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Upper Airway Edema—An Anaphylactoid Reaction to Succinylcholine?

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Succinylcholine (SCh) was reported to cause histamine release in 1957 when skin reactions were observed in four patients.[1] Since then, at least 12 additional cases of hypersensitivity to the drug have been described.[2–11] This report presents a case of probable SCh-induced upper airway edema in a patient with bronchial asthma and known penicillin allergy.

REPORT OF A CASE

A 30-year-old term-pregnant woman with history of bronchial asthma and of urticarial rash following penicillin administration required emergency cesarean section because of fetal distress. She had received no previous anesthesia. Physical examination and laboratory data were within normal limits. After preoxygenation, application of monitoring devices, and intravenous injection of 0.4 mg atropine and 3 mg *d*-tubocurarine, anesthesia was induced with ketamine (50 mg) and thiopental (100 mg), iv. Following administration of 100 mg SCh, a 7-mm single-use low-pressure cuff endotracheal tube was inserted with ease. Anesthesia was maintained with nitrous oxide–oxygen–halothane 0.5 per cent, until delivery of the infant. After clamping of the umbilical cord, halothane administration was discontinued and respiration controlled by a volume-limited ventilator. Meperidine, 50 mg, 10 mg diazepam, and 50 mg thiopental were injected iv in divided doses, and a total dose of 250 mg SCh was infused in a 0.1 per cent solution during the 70 min of surgery. Fluctuations in heart rate and blood pressure were unremarkable throughout.

At the end of the procedure, the patient was awake and responsive and the endotracheal tube was removed. Immediately thereafter, she began to show signs of respiratory distress and deepening cyanosis of the mucous membranes. Attempts to ventilate her by face mask were unsatisfactory despite insertion of oro- and nasopharyngeal airways. Laryngoscopy revealed marked edema of palate, pharynx, and larynx; the cords could no longer be visualized but it was possible, with difficulty, to insert a 6-mm endotracheal tube. Oxygen 100 per cent was administered to the spontaneously breathing patient, and 40 mg dexamethasone was injected iv. Moderate swelling of lips and eyelids was also evident, but no wheezing or skin rash was detected. The heart rate which had increased during the period of respiratory difficulty returned to normal within 5 min. Chest radiogram revealed no abnormalities, but a neck soft tissue radiogram suggested tissue swelling. An otolaryngology consultant confirmed the diagnosis of angioedema. Three hours later, the endotracheal tube was removed without problems. Steroid treatment was continued for one additional day.

Two days postpartum, skin tests were performed with 0.1 ml of all drugs used intravenously during anesthesia and with saline as control. The tests were negative for atropine, *d*-tubocurarine, thiopental, meperidine, and diazepam. There was a strongly positive reaction to SCh, both with and without preservative: wheals approximately 10 mm in

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diameter and surrounded by flares 20 mm in diameter appeared approximately 20 min after injection, lasted close to three hours, and were associated with intense itching. The next day, skin tests were performed with anesthetic and ancillary drugs not previously employed: 2-chloroprocaine-CE, bupivacaine, lidocaine, and pancuronium; these were all negative.

The complication was explained to the patient, and she was given a letter describing the probable hypersensitivity with instructions to show this letter to her physicians before any future anesthesia.

Discussion

According to Watkins,[12] the term "allergy" implies an immune-mediated reaction to a substance. In the absence of laboratory tests to elicit the underlying mechanism, clinical manifestations cannot be used to distinguish between antibody-mediated responses, complement-mediated responses, and responses secondary to release of histamine from mast cells. Therefore, on the basis of clinical observations alone, hypersensitivity-type reactions are best described as anaphylactoid, which was the term used in this case report.

Review of the 16 reported cases of hypersensitivity-type reaction to SCh reveals a wide variety of signs, with bronchospasm and cardiovascular collapse predominating. Periorbital or facial edema was mentioned in three patients whose primary problem was cardiovascular. Edema of the upper airway, however, was described only in two patients suffering from "allergy" to penicillin both of whom also had wheezing, hypotension, and tachycardia.[4,9] In our patient, the manifestations of wheezing and cardiovascular depression may have been mitigated by the anesthetic technique and the circulatory alterations associated with parturition. Wheezing may have been prevented by the bronchodilating effect of ketamine and halothane. Hypotension and heart rate changes may have been modified, first by ketamine and then by the increase in cardiac stroke volume normally following separation of the placenta. In addition, general anesthesia may suppress the signs of anaphylaxis or delay its onset or severity.[13] Finally, the sequelae of upper airway edema were obscured by the presence of the endotracheal tube. SCh and penicillin share no structural, pharmacologic, or immunologic relationship so that cross-sensitization is unlikely.[9] Possibly, the allergic diathesis predisposes to edema formation, as increased capillary permeability is one of its basic mechanisms.[14] Physical factors such as changes in temperature or humidity or pressure of the endotracheal tube could have acted as additional triggers.[14]

Skin testing in the diagnosis of anaphylactoid reactions is the chief corroborative tool employed beyond the clinical history. It is widely acknowledged to be useful for a number of purposes including assessment of possible sensitization to drugs such as penicillin and anesthetics.[14]

SCh is marketed in two forms; the liquid contains the preservative methylparaben whereas the powder does not. Hypersensitivity to methylparaben has been reported.[15] Our patient who had received both forms during the course of anesthesia produced an identical skin reaction to each. Therefore, it is very unlikely that methylparaben was a further causative agent. In conclusion, succinylcholine may have caused the development of upper airway edema in a patient with an allergic diathesis.

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