magnetic resonance spectroscopy in NARP syndrome. J Neurol Neurosurg Psychiatry 1994; 57:1492–6

10. Holt IJ, Harding AE, Petty RKH, Morgan-Hughes JA: A new mitochondrial disease associated with mitochondrial DNA heteroplasmy. Am J Hum Genet 1990; 46:428–33

11. Figarella-Branger D, Kozak-Ribbens G, Rodet L, Aubert M, Borsarelli J, Cozzone PJ, Pellessier JF: Pathological findings in 165 patients explored for malignant hyperthermia susceptibility. Neuromusc Dis 1993; 3:553–6

12. Tarba C, Cracium C: A comparative study of the effects of procaine, lidocaine, tetracaine, and dibucaine on the functions and ultrastructure of isolated rat liver mitochondria. Biochem Biophys Acta 1990; 1019:19–28

13. Maslow A, Lisbon A: Anesthetic considerations in patients with mitochondrial dysfunction. Anesth Analg 1993; 76:884–6

14. Rosaeg OP, Morrison S, MacLeod JP: Anaesthetic management of labour and delivery in the parturient with mitochondrial myopathy. Can J Anaesth 1996; 43:403–7

15. Branca D, Varotto ML, Vincenti E, Scutari G: General anesthetics: Interferences with some mitochondrial energy-dependent mechanisms. Agressologie 1989; 30:79–83

16. D'Ambra MN, Dedrick D, Savarese JJ: Kearns-Sayre syndrome and pancuronium-succinylcholine induced neuromuscular blockade. ANESTHESIOLOGY 1979; 51:343–5

17. Burns AM, Shelly MP: Anaesthesia for patients with mitochondrial myopathy. Anaesthesia 1989; 44:975–7

18. Wiesel S, Bevan JC, Samuel J, Donati F: Vecuronium neuromuscular blockade in a child with mitochondrial myopathy. Anesth Analg 1991; 72:696–9

19. Petersen E: Third-degree atrioventricular block, chronic progressive external ophthalmoplegia, pigmentary degeneration of the retina. Case report and survey of the literature. Acta Med Scand 1978; 203:39–42

20. Lauwers MH, Van Lersberghe C, Camu F: Inhalation anaesthesia and the Kearns-Sayre syndrome. Anaesthesia 1994; 49:876–8

Anesthesiology
1997; 87:1242–4

Anaphylactic Shock Induced by an Antiseptic-coated Central Nervous Catheter

Toshiyuki Oda, M.D., Ph.D., Junichiro Hamasaki M.D.,† Naomi Kanda, M.D.,† Ko Mikami M.D.†*

ANAPHYLACTIC shock is a rare but life-threatening complication in clinical practice. A number of drugs used during perioperative management have been reported to cause anaphylactic shock. Recently a non-drug-related hypersensitivity reaction, latex allergy, has been increasing in incidence during anesthesia and surgery.[1] We report a case of anaphylactic shock that occurred during the placement of an antiseptic-coated central venous catheter.

Case Report

A 47-yr-old woman with a history of uterine myoma was scheduled for hysterectomy. The patient had undergone the removal of uterine myoma at aged 30 yr, however, her medical history was free from allergic reactions. Her preoperative physical examination was significant only for well-controlled diabetes mellitus.

