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Anesthetic management of a patient with β-thalassemia intermedia undergoing splenectomy: a case report

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Abstract
A 37-year-old man with β-thalassemia intermedia (βTI), a rare disease caused by partial or complete deficiency of β-globin chain synthesis, fell into a hemolytic crisis. Severe anemia persisted despite frequent transfusions. Therefore, he was scheduled for splenectomy to alleviate the anemia. The preoperative laboratory data showed marked anemia and liver dysfunction. Echocardiography revealed hyperkinetic left ventricular motion and increased cardiac index (CI), indicating a compensatory hyperdynamic circulation induced by persistent, severe anemia. Our strategy during general anesthesia was to keep the hyperkinetic cardiovascular system steady. Hence, the hemodynamic parameters including the CI were measured using a Swan-Ganz catheter, and other physiological parameters were monitored perioperatively. Anesthesia was maintained with balanced anesthesia: isoflurane at low concentrations and fentanyl to avoid cardiovascular depression. Throughout the operation, vital signs were kept stable and the lactate/pyruvate ratio was unchanged, indicating that anaerobic metabolism did not increase. We report successful anesthetic management with attention to hemodynamic changes in a patient with βTI.

Key words Thalassemia intermedia · Severe anemia · Cardiovascular system · General anesthesia

Introduction

A patient with β-thalassemia intermedia (βTI), a rare disease caused by partial or complete deficiency of β-globin chain synthesis [1], suffered a hemolytic crisis. Severe anemia persisted despite frequent transfusions of washed red blood cells and prednisolone administration, so he was scheduled for splenectomy to restore the hemoglobin (Hb) concentration to a steady state.

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Case report

A 37-year-old man (height 158 cm, weight 41 kg) with βTI of American Society of Anesthesiologists (ASA) physical status III was scheduled for splenectomy to alleviate his anemia. Mild anemia had been present since childhood, and he was diagnosed with βTI at 30 years of age, although no treatment was required until age 36 because of no significant symptoms except mild anemia. It was not clear if his family members were carriers of a thalassemic condition because they had not been diagnosed in detail at medical facilities. At 36 years of age, he was admitted to the hospital because of edema of the lower extremities and recurrent attacks of fever. Severe anemia (Hb 3.5 g·dl^{-1}, Hct 11.4%) with an increased fraction of fetal hemoglobin (Hb F) was detected. Transfusions of washed red blood cells (RBCs) were frequently performed and prednisolone (40 mg/day) was started. This treatment for 2 months improved the anemic condition (Hb 6.4 g·dl^{-1}, Hct 20.4%) only slightly. He was thus scheduled for splenectomy to restore the Hb concentration to a steady state.

The preoperative laboratory data showed marked anemia (RBC 235 × 10^4·μl^{-1}, Hb 5.8 g·dl^{-1}, Hct 19.7%) and liver dysfunction: aspartate aminotransferase 64 IU·l^{-1}, alanine aminotransferase 118 IU·l^{-1}, γ-glutamyl transpeptidase 113 IU·l^{-1}, total bilirubin 3.4 mg·dl^{-1}, direct bilirubin 2.2 mg·dl^{-1}, albumin 3.2 g·dl^{-1}, cholinesterase 141 IU·l^{-1}, total cholesterol 114 mg·dl^{-1}. His platelet counts (21.2 × 10^4·μl^{-1}) were preserved, and the coagulation system was normal: prothrombin time 11.6 s, activated partial thromboplastin time 32.1 s, antithrombin III (AT-III) 76%. Catecholamines in the blood and urine and the lactate/pyruvate ratio were within the normal range. The electrocardiogram (ECG) showed an elevated P wave and sinus tachycardia at 103 beats/min (bpm). Echocardiography revealed mild mitral regurgitation, left atrial enlargement, increased left ventricular (LV) end-diastolic diameter, hyper-

