Changes in Hemodynamics of Anaphylactic Reaction Induced by Transfused Blood during Operation

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(Key words: anaphylactic reaction, transfusion, operation)

Many kinds of drug, such as anesthetics, muscle relaxants, blood products and others, are reported to be causes to anaphylaxis or anaphylactoid reaction during induction of anesthesia and operation[1-5]. Incompatible transfusion obviously cause hemolytic adverse reaction, and in a patient with anti-HLA antibody, transfusion of whole blood and packed cell blood including leukocytes also induce a severe allergic reaction. However, in the patient without anti-erythrocyte or anti-HLA antibody, transfusion during operation is reported to cause cardiac arrest and severe hypotension with generalized urticaria[1,2]. We experienced hypotension with generalized urticaria in prone position during a vertebral operation, the cause of which is likely to be transfusion. We report changes in hemodynamics from 1 hour to 20 hr after an aggregated anaphylactic reaction induced transfusion.

Case Report

The patient was a 26-year-old female with right lumbosacral pain scheduled for a L4-S2 laminectomy under the diagnosis of lumber vertebral superior articular process syndrome. Past history or family history were negative; physical examination and preoperative laboratory evaluation were unremarkable. She had no history of drug allergy or tendency to atopy, and had no history of transfusion or pregnancy either. She was premedicated with 50 mg pethidine chloride and 0.5 mg atropine sulfate one hour prior to an operation. General anesthesia was induced intravenously with 7.5 mg droperidol, 45 mg pentazocine, 200 mg sodium thiopental and 40 mg succinylcholine. Anesthesia was maintained with 4 $l \cdot min^{-1}$ oxygen, 2 $l \cdot min^{-1}$ nitrous oxide and 0.8–2% enflurane as needed. The operative position was prone, and the operation started at 10:20. On about 5 hrs after the beginning of the operation, arterial blood pressure gradually decreased to 60/40, and pulse rate increased suddenly to 150, which was shown sinus tachycardia in ECG. No ST or T changes were not shown in ECG. No rales were not audible, and blood gas analysis, pH 7.396, P_{O_2} 218.3, P_{CO_2} 46.5 and BE 0.0, revealed no respiratory distress. There were no signs of bronchospasm, either.

Anesthetic record before and after the reaction is shown in figure 1. Firstly this fall of blood pressure was thought to be due to bleeding because of the bleeding volume being 900 ml at this time. One hundred and eighty ml whole blood was accordingly transfused, however, blood pressure did not increase, moreover decreased to 50 mmHg of systolic blood pressure. At this point

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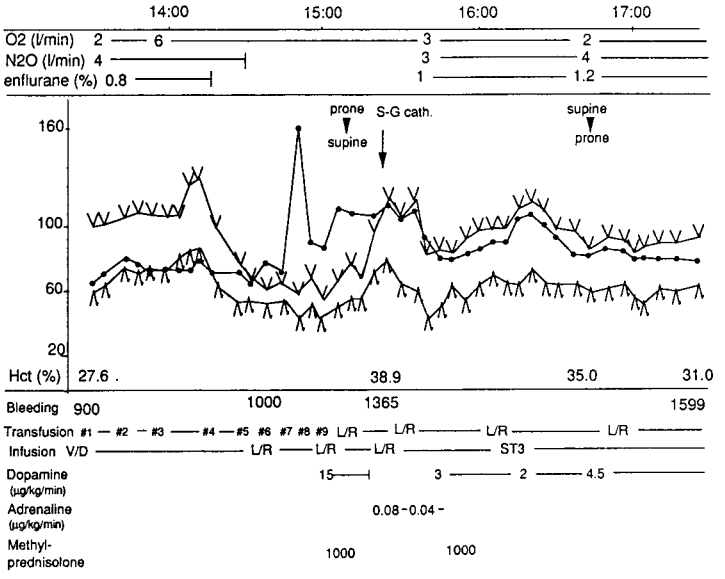

Fig. 1. Anesthetic record before and during anaphylactic reaction.
L/R: 500 ml of Lactec (Otuka, Tokyo); V/D: 500 ml of Veen D Inj. (Nikkennkagaku, Tokyo); ST3: 500 ml of Solita T3 (Shimizu, Tokyo) #1 to #9: Whole blood; S-G Cath.: insertion of Swan-Ganz catheter.