The patient was brought to the operating room after being premedicated with oral diazepam, 5 mg. Before induction of anesthesia, an epidural catheter was placed in the second lumbar interspace, and 2 ml of 1% mepivacaine was given as a test dose. Her preinduction blood pressure was 126/82 mmHg, with a heart rate of 82 beats/min in normal sinus rhythm. Anesthesia was induced with propofol (1.5 mg/kg), and tracheal intubation was facilitated with vecuronium (0.1 mg/kg). Anesthesia was maintained with sevoflurane in nitrous oxide and oxygen. After induction of anesthesia, an antiseptic-coated central venous catheter (ARROWgard Blue™, 14-gauge, Arrow International Inc., Reading, PA), a type that is treated with chlorhexidine and sulfadiazine silver, was introduced *via* the right subclavian vein. During placement of the catheter, we recognized arterial hypotension (from 120/68 mmHg to 102/60 mmHg in 5 min) and reaching as low as 70/40 mmHg within 10 min, together with tachycardia (120 beats/min). The hypotension was refractory, despite treatment with vasoactive agents (ephedrine, dopamine, norepinephrine), fluid replacement, or treatment with corticosteroid (methylprednisolone). We also noted a generalized irregular, raised erythema. There was no evidence of bronchoconstriction. We made a diagnosis of hypersensitivity reaction on the basis of the clinical manifestations and postponed the surgical operation. Thirty minutes later, the blood pressure rose to 130/70 mmHg with the aid of dopamine (5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and became stable 40 min later without dopamine. The generalized erythema gradually subsided within 2 h. The central venous catheter

* Associate Professor.

† Staff Anesthesiologist.

Received from the Department of Anesthesiology and Critical Care Medicine, Kagoshima University, Faculty of Medicine, Kagoshima-Shi, Japna. Submitted for publication February 3, 1997. Accepted for publication June 11, 1997.

Address reprint requests to Dr. Oda: Department of Anesthesiology and Critical Care Medicine, Faculty of Medicine, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima-Shi, 890, Japan. Address electronic mail to: odat@med4.kufm.kagoshima-u.ac.jp

Key words: Anaphylactic shock. Antiseptic-coated central venous catheter.

remained in place for 2 days, however, we had not noted further clinical manifestation of anaphylaxis.

To identify the causative mechanism, a prick test was performed using the substances associated with the period of anesthesia—propofol, mepivacaine, vecuronium, atropine, Ringer's acetate, povidone iodine, chlorhexidine, sulfadiazine silver, and latex. The first time prick test was performed 1 week after the episode, and it produced a negative response for each substance. The prick test was repeated 6 weeks later, when a significant positive reaction to chlorhexidine was obtained.

The surgical operation was scheduled again for 6 weeks later. Unfortunately, the result of the second prick test had not been reported to the anesthesiologists, therefore they chose the drugs that resulted in negative response in first prick test. Consequently, the anesthesia was planned to follow the same procedures used on the previous occasion. Severe hypotension with tachycardia occurred again as soon as the central venous catheter was inserted into the vein. The catheter was removed immediately. The blood pressure recovered within 15 min under treatment with epinephrine and norepinephrine. After obtaining stable hemodynamics, a central venous catheter without antiseptic surface treatment (Blue FlexTip,™ 14-gauge, Arrow International Inc.) was placed uneventfully, and the surgical operation was then performed. The perioperative period was uneventful. Blood analysis during the second-time anesthesia revealed a significantly increased histamine concentration immediately after the hypotension (from 3.3 nM/l before induction of anesthesia to 540.0 nM/l immediately after hypotension, respectively; reference level = 0.1–0.5 nM/l) and a reduction in C3 (from 108 mg/dl to 38 mg/dl, respectively; reference level = 60–116 mg/dl) and in C4 (from 33 mg/dl to 18 mg/dl, respectively; reference level = 15–44 mg/dl). Immunoglobulin E (IgE) showed as low as 15 U/ml before induction of anesthesia, and it reduced to 9 U/ml after hypotension. IgE recovered to 17 U/ml in the next day. The lymphocyte count reduced from 2,800 counts/μl (before induction of anesthesia) to 400 counts/μl (3 h after hypotension).

Discussion

The clinical manifestations seen in this patient can be accepted as anaphylactic shock for the following reasons. First, the clinical features (rapid onset of hypotension and tachycardia, refractory hypotension, and skin erythemas) are those normally associated with a hypersensitivity reaction. Second, the blood analysis revealed a high histamine concentration and reduced levels of complements (C3 and C4). Third, the reaction reoccurred when an antiseptic-coated central venous catheter was again used.