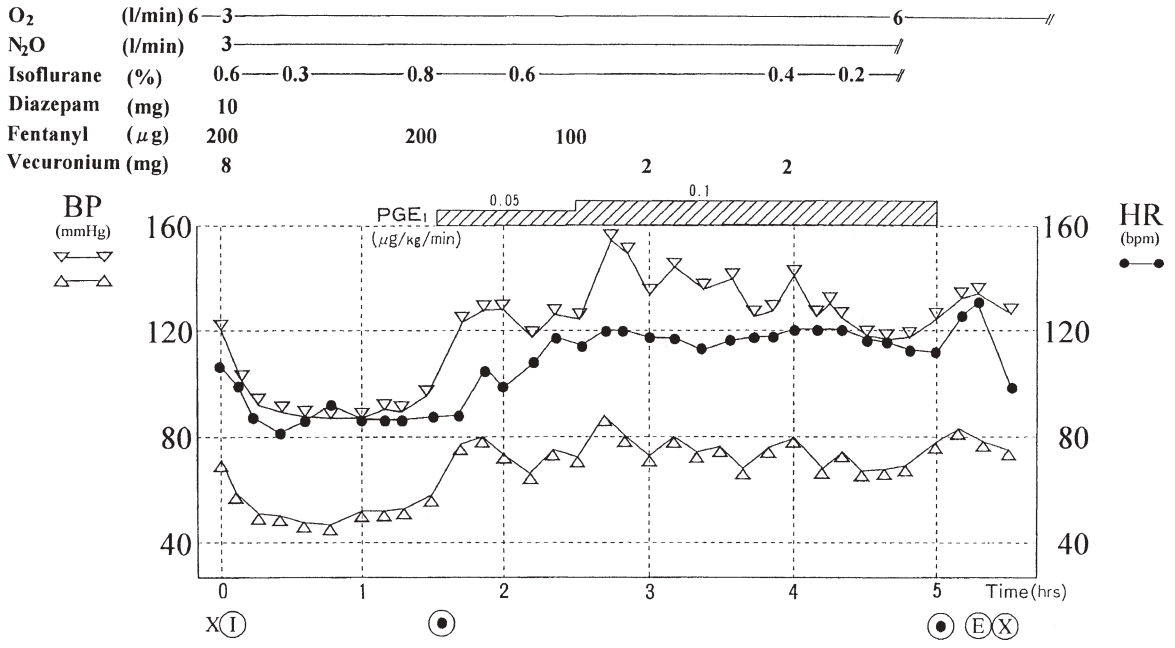

Fig. 1. Time course of anesthesia with isoflurane and fentanyl for a β-thalassemia intermedia patient. *Open triangles* show the blood pressure (*BP*). *Upper and lower triangles* show the systolic and diastolic BP, respectively. *Filled circles* show the heart rate (*HR*). *Open circles with a center dot* indicate the beginning and end of surgery. *I*, tracheal intubation; *E*, extubation. The *striped bar* depicts the onset and the flow ($\mu g \cdot kg^{-1} \cdot min^{-1}$) of the prostaglandin E_1 (PGE_1) infusion

kinetic LV motion, and increased cardiac index (CI $8.4 l \cdot min^{-1} \cdot m^{-2}$) and cardiac output (CO $11.7 l \cdot min^{-1}$), although the LV ejection fraction (0.74) was within the normal range. Chest radiographs demonstrated slight cardiomegaly (cardiothoracic ratio 0.58) without obvious pulmonary venous congestion.

Figure 1 shows the anesthesia time course. Scopolamine 0.25 mg and pethidine 17.5 mg were given intramuscularly 30 min before induction of anesthesia. On arrival at the operating room the patient's blood pressure was 120/65 mmHg, and his heart rate was regular at 80 bpm. Anesthesia was induced intravenously with diazepam 10 mg and fentanyl 200 μg. Intravenous vecuronium 8 mg facilitated tracheal intubation. No facial bone deformity was observed in the patient, and tracheal intubation was performed uneventfully. Anesthesia maintenance consisted of isoflurane (0.2%–0.8%), nitrous oxide ($3 l \cdot min^{-1}$), oxygen ($3 l \cdot min^{-1}$), and intermittent intravenous doses of fentanyl (100–200 μg) and vecuronium. Prostaglandin E_1 (PGE_1) was administered continuously ($0.05–0.10 \mu g \cdot kg^{-1} \cdot min^{-1}$) to reduce the afterload.

Intraoperative monitoring included ECG, direct arterial pressure, arterial hemoglobin oxygen saturation (Sp_{O_2}), end-tidal carbon dioxide tension (ET_{CO_2}), urine output, CO, CI, and mixed venous blood oxygen saturation (Sv_{O_2}) with a fiberoptic Swan-Ganz catheter. In addition, the lactate/pyruvate ratio was calculated as an index of anaerobic metabolism. Methylprednisolone 1000 mg, urinastatin 300 000 U for maintaining the microcirculation, human haptoglobin 4000 U for preventing renal dysfunction due to hemolysis, and human freeze-dried concentrated AT-III 4000 U to reduce the transient thrombotic risk were given intraoperatively.

