

CORRESPONDENCE

Novel mechanism of B cell-mediated anaphylaxis after spinal anesthesia with bupivacaine

Dear Editor,

The estimated incidence of perioperative grade 3–5 anaphylaxis is 1 per 10,000 patients administered anesthesia, with the leading causes being antibiotics, neuromuscular blocking agents, and chlorhexidine.¹ Reports on severe allergic reactions to local anesthetics are rare,^{1,2} and few case reports have presented bupivacaine-induced anaphylaxis through symptomatic diagnosis and the lymphocyte stimulation test.³ To prevent anaphylaxis recurrence, diagnostic tests should be performed for culprit drug identification,⁴ including skin tests, intracutaneous tests, serum drug-specific immunoglobulin E (IgE) quantification, and basophil activation test.

The Tri-Service General Hospital Institutional Review Board (TSGHIRB-A202005103) waived patient informed consent because no identifiable personal medical information of patients was obtained in this study. A 69-year-old Taiwanese woman, with a height of 148.5 cm and a weight of 44.6 kg, was admitted for left hip replacement. She had undergone a similar procedure for her right hip uneventfully under spinal anesthesia with 15 mg isobaric bupivacaine

9 months ago. Her medical history revealed diabetes mellitus and occasional high blood pressure. On arrival to the operation room, standard monitoring was applied, which included the use of three-lead electrocardiography, noninvasive blood pressure monitors, and pulse oximetry. Spinal anesthesia was performed at the L4/5 interspace without any intravenous premedication and antibiotics following oxygen supplementation through a face mask when blood pressure was 150/70 mmHg and heart rate was 60 beats per minute. Approximately 10 min after intrathecal injection of 13 mg 0.5% isobaric bupivacaine, the patient complained of breathing difficulty, and her blood pressure drastically decreased to 58/42 mmHg (heart rate 65 beats per min) from 150/60 mmHg (heart rate 77 beats per min) within 3 min. The initial intravenous injection of ephedrine (10 + 10 mg) and norepinephrine (incremental from 0.01 to 0.04 mg until a total of 0.1 mg) could barely maintain her systolic blood pressure to >60 mmHg in the following 20 min. Because of severe hypotension with a poor response to vasopressors, 30 mg diphenhydramine and 200 mg hydrocortisone were administered based on the high suspicion of anaphylactic shock. Subsequent intravenous epinephrine

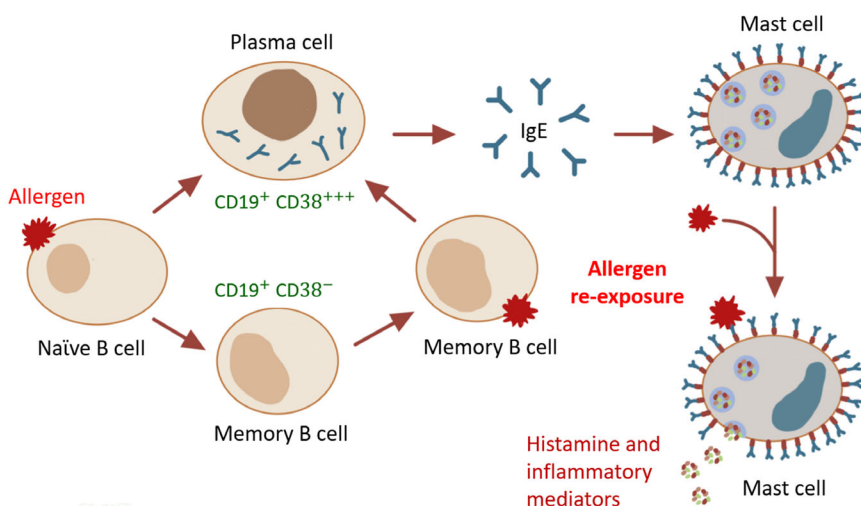


FIGURE 1 Skin redness and blanching test results (yellow arrow) approximately 30 min after intrathecal injection of isobaric bupivacaine for spinal anesthesia (left); B cell-mediated allergic mechanism (right). B cell-differentiated plasma cells produce specific immunoglobulin E (IgE) antibodies. Re-exposure to the same allergen induced degranulation and the release of histamine in mast cells. Memory B cells may rapidly respond to allergen re-exposure with the generation of new plasma cells

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(incremental from 0.01 to 0.2 mg until a total of 0.36 mg) and simultaneous fluid resuscitation (2000 ml) through a newly inserted femoral central venous catheter finally maintained her systolic blood pressure at >100 mmHg. Approximately 30 min after intrathecal injection of bupivacaine, skin flushing was observed on her face, trunk, and limbs (Figure 1). The procedure was terminated despite clear consciousness and clear breathing sounds. Her vital signs became stable in the following 3 h, with vasopressor therapy tapered to zero. After discharge, she was referred to the Drug Hypersensitivity Clinical and Research Center, Linkou Chang Gung Memorial Hospital, Taiwan. Hypersensitivity to bupivacaine was identified through positive and negative results in cluster of differentiation (CD)19/CD45 and CD38 tests, respectively, of the B cell culture, along with negative results in the basophil activation (CD63) and histamine/leukotriene 4 release tests. In addition, negative hypersensitive reactions to other anesthetics, including fentanyl, lidocaine, propofol, cis-atracurium, rocuronium, succinylcholine, and midazolam, were confirmed for further general anesthesia. The left hip operation was then completed smoothly under general anesthesia 3 months later.

In conclusion, the patient experienced grade 5 anaphylaxis with severe hypotension following the second exposure to isobaric bupivacaine for spinal anesthesia, which was confirmed through positive and negative hypersensitivity reaction results in CD19/CD45 and CD38 tests, respectively, of B cell culture. In the first exposure, the allergen triggers naïve B cells to differentiate into plasma cells (CD19⁺ CD38⁺⁺⁺) and memory B cells (CD19⁺ CD38⁻).⁵ Plasma cells produce specific IgE antibodies to bind to the surface of circulating mast cells. Subsequent exposure to the same allergen may induce widespread mast cell sensitization and histamine release, resulting in a classical anaphylactic reaction (Figure 1). Memory B cells may rapidly respond to allergen re-exposure through the generation of new plasma and memory B cells to induce a nonclassical allergic IgE reaction.⁵ The culprit drugs were identified for the prevention of recurrent anaphylaxis during subsequent anesthesia and operations.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

Meng-Ta Yang^{1,2}

Su-Yang Hwa³

Feng-Cheng Liu⁴

Tso-Chou Lin¹ 

¹Department of Anesthesiology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

²Division of Anesthesiology, Hualien Armed Forces General Hospital, Hualien, Taiwan

³Department of Orthopedic, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

⁴Division of Rheumatology, Immunology and Allergy, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

Correspondence

Tso-Chou Lin, Department of Anesthesiology, Tri-Service General Hospital, National Defense Medical Center, No. 325, Section 2, Cheng-Gong Road, Taipei 11490, Taiwan.
Email: tclin@mail.ndmctsgh.edu.tw

ORCID

Tso-Chou Lin  <https://orcid.org/0000-0003-0131-2586>

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