IMMEDIATELY after induction of anesthesia, a generalized maculopapular exanthema with facial edema, hypotension, and tachycardia developed in a 19-yr-old man undergoing left hip debridement for Perthe's disease. The clinical circumstances and the studies performed to establish the diagnosis of cold urticaria are described.

Case Report

A 19-yr-old man (weight, 72 kg) with Down syndrome, hypothyroid disease controlled with levothyroxine, and no known allergies had undergone general anesthesia on three previous occasions without complications. At the time of the procedure described, he was taking amoxycillin–clavulanic acid and diclofenac for a left hip infection. The patient, classified as American Society of Anesthesiologists physical status II, was scheduled for left hip debridement surgery. Anesthesia was induced with 1 mg atropine, 2 mg midazolam, 0.10 mg fentanyl, 300 mg thiopental, and 50 mg atracurium. The latter was injected as a bolus, at a temperature of approximately 6°C (taken directly from the refrigerator).

Less than 30 s after the drugs used for induction were administered, a generalized maculopapular exanthema, facial edema, hypotension (systolic/diastolic arterial pressure of 66/34 mmHg) and sinus tachycardia (144 beats/min) developed in the patient. Orotracheal intubation was performed immediately, but no edema of the glottis was noted during laryngoscopy, and there were no subsequent signs of bronchospasm with controlled ventilation. The condition improved after the intravenous infusion of 500 ml crystalloid (at room temperature [21°C]) during a period of 30 min and 125 mg methylprednisolone. No other anesthesia-related incidents occurred during the 70 min of surgery, in which anesthesia was maintained with isoflurane and nitrous oxide–oxygen. The patient’s trachea was extubated at the end of the procedure.

When questioned, the patient’s family reported the occasional appearance of urticaria when he participated in aquatic activities. No personal or family atopy was observed. The family rejected a study of possible allergies, and the episode was regarded as a consequence of histamine release triggered by the drugs administered during anesthesia induction.

Seven months later, the patient again required left hip debridement. The anesthetic was induced using the same drugs as before but in a different sequence: 2 mg midazolam, 0.12 mg fentanyl, 10 mg atracurium, 100 mg thiopental, 15 mg atracurium, and 150 mg thiopental. On this occasion, atracurium was administered at room temperature (21°C). Orotracheal intubation was performed without difficulty after muscle relaxation was achieved. Eight minutes after induction, exanthematous papular lesions were observed distributed on the patient’s trunk and upper limbs. The lesions disappeared without treatment, and no hemodynamic or respiratory changes were observed. Anesthesia was maintained with isoflurane, nitrous oxide–oxygen, fentanyl, and pancuronium for the 3.5 h duration of the operation. The patient was extubated in the operating room and transferred to the recovery ward for routine postoperative monitoring. Blood samples were obtained 45 min after induction, and the following results were obtained: serum tryptase, 6.8 μg/l (normal range: <15.5 μg/l); C3, 154.7 mg/dl (normal range, 90–180 mg/dl); C4, 33.8 μg/dl (normal range, 10–40 μg/dl); immunoglobulin E, 209 KU/l (normal range, 0–100 KU/l); and 24-h urine methylhistamine level, 178.4 μg/24 h (normal range, 0–172 μg/24 h). Therefore, only the immunoglobulin E levels were abnormally increased. One week later, similar normal test values were obtained, although the immunoglobulin E level remained elevated (329 KU/l).

After the family gave their consent, the patient was referred to the allergy department of the hospital for further study and diagnosis. Sensitization skin tests (prick tests and intradermal reactions) were performed for the drugs and products used during standard surgical procedures: muscle relaxants (atracurium, pancuronium, succinylcholine, and vecuronium), thiopental, midazolam, fentanyl, and latex. The results of all the skin tests were negative. A cold stimulation test applied to the skin of the forearm was immediately positive with an exposure time of 2 min. No clinical manifestations suggested cryoglobulinemia or vasculitis. Results of the laboratory tests, the hemogram, the globular sedimentation rate, and the proteinogram were normal, as were complement, cryoglobulins, antinuclear antibodies, rheumatoid factor, and serology for mononucleosis, cytomegalovirus, syphilis, mycoplasma, and hepatitis.

The case history, a cold-stimulation test positivity with a 2-min exposure time, and the absence of clinical evidence of associated disease suggested the diagnosis of primary cold urticaria triggered by
the intravenous injection of atracurium at a low temperature (approximately 6°C). The temperatures of the other infused fluids and the operating room were similar during both procedures.

Discussion

Histamine release induced by the administration of drugs used in routine anesthesia practice is common, and muscle relaxants are often implicated. Most reactions affect the skin, although there have been reports of histamine release triggering severe systemic reactions. According to Fisher and Baldo, the incidence of significant perioperative reactions ranges from 1 in every 10,000–20,000 anesthetic sessions.