Throughout the operation, vital signs and physiological parameters were stable (blood pressure 90–150/50–90 mmHg, heart rate 90–120 bpm, Sp_{O_2} 99%–100%, ET_{CO_2} 34–37 mmHg, and Sv_{O_2} 80%–92%) as shown in Fig. 1 and Table 1. The operation lasted 3 h 30 min. After spontaneous ventilation was recovered, neuromuscular blockade was reversed by injecting neostigmine 2 mg and atropine 1 mg intravenously. Patient was allowed to regain consciousness, and the trachea was extubated after the return of protective reflexes. A total of 1750 ml of fluid was administered throughout the anesthesia. Washed red blood cells 600 ml and human plasma protein fraction 500 ml were transfused. The estimated total blood loss and urinary output were 320 ml and 590 ml, respectively. No untoward events related to anesthesia or surgery occurred.

His postoperative course was generally uncomplicated. The Hb and Hct levels rose to $7.2 g \cdot dl^{-1}$ and 22.4%, respectively. The CI decreased ($7.0 l \cdot min^{-1} \cdot mm^{-2}$) compared to the preoperative value. Maintenance therapy including prednisolone (5 mg/

Table 1. Perioperative and postoperative physiological parameters of a βTI patient

Parameter	After induction of anesthesia		Immediately after the operation	Postoperative day 1
	1 h	3 h		
Hb ($g \cdot dl^{-1}$)	6.6 ↓		8.7 ↓	9.5 ↓
Hct (%)	21.3 ↓		29.5 ↓	31.4 ↓
Pa_{O_2} (mmHg) (FI_{O_2})	184.9 (0.5)	200.8 (0.5)	104.1 (0.25)	
Pa_{CO_2} (mmHg)	36.3	32.2	36.6	
BE ($mEq \cdot l^{-1}$)	–1.4	–3.8	–2.8	
Glu ($mg \cdot dl^{-1}$)	172 ↑	242 ↑		97
L/P ratio	12.8	14.1		
PT (s)	12.3	11.9	12.5	
APTT (s)	40.3	31.7	31.0	
Fib ($mg \cdot dl^{-1}$)	173	154	154	
FDP ($\mu g \cdot ml^{-1}$)	<2.6	<2.6	4.0	
AT-III (%)	89	79	117	
CO ($l \cdot min^{-1}$)	10.3 ↑	11.5 ↑	10.0 ↑	8.2 ↑
CI ($l \cdot min^{-1} \cdot m^{-2}$)	7.5 ↑	8.3 ↑	7.3 ↑	6.0 ↑
Sv_{O_2} (%)	80	85	84	77
Epinephrine ($ng \cdot ml^{-1}$)	0.02	0.06		
Norepinephrine ($ng \cdot ml^{-1}$)	0.16	0.99 ↑		

βTI, β-thalassemia intermedia; Hb, hemoglobin; Hct, hematocrit; Pa_{O_2}, oxygen partial pressure; FI_{O_2}, fractional concentration of oxygen in inspired gas; Pa_{CO_2}, carbon dioxide partial pressure; BE, base excess; Glu, serum glucose; L/P, lactate/pyruvate; Fib, fibrinogen; PT, prothrombin time; APTT, activated partial thromboplastin time; FDP, fibrin degradation product; AT-III, antithrombin III; CO, cardiac output; CI, cardiac index; Sv_{O_2}, mixed venous blood oxygen saturation. *Arrows* indicate that the value is beyond the normal limits

day) and deferoxamine mesilate was commenced. He stayed in the hospital for approximately 3 weeks after splenectomy.

Discussion

Thalassemia is a congenital hemolytic disorder caused by partial or complete deficiency of globin chain synthesis [1]. βTI is a clinical term used to describe patients who have mild thalassemia without regular transfusion requirements except on certain occasions, such as the presence of intercurrent infections, hypersplenism, or other illnesses. Patients with βTI have diverse symptoms, and some have severe anemia [2]. In this patient with βTI, severe anemia persisted despite frequent transfusion and prednisolone administration. Therefore, he was scheduled for splenectomy to restore the Hb concentration to a steady state. It should be noted that there are possible difficulties with intubation due to facial bone deformity, especially in thalassemia major patients [3] and hemodynamic changes in response to chronic severe anemia. There have been reports [3, 4] describing management of the difficult airway caused by facial bone deformity in thalassemia patients. However, few reports have presented perioperative hemodynamic parameters in detail to our knowledge. In this case report, we described anesthetic management with attention to hemodynamic changes in a patient with βTI.

