

Adverse reaction to bupivacaine

ADVERSE reactions to local anesthetics (LA) have been widely described, and various mechanisms have been proposed to explain such reactions (1). Most of them are thought to be toxic, mainly after unintentional intravascular injection, eliciting cardiovascular and neurologic symptoms; other clinical manifestations include cutaneous and respiratory symptoms. Allergic reactions are rare (2), and contact dermatitis is the most frequently described allergic reaction, mainly due to the ester class of LA.

Bupivacaine is one of the LA most frequently used in medicine. In this paper, we report on a bizarre adverse reaction to bupivacaine.

■ A 69-year-old woman was referred for allergologic investigation, in order to select at least one LA which could be safely used before surgery. Her medical history was negative for atopic diseases, but she had had episodes of bronchospasm related to nonsteroidal anti-inflammatory drug administration. Her surgical history included cholecystectomy, cataract surgery, and hallux valgus surgery. She denied atopy or allergic diseases in her family.

Skin prick tests (SPT) were performed with three different undiluted LA: Lidocaina Braun 2%[®] (lidocaine), Scandibsa 2%[®] (mepivacaine), and Svedocain 0.75%[®] (bupivacaine). As this step yielded a negative reaction, each LA was subsequently administered as a subcutaneous challenge test (simple blind), carried out with increasing doses, injected in the lateral side of her arm. Blood pressure, pulse rate, and symptoms were recorded before and during the challenge tests.

Challenge tests with lidocaine and mepivacaine were carried out without adverse reactions. Approximately 30 min after the 0.1-ml dose (1:100 diluted), bupivacaine elicited heavy feeling in her arms and itching in her eyes. Changes in blood pressure and in pulse rate were not observed. Since anxiety might influence the appearance of the non-cutaneous signs and symptoms, our patient was rechallenged 1 month later with bupivacaine, under the same protocol. This time the 0.1-ml dose (1:100 diluted) also elicited clinical manifestations (heavy feeling, cough, sneezes, and itching in her eyes)

30 min later, without changes in blood pressure or in pulse rate. Specific serum IgE to bupivacaine was negative (RAST <0.35 kU/l).

In order to exclude other sensitizations, SPT with common inhalant allergens (pollens, house-dust mites, molds, and animal epithelia) were performed with commercially available extracts (ALK-Abelló, Madrid, Spain). All of them were negative.

■ The diagnosis of adverse reactions to LA is based on clinical history, skin tests, and challenge tests. Nevertheless, skin tests have limited value, specific IgE has not been described in adverse reactions to LA (2), and clinical history alone often does not

allow sufficient accuracy for diagnosis. Therefore, the subcutaneous challenge test is our most important tool for the diagnosis of adverse reactions to LA.

Several cases of adverse reactions to bupivacaine have been reported. Most of them are thought to be toxic (respiratory arrest [3], cardiovascular toxicity [4, 5], myotoxicity [6], and neurologic symptoms [7]). Other cases include anaphylactoid reactions (8, 9) and delayed cutaneous reactions (10). As far as we know, rhinitis and/or conjunctivitis have not been reported as adverse reaction to bupivacaine.

Since LA commercial preparations often contain preservative agents, clinical manifestations might be elicited by sensitization to such substances. That circumstance is unlikely in our patient, since all three LA used (Lidocaina Braun[®], Scandibsa[®], and Svedocain[®]) had the same preservative agent (sulfites), and only Svedocain 0.75% twice elicited clinical manifestations. Nevertheless, Simon (11) suggests that sulfite concentration in common doses of LA does not elicit bronchospasm in patients with asthma and sensitization to sulfites.

The role of psychological aspects in adverse reactions to drugs is difficult to assess. We tried to avoid such a possibility by performing challenge tests by the simple-blind method. In fact, under the same protocol with all three LA tested, only bupivacaine elicited adverse reaction.

In summary, in this patient, bupivacaine could be identified as the cause of the adverse reaction, but an IgE-mediated mechanism could not be dem-

A probable non-IgE-mediated reaction to a local anesthetic.

onstrated. As expected, since all of the three LA used belong to the amide class, cross-reactivity among them did not appear.

Key words: adverse reactions; bupivacaine; challenge tests; local anesthetics.

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Intolerance to sodium metabisulfite in beer

Where report on a patient who developed facial erythema and edema shortly after consumption of alcoholic beverages, namely, one specific brand of beer. Extensive allergologic testing identified sodium metabisulfite as the causative agent of the patient's symptoms and the pseudo-allergic pathogenesis of his symptoms.

■ In 1993, a then 25-year-old white man began to experience numerous episodes of itchy erythematous rashes and swelling in the face, namely, over the zygomatic arches and periorbitally. These symptoms developed within minutes after consumption of various brands of wine and most often after

enjoying his favorite brand of beer. All symptoms resolved spontaneously within 1-2 h. Prick tests of relevant cereals (malt, barley, rice, rye, wheat), hops, and brewer's yeast, along with food preservatives, the food dye tartrazine, and the implicated brand of beer (Irseer Klosterbräu®), were negative.

To test whether ethanol or its metabolites acetaldehyde or acetic acid might be the relevant agents, the respective prick tests were performed and yielded negative results (Table 1). Oral challenge with food preservatives (including 500 mg of *p*-hydroxybenzoic acid and 500 mg of sodium salicylate) and 100 mg of tartrazine did not result in any reactions, nor did oral challenge with 50 ml of the accused beer. Thirty minutes later, the patient was challenged with another 50 ml of the beer and developed pronounced erythema and edema over the zygomatic arches and periorbitally within 10 min. The symptoms were accompanied by a significant ($P < 0.01$; Student's *t*-test) increase of serum histamine from a value of 9.8 nM before exposure to 26.3 nM after exposure (normal range: < 10 nM), as detected by radioimmunoassay (Immunotech, Hamburg, Germany). Identical symptoms were observed after oral exposure to the amount of 10 mg sodium metabisulfite, a dose recommended by others (1). No specific IgE or IgG antibodies to sodium metabisulfite could be detected in the patient's serum by the radioimmunosorbent test (Pharmacia, Uppsala, Sweden). Since sodium metabisulfite was capable of inducing the clinical symptoms also realized after consumption of beer, a fresh sample of the beer preferred by the patient was analyzed for its sulfite content by means of distillation and subsequent

No need to panic. You can still enjoy a beer or two.

Table 1 Results of allergologic tests

Mode	Substance	Result
Skin prick	5% Sodium metabisulfite	Neg
	1% <i>p</i> -Hydroxybenzoic acid	Neg
	Tartrazine	Neg
	Brewer's yeast	Neg
	Cereals	Neg
	Ethanol 96% and 9.6%	Neg
	Acetaldehyde 100%	Neg
	Acetic acid 9.6% and 0.96%	Neg
	Beer	Neg
	<i>p</i> -Hydroxybenzoic acid (500 mg)	Neg
Oral challenge	Sodium salicylate (500 mg)	Neg
	Tartrazine (100 mg)	Neg
	Beer (100 ml)	Pos *
	Sodium metabisulfite (10 mg)	Pos *

*Erythema and edema over zygomatic arches and periorbitally.

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