative produced no wheal or flare. Application of the arterial tourniquet to the arm not operated on and subsequent injection of 50 ml of the preservative methylparaben, 0.1 per cent in 0.9 per cent saline solution, produced no reaction. The patient refused to have his arm reanesthetized with lidocaine without preservative. When the sizes of the wheals resulting from histamine release on the not operated on arm after intradermal injection of 0.02 ml d-tubocurarine, 1 mg/ml, 0.1 mg/ml, and 0.01 mg/ml, were compared with the reactions of six normal controls, no significant difference between wheal sizes was found. A random skin biopsy on the arm not operated on did not reveal any increase in mast cells.

**DISCUSSION**

Although few patients with mastocytosis will come to surgery in any one institution, Sagher has nevertheless observed that those with systemic mastocytosis "may run an increased risk of collapse and shock during surgical operations." Holli reported a patient with systemic mastocytosis who failed to regain consciousness after abdominal surgery. Demis documented a fourfold increase in urinary free histamine in a patient with cutaneous mastocytosis during the 24-hour period after operation. The patient received known histamine releasers such as morphine, codeine, and scopolamine in addition to thiopental-nitrous oxide-ether anesthesia. Neither Holt nor Demis discusses the anesthetic course of the patient. As with pheochromocytoma and carcinoid syndrome, surgical procedures have been performed in some patients with mastocytosis without mention of any anesthetic catastrophe, although no specific comment was made regarding anesthesia.
mastocytosis are abnormal not only in numbers but in their response to stimuli seems likely in view of the wide range of minor stimuli which may precipitate signs of histamine release. In addition, these stimuli may normally release small amounts of histamine that do not result in signs or symptoms except when numerous mast cells are present. Thus, a substance not normally considered a histamine-releaser, such as lidocaine, might produce symptoms in a particular patient with mastocytosis. Although there is evidence for the histamine-releasing capability of procaine in normal man and animals, similar data for lidocaine could not be found. A severe, unspecified intolerance to both procaine and lidocaine in a patient with mastocytosis has been reported; however, this is not a general characteristic of the disease.

Sufficient data to recommend a specific anesthetic agent or technique are not available. In anesthetizing patients with mastocytosis, the prime concern is avoidance of histamine release. It cannot assuredly be prevented with any particular anesthetic, since the symptoms of histamine release may occur seemingly spontaneously or from psychological, chemical, or physical stimuli even in unanesthetized patients. Avoidance of known histamine-releasing drugs, especially their rapid intravenous administration, is recommended if possible. Patient responses to the use of histamine-releasing drugs tried as possible therapy in mastocytosis have ranged from no effect to frank anaphylaxis. Those anesthetic drugs with histamine-releasing potential include the opiates, atropine derivatives, d-tubocurarine, gallamine, decamethonium, and dextran. When a narcotic or muscle relaxant is necessary, meperidine or succinylcholine, which will produce minimal histamine release, is appropriate.

Fortunately, the inhalational anesthetics do not release histamine. Although either may exert a slight protective effect against direct histamine-releasing drugs, to our knowledge other agents have not been similarly tested. The use of halothane for the removal of mastocytes in dogs, a relatively common tumor, has not been accompanied by a noticeable increased incidence of hypotension. However, if significant histamine release should occur, the resulting hypotension might be more severe and prolonged when compensatory reflexes are compromised under deep inhalational anesthesia with halothane. Since hypotension would be a more likely complication than bronchoconstriction, we would recommend a light plane of anesthesia regardless of the agent chosen. However, since bronchoconstriction remains a possibility, the agent should be compatible with beta-adrenergic stimulants should such therapy be necessary.

Chronic antihistamine administration has been very valuable in decreasing symptoms, including histamine shock, in ambulatory patients with mastocytosis. Maximal doses, which may be necessary, can be used in a surgical patient for premedication and intraoperatively. Although antihistamines interfere with tissue binding rather than release of histamine, prophylactic administration still seems preferable to waiting for release to occur. If significant hypotension or bronchoconstriction should nevertheless occur, we would expect therapy with alpha- and beta-sympathomimetics to be effective. Steroids are rarely beneficial in reducing symptoms.

**References**

Expanding Aneurysm of the Radial Artery after Frequent Puncture

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The radial artery at the wrist is commonly used for arterial blood sampling and hemodynamic measurement. The techniques of intermittent needle puncture or placement of an indwelling plastic catheter are infrequently associated with serious complications. This report describes an expanding aneurysmal dilatation of the radial artery following repeated puncture and cannulation, necessitating excision of the involved segment of the vessel.

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REPORT OF A CASE

A 79-year-old woman was admitted to the Massachusetts General Hospital in respiratory distress due to fracture of the larynx after an automobile accident. Emergency tracheostomy and operative repair were performed. The postoperative course was complicated by both pneumonia and intermittent pulmonary edema, for which the patient was treated with mechanical ventilation, antibiotics, digitalis, and diuretics. Early during her postoperative course the patient's right radial artery was punctured ten times with a 20-gauge needle for arterial blood-gas analysis. When the need for prolonged respiratory care became evident, an indwelling arterial catheter (size 18 Argyle) * was placed percutaneously at this site. It remained in situ for ten days. Eighteen days after removal of

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