Table 1. Changes in hemodynamics and blood gas analysis after the reaction

time after the reaction	1 h[a]	5 h[b]	6 h[b]	9 h[b]	15 h[c]	20 h
Blood pressure (mmHg)	94/46	108/60	91/55	100/64	120/74	143/82
Heart rate (beats/min)	82	94	135	97	140	110
PWP (mmHg)	3.0	1.0	1.0	2.0	3.0	4.0
RAP (mmHg)	2.0	0.5	0.5	1.0	0.5	1.0
CI ($l \cdot min^{-1} \cdot m^{-2}$)	6.69	3.40	3.61	3.57	3.71	4.02
SV (ml)	119	53	39	54	39	54
SVRI (dyne sec$\cdot cm^{-5} \cdot m^{-2}$)	716	1772	1473	1677	1913	2012
PVRI (dyne sec$\cdot cm^{-5} \cdot m^{-2}$)	87.6	133	177	127	108	33
LVSWI (g $m \cdot m^{-2}$)	165.5	36.9	24.0	37.0	31.1	48.9
RVSWI (g $m \cdot m^{-2}$)	9.24	3.04	3.09	3.34	2.70	2.32
FI_{O_2}	0.5	0.35	0.35	0.35	0.35	0.4
PH	7.372	7.402	7.421	7.463	7.475	7.443
P_{O_2}	336.2	222.7	208.4	223.5	215.6	234.9
P_{CO_2}	32.2	33.6	30.4	32.4	32.7	34.9
BE	− 5.6	−3.1	− 3.8	0.1	1.0	0.2

a: adrenaline 0.04 $\mu g \cdot kg^{-1} \cdot min^{-1}$; b: dopamine 4.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$; c: dopamine 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$

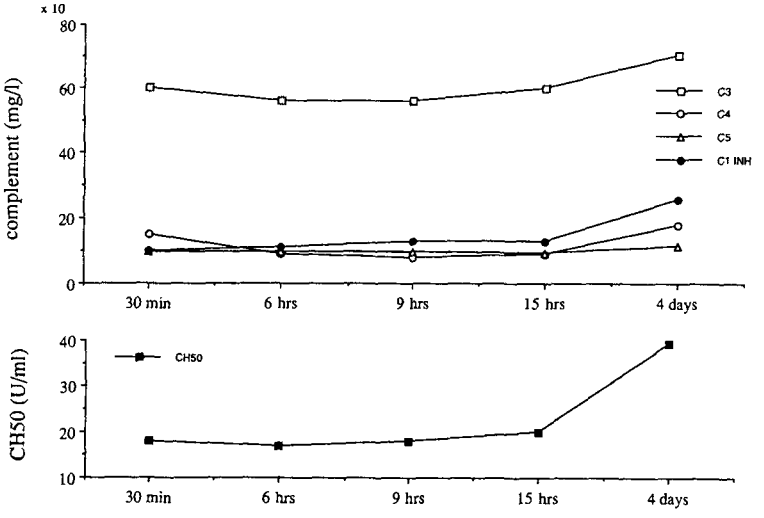

Fig. 2. Changes in complement factors at 30 min to 4 days after the reaction.
C3: complement 3 factor; C4: complement 4 factor; C5: complement 5 factor; C1 INH: complement 1 esterase inhibitor.

we noticed severe generalized flushing over her extremities just in time for uncovered surgical drapes with a suspicion of the adverse reaction of transfusion. Then we diagnosed anaphylactoid reaction to transfusion because she was administered only Lactec (Ringer's solution, Otuka, Tokyo) and whole blood in this period. Immediately after diagnosis of adverse reaction, the operation was temporary suspended, and 100% oxygen was administered, nitrous oxide and enflurane being off. One gram of methylprednisolone, 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine were administered. After the position be changed to supine, fused urticaria was detected to be spread over whole body and face. Adrenalin which is first-line drug for treatment of anaphylaxis was infused at a rate of 0.08 $mg \cdot kg^{-1} \cdot min^{-1}$ instead of dopamine. At the same time Lactec was administered rapidly to improve plasma loss due to generalized urticaria. Infused volume of fluid until blood pressure maintained were 2,500 ml. Swan-Ganz catheter was inserted to recognize accurate hemodynamics during the treatment of shock. Changes in hemodynamics and blood gas analyses between 1 hour to 20 hr after the episode of anaphylactic reaction is shown in table 1. One hour after the reaction, hemodynamic data, systemic vascular resistance being 716 dyne $sec \cdot cm^{-5} \cdot m^{-2}$ and cardiac index 6.69 $l \cdot min^{-1} \cdot m^{-2}$, revealed still peripheral vasodilatation, despite of the infusion of 0.04 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of adrenaline, and hyperdynamic state. Since loss of effective circulatory volume was verified, rapid infusion was continued. Infusion of adrenaline was changed to 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine when systolic blood pressure was maintained to over 100 mmHg. Two hours after the shock, operation was re-started in prone position because of stable hemodynamics. The rest of operation was uneventful without complications. After the shock 3500 ml of fluid were needed to maintain blood pressure. Total infused fluids, transfused bloods, bleeding volume during the operation were 5,885 ml, 2,320 ml, and 2,037 respectively. She was ventilated with intermittent positive pressure till 20 hr after the anaphylactic shock. Seven hours after the shock, generalized urticaria over her torso and extremities was disappeared, however, edema on her face still was admitted and continued on second day postoperatively.