The anaphylactic shock in this patient was considered to be caused by the chlorhexidine for the following reasons. First, the second prick test revealed a positive response to chlorhexidine. Second, the circulatory disturbance occurred immediately after the insertion of the chlorhexidine-treated catheter. Third, the response reoccurred on the use of the catheter. There was no abnormal response to the placement of an untreated polyurethane central venous catheter supplied by same manufacturer. This suggests that the material of the catheter itself was not the cause.

Anaphylactic shock caused by chlorhexidine has been described previously.[2–4] However, in those cases the chlorhexidine was used for disinfection of the skin, a mucous area, or a wound. We could find no previous report that anaphylactic shock can be caused by an antiseptic-coated central venous catheter.

The release of chlorhexidine from antiseptic catheters was described by Modak *et al.*[5] According to this report, chlorhexidine is released into the surrounding tissue or blood, although the amount would be significantly below the toxic concentration.[6] However, the allergic reaction to drugs is usually dose-independent,[7] and so even a small amount of chlorhexidine released from the catheter could be the cause of anaphylactic shock.

A preoperative prick test would seem to the way of predicting the occurrence of anaphylactic shock. However, we failed to elicit a positive response to chlorhexidine in the first test, performed 1 week after the episode. Monneret-Vautrin *et al.*[8] estimated that the optimal time for the test was 6–12 weeks after the episode. The second test performed in this patient 6 weeks after the episode produced the positive response in accord with the observation of Monneret-Vaurin *et al.*

There are two questions to answer before recognizing this clinical manifestations as anaphylactic shock. First, this patient showed low IgE concentration. IgE in the patients with a type I allergic reaction usually shows high plasma concentration. Interestingly, Watkins described that 10–20% of the population exhibits low IgE concentrations.[9] These individuals appeared to be prone to hypersensitivity reactions.[10] We considered that this patient may have the low IgE trait. Second, why did the clinical signs subsided with the catheter still in place? Although the specific answer to the question is not postulated, the possible mechanisms could be explained by the exhaustion of circulating antibody or Immunoglobulin, by the exhaustion of preformed histamine in the mast cells or basophils, or by the reduction of the lymphocyte-mediated immune reactions.

In summary, anaphylactic shock induced by the chlorhexidine coating on surface of a central venous catheter may be a rare but significant complication during the perioperative period.

References

1. Slater JE: Latex allergy. J Allergy Clin Immunol 1994; 94:139–49

2. Okano M, Nomura M, Hata S, Okada N, Sato K, Kitano Y, Tashiro M, Yoshimoto Y, Hama R, Aoki: Anaphylactic symptoms due to chlorhexidine gluconate. Arch Dermatol 1989; 125:50-2

3. Ohtoshi T, Yamauchi N, Tadokoro K, Miyachi S, Suzuki S, Miyamoto T, Muranaka M: IgE antibody-mediated shock reaction caused by topical application of chlorhexidine. Clin Allergy 1986; 16:155-61

4. Cheung J, O'Leary JJ: Allergic reaction to chlorhexidine in an anaesthetised patient. Anaesth Intensive Care 1985; 13:429-30

5. Modak SM, Sampath L: Development and evaluation of a new polyurethane central venous antiseptic catheter: Reducing central venous catheter infections. Complications Surg 1992; 11:23-4

6. Gabler WL, Roberts D, Harold W: The effect of chlorhexidine on blood cells. J Periodontal Res 1987; 22:150-5

7. DeSwarte RD: Drug allergy—Problems and strategies. J Allergy Clin Immunol 1984; 74:209-24

8. Moneret-Vautrin DA, Laxenaire MC, Moeller R: Anaphylaxis due to succinylcholine. Immunoallergological study of thirteen cases. Clin Allergy 1981; 11:175-83

9. Watkins J: Investigation of allergic and hypersensitivity reactions to anaesthetic agents. Br J Anaesth 1987; 59:104-11

