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CLINICAL REPORT

Anesthesia protocols for early vitrectomy in former preterm infants diagnosed with aggressive posterior retinopathy of prematurity

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Abstract Aggressive posterior retinopathy of prematurity (ROP) can, if left untreated, rapidly progress to total retinal detachment within 1–2 weeks. Early surgical intervention with vitrectomy has been attempted to treat and prevent further retinal detachment. We investigated the anesthetic management of 29 infants with aggressive posterior ROP undergoing early vitrectomy. Postmenstrual age at surgery ranged from 35 to 47 weeks (median 41). Weight ranged from 1408 to 3478 g (median 1875). All infants underwent general anesthesia with fentanyl and sevoflurane. Mean surgical and anesthetic times were 88.6 and 143.6 min, respectively. In two patients, vitrectomy was postponed for one week due to enteric perforation in one patient and meningitis in the other, because the anticipated perioperative risk was deemed high. There were no intraoperative complications, except in one patient who developed pulmonary edema following upper airway obstruction. All patients survived to be discharged from NICU or transferred to the referring hospital. In all cases, complete or partial retinal reattachment was successfully achieved. Early vitrectomy for aggressive posterior ROP may be effective despite associated perioperative risks. As this condition progresses rapidly, prompt preoperative organization, including anesthetic planning, is important and useful. Anesthesiologists can play an important role in the perioperative management of such high-risk infants.

Keywords Aggressive posterior ROP · Early vitrectomy · Perioperative management

Introduction

Recently, the number of patients diagnosed with severe retinopathy of prematurity (ROP) has increased concurrently with the improved survival of extremely low birth weight infants. According to the International Classification of ROP (Table 1), "aggressive posterior ROP" can, if left untreated, rapidly progress to total retinal detachment within 1–2 weeks [1]. One particular characteristic of aggressive posterior ROP is that it may progress to Stage 5 without exhibiting the classical course from Stage 1 to Stage 3. Early intervention, with photocoagulation, is necessary but often fails to stop the progression of ROP to Stage 5. As a consequence, early surgical intervention with vitrectomy has been attempted in order to treat and prevent further retinal detachment associated with such severe forms of ROP [2]. However, early surgical intervention in premature infants carries perioperative risks related to extraocular pathology. The following case report was approved by the Institutional Clinical Research Ethics Board.

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Table 1 The international classification of retinopathy of prematurity revisited [1]

Stage 1	Demarcation line
Stage 2	Ridge
Stage 3	Extraretinal fibrovascular proliferation
	Mild
	Moderate
	Severe
Stage 4	Partial retinal detachment
4A	Extrafoveal
4B	Foveal
Stage 5	Total retinal detachment
Severity	Plus disease: sufficient vascular dilatation and tortuosity in at least 2 quadrants of the eye
	Pre-plus disease: insufficient vascular dilatation, and tortuosity less than in plus disease
Aggressive posterior ROP	

Table 2 Gestational or postmenstrual age and weight at birth and at surgery, expressed as median values and ranges

	Median
At birth	
Gestational age	24 weeks (22–30)
Weight	712 g (466–1676)
At surgery	
Postmenstrual age	41 weeks (35–47)
Weight	1857 g (1408–3478)

Cases

We retrospectively reviewed clinical charts and the perioperative course of infants diagnosed with aggressive posterior ROP who underwent early vitrectomy between January 2005 and February 2007 at the National Center for Child Health and Development, Tokyo. We investigated gestational age and weight at both birth and surgery, preoperative respiratory status, surgical and anesthetic times, dose of fentanyl during the surgery, and perioperative complications.

We investigated the anesthetic management of 29 infants. Gestational age and weight at both birth and surgery are given in Table 2. The minimum postmenstrual age and weight at surgery were 35 weeks and 1408 g, respectively. Twenty-five infants were transferred to our center from other medical centers. Chronic lung disease was diagnosed in 21 infants. None of our patients were intubated preoperatively. All of our infants underwent general anesthesia with fentanyl and sevoflurane; the mean dose of fentanyl was 4.6 mcg/kg. The mean surgical and anesthetic times were 88.6 and 143.6 min, respectively.

In two cases, the planned vitrectomy was postponed for one week due to GI tract perforation in one infant and meningitis in the other, because the anticipated perioperative risk was deemed high. Peritoneal drainage was successfully performed preoperatively in the one infant suffering from enteric perforation. Six days after peritoneal drainage, hemodynamic status and laboratory findings were stable. Antibiotic treatment was commenced in the patient suffering from meningitis. Laboratory findings and the general condition of this patient improved within a week of the start of antibiotic treatment beginning. Following treatment, both patients were scheduled for surgery.