Each blood at 30 min, 6 hr, 9 hr and 4 days after the anaphylactic reaction were saved to measure levels of histamine, serotonin, complement 3 (C3), complement 4 (C4), complement 5 (C5) and complement 1 esterase inhibitor (C1 INH).

Examination of anti-erythrocyte antibody

Screening of anti-erythroyte antibodies

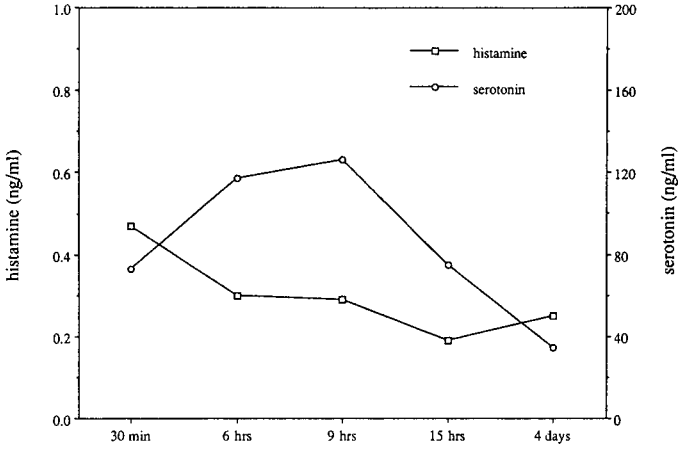

Fig. 3. Changes in levels of histamine and serotonin at 30 min to 4 days after the reaction.

and cross-matched tests in all transfused bloods were performed again with saved preoperative blood of the patient. The results were negative and showed all transfused bloods were compatible. Cross-matched test were also performed among all transfused bloods each other, and confirmed they were compatible.

Examination of anti-HLA antibody

Lymphocytotoxic test using random lymphocyte revealed no anti-HLA antibody in the patient. These results showed that in the term of anti-erythrocyte and anti-HLA antibody, all the transfused blood were compatible to the patient.

Changes in complements and chemical mediators

Changes in complements after the reaction are shown in figure 2. Decreases of C4, C1 INH and CH50 during 30 min to 15 hr after shock compared with those value in 4 days indicated an activation of classical pathway of complement system. No change of C5 compared with the value in 4 days implied that this activation of complement system completed at the level of C3. Serial changes in the concentration of histamine and serotonin are shown in figure 3. Level of histamine at 30 min after the reaction was higher than at other measured points, however was not enough concentration to induce systemic reaction in man. Levels of serotonin were compatible during the course.

Discussion

Various kinds of drug are reported to be causes of anaphylactic or anaphylactoid reactions during an operation[1-5]. When anaphylaxis or anaphylactoid reaction would occur during an operation, it should be difficult to detect early signs of the adverse reaction induced by drugs because of many factors being influencing hemodynamics, and urticarial eruptions may be also obscured by surgical drapes covered over whole body except surgical lesion. In this case we diagnosed that at first the decrease of blood pressure was due to bleeding. However, recognition of generalized urticaria when uncovered the surgical drapes and the finding of no improvement of blood pressure despite of transfusion accordingly made the correct diagnosis of anaphylactoid reaction.