10. Lavery GG, Clarke RS, Watkins J: Histaminoid responses to atracurium, vecuronium and tubocurarine. Ann Fr Anesth Reanim 1985; 4:180-3

Anesthesiology
1997; 87:1244-7

Air Embolization in Seated, Sedated, Spontaneously Breathing, Neurosurgical Patients

J. Gilbert Stone, M.D., Arthur E. Schwartz, M.D.,† Mitchell F. Berman, M.D.,† Vincent S. Lenczewski, M.D.,‡ Shabina M. Ahmad, M.D.,‡ Jeffrey N. Bruce, M.D.,§ Robert R. Goodman, M.D., Ph.D.‖*

INNOVATIVE neurosurgical operations are performed with increasing frequency in semi-sitting or head-up positions and without general anesthesia or extensive monitoring.[1-5] To demonstrate the necessity for proper monitoring, we present two cases of venous air embolism that developed in seated, sedated, spontaneously breathing patients soon after a cranial burr hole was placed and the dura was opened.

Case 1

A 47-yr-old man with progressive, medication-resistant Parkinson's disease underwent a pallidotomy with local anesthesia and conscious sedation. He was otherwise in good health. Intravenous midazolam, 1 mg, and fentanyl, 50 μg were administered to apply a preoperative stereotactic headframe for computed tomography. In the operating room, unconsciousness was induced with a 30 $\mu g \cdot kg^{-1} \cdot min^{-1}$ infusion of propofol. The patient became unresponsive to verbal commands, although breathing remained spontaneous and regular. O_2 was delivered *via* nasal prongs at 4 l/min. Electrocardiograph (ECG), blood pressure, O_2 saturation, and end-expired PCO_2 (infrared) were monitored with the respiratory gas sampling port in the posterior nasopharynx, 8 cm from the nares.[6] Data were obtained every 10 s, with median values recorded every 50 s (fig. 1). The scalp was incised with the patient in a 45° semi-sitting position, and a 0.5-inch cranial burr hole was drilled. Bone wax was applied, and the dura cauterized before a microelectrode was inserted into the brain. Soon thereafter, the patient began to cough and hyperventilate. Chest auscultation revealed normal heart and breath sounds. End-expired PCO_2 and O_2 saturation rapidly decreased from 40 to 11 mmHg and from 98 to 88%, respectively. Concurrently, respiratory rate increased from 14 to 38 breaths/min, and heart rate increased from 65 to 91 beats/min. The surgeons were notified, and the operative field was irrigated. The propofol infusion was discontinued. Blood pressure increased slightly at first and then decreased to 80/45 mmHg over 10 min. As consciousness was regained, coughing subsided, and vague chest discomfort was reported. The ST segments were unchanged. Without additional therapy, vital signs gradually returned toward baseline, and surgery proceeded without further complication.

Case 2

A 65-yr-old woman with an expressive aphasia and progressive hemiparesis had a brain biopsy with local anesthesia and conscious sedation. She received midazolam, 1.5 mg, fentanyl, 125 μg, and nasal O_2. She was placed in a 45° semi-sitting position.

* Professor of Anesthesiology.

† Assistant Professor of Anesthesiology.

‡ Resident of Anesthesiology.

§ Associate Professor of Neurosurgery.

‖ Assistant Professor of Neurosurgery.

Received from the Departments of Anesthesiology and Neurosurgery, Columbia University, College of Physicians and Surgeons, New York, New York. Submitted for publication February 18, 1997. Accepted for publication June 12, 1997.

Address reprint requests to Dr. Stone: Department of Anesthesia, College of Physicians and Surgeons, Columbia University, 630 West 168th Street, New York, New York 10032. Address electronic mail to: JGS3@Columbia.edu

Key words: Anesthesia: conscious or semi-conscious sedation. Monitoring: end-expired PCO_2; capnometry; O_2 saturation; pulse oximetry. Neurosurgery: craniotomy. Position: sitting. Respiration: spontaneous. Venous air embolism.