After these experiences of two infants who needed additional preoperative treatment, we developed a preoperative checklist (Fig. 1) and an anesthesia protocol for aggressive ROP (Fig. 2) in order to promote effective and safe preoperative management. The preoperative checklist includes maternal information during the pregnancy, perinatal course of the patient, and present clinical status. The roles of the anesthesiologist, the neonatologist and the ophthalmologist are outlined during the perioperative timeline in the anesthesia protocol. We first introduced this system for the fifteenth patient in the case series, and continued to use it for all subsequent patients. After this system had been introduced, none of the patients needed additional preoperative treatment after transportation to our center.

Thirteen patients were extubated in the operating room or in the NICU on the day of surgery, and 10 were extubated the following day. The six remaining patients required postoperative ventilatory support for more than 2 days in the NICU. There was one intraoperative complication; the patient developed an upper airway obstruction and pulmonary edema associated with post-extubation laryngeal edema. This particular infant was born after 23 weeks of gestation and weighed 754 g at birth. On the day of surgery, this patient's weight was 2460 g and was aged 40 weeks postconception. During surgery, the drip chamber was filled with 100 ml of Ringer's acetate at the start of anesthesia. Unfortunately, 80 ml of this solution was accidentally injected during the induction of anesthesia. As a result, the patient's volume status was a plus balance of 15 ml/kg per hour at the end of surgery. After extubation, the patient presented with desaturation because of negative pressure pulmonary edema accompanied with hypervolume status and upper airway obstruction. He was reintubated and required a few more days of ventilatory support.

There was no severe apnea resulting in desaturation or bradycardia due to apnea during the postoperative course. No patients needed reintubation or experienced postoperative complications. All patients survived to be discharged from the NICU or transferred back to the referring center.

Fig. 1 Information for the transportation and admission of patients with ROP

Medical center :

Neonatologist : Ophthalmologist :

Tel : Fax :

Name of patient : Sex : Male ,Female

Phone number of patient :

Date of birth :

Gestational age at birth : Apgar Score : /1min、 / 5 min

Postmenstrual age at the day providing this information :

Body weight at birth : g Body weight at present time : g

Type of blood : A B O AB 、Rh（+、－）

Please give a circle all that apply on the below

１. Maternal information about infection

Syphilis : Wa（+、－）、TPHA（+、－）

Hepatitis B : HbsAg（+、－）、HbeAg（+、－）

Hepatitis C : HCVAb（+、－）

HIV :（+、－）

HTLV: :（+、－）

２. Family information

fever、 diarrhea、 rash、 nasal discharge、 tuberculosis、 influenza

３. Patient information（current status）

・chromosome abnormality、 other abnormality

・ Nerve system： Intraventricular hemorrhage（Ⅰ、Ⅱ、Ⅲ、Ⅳ）、 Ventricular dilatation、 Intracranial hemorrhage、 VP shunt、 Periventricular leukomalacia（１、２、３）、 Central neurological abnormality、 Convulsion

・Facial surface： Facial anomaly、 Cleft lip and plate

・Respiratory system： Abnormality of respiratory tract、 CLD、 Apnea（use of thoeophyline）

In all cases, complete or partial retinal reattachment was successfully achieved when assessed at the follow-up examination at six months postsurgery.

Discussion

The most important risk factor for developing ROP is prematurity [3]. Because the chance of an extremely low birth weight infant surviving has increased in recent years, the incidence of patients with severe types of ROP has also increased. These patients often experience blindness during the progression of ROP, which ultimately leads to retinal detachment. When ROP progresses to Stage 3, retinal photocoagulation or cryotherapy is performed as an initial treatment. Compared to cryotherapy, the clinical outcome in cases where the eyes have been treated with photocoagulation include better visual acuity and fewer complications following the procedure [4, 5]. In the case of Stage 5, buckling or vitrectomy may be used to treat retinal detachment, but this often fails to provide useful vision [6].

Fig. 1 continued

◇Mechanical ventilation support

◆HFO： days (going on or not)

◆IMV： days (going on or not)

◆Total trial times of extubation（including accidental extubation）： times

◆The date of current extubation：

◆If the patient depends on mechanical ventilation support,

・Size of ETT：

・Setting of mechanical ventilation

◇NCPAP ： days (going on or not)

◇Oxygen administration： days (going on or not)

・Cardiovascular system： PDA、 CHD (excluding PDA)、 PH、 CHF (controlled with medication)

◇Name and dose of medication

・Gastrointestinal system： Gastric rupture、 NEC、 Artificial anus

◇Dysfunction of the liver：T-Bil mg/dl、 D-Bil mg/dl
AST IU/l、 ALT IU/l、LDH IU/l

・Nutrition management： Tubal、 Oral、 Parenteral

◇Type of milk：

◇Dose and times of milk： ml× times

◇Type and insertion site of catheter：

◇Type and infusion rate of Parenteral nutrition：

・Renal and urological system： Urinary tract anomaly、 Urinary tract infection

◇Renal dysfunction：BUN mg/dl、 Cre mg/dl

◇Electrolyte abnormality：Na mEq/l、 K mEq/l、 Cl mEq/l
Ca 、 P mg/dl

・Hematological status： hemorrhagic tendency

◇Anemia：RBC 10^3/mm^3、 Hb g/dl、 Hct %、 Fe μg/dl

◇Thrombocytopenia：platelet count 10^4/mm^3

・Infection：Positive culture of MRSA、 Bacterial infection、 Fungal infection、 Viral infection、 Chlamydia infection