When the hypotension occurred in this case, no drug except whole blood were administered. Then, we had thought that the cause of this reaction had been anti-erythrocyte or anti-HLA antibody, and investigated these antibodies after the operation. However, the results denied these antibodies being cause of this reaction. This reaction was thought to be related with immunological factor because changes in complement indicated activation of classical pathway. Level of histamine after the anaphylactic reaction is reported to return to normal level within 20 min[6]. Sudden tachycardia coincided with hypotension is also reported to be due to

elevated level of histamine immediately after a reaction[7]. In this case, level of histamine at 30 min after the reaction was not enough high to induce systemic reaction, nevertheless, level of histamine at reaction occurred was thought to be high compared with that at 30 min. This was supported with sudden tachycardia associated with hypotension. Since the activation of complement and the elevation of histamine concentration, therefore, this reaction is thought to be due to aggregated anaphylaxis[7,8]. When any kind of blood, even cross-matched blood, would be administered during an operation, we have to recognize and redirect to the omnipresence of the possibility of occurrence of anaphylaxis.

Hemodynamic change in systemic anaphylactic reaction is poorly understood and controversial. Our data showed that hypotension was primarily caused by peripheral vasodilatation and acute reduction in intravascular fluid volume, which is in accordance with the observation made by Fisher[9]. Enjeti et al.[10] also reported myocardial dysfunction in anaphylactic shock is not major initiating mechanism. Increased pulmonary vascular resistance (PVR) is reported only in anaphylactic shock with a bronchospasm[7]. PVR in this case was not increased on account of no involvement of lung, either.

Early recognition and immediate initiation of treatment for systemic reaction may prevent progression of the reaction[11]. However, during operation it is not easy to detect urticaria because of covering whole body with surgical drapes. First- line drug against anaphylaxis is recommended to be adrenaline, and rapid enormous infusion of fluid be administered to restore blood pressure[1,2,5]. Swan-Ganz catheter is crucial to recognize accurate hemodynamic condition and to proper treatment for anaphylaxis.

In summary, since during an operation we can not take complains of a patient about symptoms of anaphylaxis and first sign of reaction should appear only hypotension, generalized urticaria is important sign to diagnose allergic reaction. Our data showed that hypotension occurred in anaphylactic reaction was primarily caused by peripheral vasodilatation and acute reduction in intravascular fluid volume.

(Received Sep. 10, 1990, accepted for publication Nov. 15, 1990)

References

1. Konishi A, Kotaki M, Fujii M, Suzuki M, Okuaki A: Cases of diffuse urticaria and severe hypotension due to blood transfusion during operation. Hiroshima J Anesthesia 17:99–103, 1981
2. Ogino R, Matsuki H, Oyama T: Cardiac arrest secondary to anaphylactic shock caused by blood transfusion. Masui (Jpn J Anesthesiol) 33:302–308, 1984
3. Sale SR, Greenberger PA, Patterson R: Idiopathic anaphylactoid reactions. A clinical summary. JAMA 246:2336–2339, 1981
4. Stoeling RK: Allergic reactions during anesthesia. Anesth Analg 62:341–356, 1983
5. Moudgil GC: Anaesthesia and allergic drug reactions. Can Anaesth Soc J 33: 399–415, 1986
6. Moss J, Fahmy NR, Sunder N, Beaven MA: Hormonal and hemodynamic profile of an anaphylactic reaction in man. Circulation 63:210–213, 1981
7. Pavek K, Wegmann A, Nordström L, Schwander D: Cardiovascular and respiratory mechanisms in anaphylactic and anaphylactoid shock reactions. Klin Wochenschr 60:941–947, 1982
8. Watkins J: Investigation of allergic and hypersensitivity reactions to anaesthetic agents. Br J Anaesth 59:104–111, 1987
9. Fisher MM: Clinical observation on the pathophysiology and treatment of anaphylactic cardiovascular collapse. Anaesth Intens Care 14:17–21, 1986
10. Enjeti S, Bleecker ER, Smith PL, Rabson J, Permutt S, Traystman RJ: Hemodynamic mechanism in anaphylaxis. Circulatory Shock 11:297–309, 1983
11. Salo M, Clarke RSJ: Practical management of the immediate reaction, Guide to immediate anaesthetic reactions. Edited by Watkins J, Levy CJ. London, Butterworths, 1988, pp. 41–57
12. Levy J: Anaphylactic reactions in anesthesia and intensive care, London, Butterworth, 1986, p. 129