We described a young patient in whom urticarial lesions developed in response to the administration of the same drugs on two separate occasions. The adverse reactions differed in terms of severity: An anaphylactoid-like reaction was observed after the initial exposure, whereas the subsequent event was a limited skin reaction. The condition was more severe in the first episode and was triggered by the injection of atracurium at a low temperature (approximately 6°C). This phenomenon was observed only partially on the second occasion, when all drugs were administered at room temperature (21°C), which suggests that the intensity of the stimulus was a determining factor. Having dismissed hypersensitivity to the drugs used and disease associated with cold syndromes, the clinical findings of our patient suggest a severe primary acquired cold urticaria. However, in the absence of a history of severe reactions to low temperatures, cold urticaria is not usually suspected in the presence of manifestations compatible with anaphylactic shock during surgery.

Cold urticaria accounts for 3–5% of all physical urticarias. The first report dates back to 1866, although it was not until 1936 that Horton et al described the possibility that shock-like complications can develop in response to aquatic activities. Severe cold urticaria is a life-threatening condition that is difficult to diagnose when observed in the operating room. Lockhart reported a case that occurred when fluid infusion was initiated before anesthesia was induced. The condition is characterized by the development of urticaria, angioedema after exposure to local and environmental cold, or both conditions. The most common triggering factors are cold air current, rain, aquatic activities, snow, cold foods and drinks, contact with cold objects, aerosols, and so forth.

The following classification has been proposed according to the severity of the symptoms: type 1 (localized urticaria, angioedema, or both: 30% of cases), type 2 (generalized urticaria, angioedema, or both: 32% of cases), and type 3 (urticaria, angioedema, or both associated with systemic alterations in the form of arterial hypotension, vertigo, loss of consciousness, disorientation, or shock: 38-42% of cases).

Diagnostic tests have been developed based on skin stimulation with temperatures of 0–4°C for a period of 1–5 min (the cold stimulation test). Wanderer et al observed a 57% incidence of type 3 hypersensitivity reactions in patients with cold stimulation tests found to be positive in less than 3 min, compared with a 24% incidence when positivity was recorded after 3 min. Thus, an inverse relation appears to exist between the time elapsed to a positive cold-stimulation test result and the appearance of severe reactions induced by cold.

Several studies have implicated immunologic mechanisms in acquired cold urticaria, a finding that could account for the increased immunoglobulin E levels that we observed in our patient. Gruber et al reported the presence of autoantibodies in patients with primary cold urticaria. In some instances, clinical induction has been possible by passive transfer. Cutaneous mast cells rather than blood basophils are clearly the target cells in the primary syndrome. However, basophil degranulation has been found in a patient’s blood that was stored at 0°C; similarly, many authors have reported increases in blood histamine and other mediators after challenge. No studies have been published to date regarding the release of tryptase, the most important mast cell activation marker.

The primary objective of treatment is to prevent systemic reactions caused by the triggering mechanisms (aquatic activities, a cold surgical environment, and so on). Patients with negative results of cold-stimulation tests (atypical presentations) also can have shock-like reactions. Medication is effective in suppressing the symptoms; for example, the administration of antihistamines reduces the number of recurrences and prolongs the time to a positive cold-stimulation test result. In this context, a case has been reported of successful treatment with combined anti-H1 and anti-H2 drugs and corticoids, before the induction of hypothermia required for coronary bypass graft.

Therefore, in patients with suspected or known primary cold urticaria who are undergoing surgery, drugs requiring cold storage should be avoided or warmed before injection. Further prophylactic measures include warming all perfused fluids, increasing the temperature of the operating room, and administering antihistamines and corticoids before surgery.
References


Hemofiltration in Parallel to the Venovenous Bypass Circuit for Oliguric Hypervolemia during Liver Transplantation

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PATIENTS undergoing liver transplantation often require blood components perioperatively for the treatment of coagulation factor deficiencies, thrombocytopenia, and anemia. Preexisting hypervolemia may limit this therapy, particularly when oliguric renal failure complicates end-stage liver disease. Intravascular volume reduction is then often accomplished with continuous arteriovenous hemodialysis (CAVHD), continuous arteriovenous hemofiltration (CAVH) or continuous venovenous hemofiltration (CVVH). This report concerns intraoperative CVVH, in parallel to the venovenous bypass (VVV) system, without anticoagulants during liver transplantation. With this CVVH technique, transmembranal pressure gradients and ultrafiltration rates resemble that of CAVH.

Case Report

A 58-yr-old man was awaiting liver transplantation for the treatment of cirrhosis secondary to chronic hepatitis C virus infection. Spontaneous retroperitoneal and gastrointestinal hemorrhages had previously developed in the patient and he had received more than 50 units of packed red blood cells and fresh frozen plasma (FFP), in the medical intensive care unit over 5 days. Encephalopathy, shortness of breath and hypoxemia ensued, requiring tracheal intubation and mechanical ventilation. Serial