Thalassemia syndromes often are complicated by cardiac involvement related to iron overload in tissues as a result of hemolysis and multiple transfusions [5]. In addition, chronic anemia results in a high cardiac output state. The diminished capacity of the blood to carry oxygen to peripheral tissues was overcome by increasing cardiac output [6]. Coagulopathy due to hemodilution [7] induced by severe anemia or the hypercoagulable state [8] may also exist. Because of these possibilities, the preoperative physiological condition of the patient was evaluated carefully.

In the present case, not only severe anemia but liver dysfunction, which might be caused by multitransfusional iron overload [9], were indicated preoperatively. On the other hand, the platelet counts and coagulation system were normal. The existence of a chronic hypercoagulable state in thalassemia, particularly in splenectomized patients with βTI, has been indicated [8]. Accordingly, AT-III was administered to prevent the hypercoagulable state, which may be evoked by splenectomy [10]. The possibilities of additional anticoagulant or antiplatelet therapy to the hypercoagulable state during general anesthesia had to be considered. Therefore, epidural anesthesia was not performed in this case.

Echocardiography showed increased CI, left atrial enlargement, increased LV end-diastolic diameter, and hyperkinetic LV motion, although the LV ejection fraction was preserved within the normal range, suggesting a hyperkinetic circulation due to the chronic severe ane-

mia. In other words, increased cardiac output in the βTI patient with severe anemia probably was a compensatory mechanism to maintain oxygen delivery to peripheral tissues. Therefore, our strategy during general anesthesia for the βTI patient was to keep the cardiovascular system hyperdynamic, because cardiovascular depression can easily cause hypoxia in peripheral tissues. Hence, the CI and cardiac output were measured using the Swan-Ganz catheter.

Anesthesia was maintained with balanced anesthesia using isoflurane at a low concentration and fentanyl to avoid cardiovascular depression, because with severe anemia tolerance to volatile anesthetic-induced cardiovascular depression might be limited [11–13]. In other words, balanced anesthesia with a volatile anesthetic at low concentrations and fentanyl, which is known to decrease the minimum alveolar concentration of volatile anesthetics [14], may help stabilize hemodynamic parameters by minimizing noxious sympathetic responses during surgery [15] and by avoiding a decrease in the cardiac output induced by a high concentration of volatile anesthetic. In addition, PGE_1 was continuously administered to reduce cardiac work by decreasing vascular resistance. Proper red blood cell transfusions to improve inadequate oxygen delivery may also be necessary. Therefore, we intended to maintain not only compensatory increases in cardiac output but also the hemoglobin concentration at more than $6.6\,g \cdot dl^{-1}$, which was the initial concentration after induction of general anesthesia, although the lower limit of human tolerance to anemia has not been established [16]. Throughout the operation, vital signs were kept stable, and the lactate/pyruvate ratio was unchanged, indicating that anaerobic metabolism did not increase, as shown in Table 1. No untoward events related to the anesthesia or the surgery occurred.

Plasma catecholamine levels in our patient before surgery were within normal limits. These results were consistent with the report showing that both epinephrine and norepinephrine in patients with chronic anemia are within the normal range, suggesting that the compensatory augmentation of cardiac output due to chronic anemia may be mediated by a noncatecholamine factor that increases contractility [17].

Theoretically, abnormal hemoglobin and severe anemia are expected to affect the accuracy of oximeter monitors [18]. However, the influence of Hb F with high oxygen affinity on pulse oximetry is insignificant: in the range of 75%–100% oxygen saturation [19]. In addition, when the hematocrit is > 15%, bias values of the continuous saturation monitoring are small [20]. Therefore, the Sp_{O_2} and Sv_{O_2} values were probably of acceptable accuracy in this case, although the results may be viewed with caution.

Conclusions

Compensatory hemodynamic changes should be evaluated with caution during the perioperative management of patients with βTI, even if they do not have clinical signs of cardiovascular involvement. Minimizing cardiovascular suppression caused by anesthetics seems to be important.

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