・Endocrine system

◇Rickets：ALP IU/l

◇Hypoglycemia：BS mg/dl

◇Hypothyroidism：TSH μU/ml、 T3 ng/dl、 T4 μg/dl
fT3 pg/ml、 fT4 ng/dl

・Other complication

・Current internal remedy

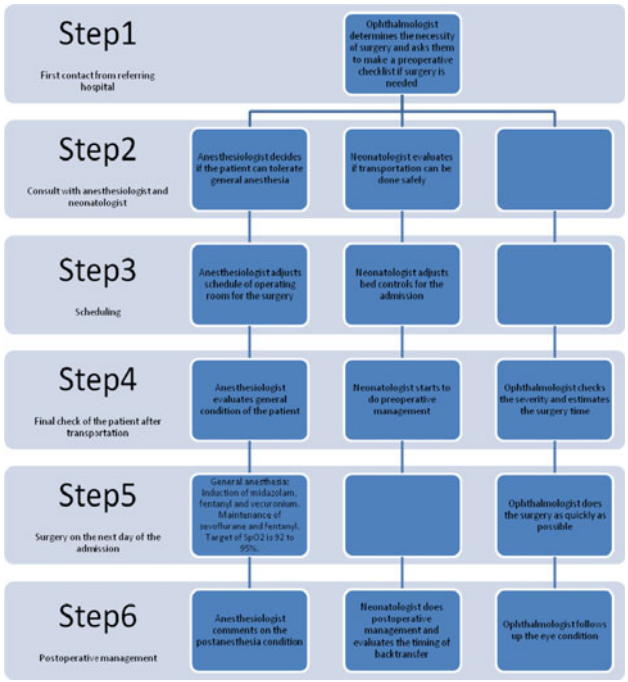

Fig. 2 Flowchart for our aggressive ROP protocol

Aggressive posterior ROP exhibits rapid progression to total retinal detachment within 1–2 weeks if left untreated [1]. Thus, early intervention with photocoagulation and vitrectomy has been attempted in order to treat and prevent further retinal detachment associated with such severe forms of ROP [2]. Azuma et al. [2] reported that their study indicated great benefit from early surgery for the treatment of aggressive posterior ROP, in comparison to poor visual outcomes following vitreous surgery for Stage 5 ROP, despite surgical and anesthetic intervention on very small infants. Anesthesiologists must perform a comprehensive evaluation to determine whether the timing of surgery is adequate, as aggressive posterior ROP requires urgent surgery, and such premature infants often exhibit multisystem disease.

As almost all of our patients were transferred from another hospital, assessment prior to transport was very important as a primary means of assessing perioperative risk. We experienced two infants who had already been transported to our center but required treatment prior to surgery. As a result, surgery was postponed and these particular infants' complications required swift treatment. Neither of these infants missed the chance and timing of early vitrectomy, despite the loss of several days that were required to treat their complications. The patients were then rescheduled for surgery. We then began to send a checklist facilitating a systematic review of any patient with aggressive posterior ROP to the referring hospital, and requested updated status reports (Fig. 1). It is important to gather as much information and preoperative assistance as possible in the hope of reducing the incidence of complications. Based on this checklist, anesthesiologists and neonatologists can determine whether the patient can tolerate transport and anesthesia. In fact, if the anesthesiologist does not permit the patient to receive general anesthesia, the neonatologist cannot decide to transport the patient by themselves. It is both important and necessary that anesthesiologists, neonatologists and ophthalmologists work together for the safe perioperative management of patients (Fig. 2). After the introduction of the checklist, there was no case for which the surgery was postponed after transportation and admission to our hospital.

All patients go back to the NICU after the surgery, and monitors and mechanical ventilator support are always available. Thus, we think that opiate should not be limited for the purpose of extubation in the operating room. Besides, it was revealed that about half of the patients ware extubated in the operating room and that these patients had no postoperative respiratory complications in this study. Anesthesiologists can nonforcibly extubate such premature infants by concurrently providing sufficient analgesia. In the case of intubated patients after the surgery, it is important that anesthesiologists inform neonatologists about mechanical ventilator support, based on each patient's respiratory status during the surgery.

Anesthesia for premature infants is often difficult because of coexisting multisystem disease, as investigated via the checklist (Fig. 1), and because multiple organ function is only at a developmental stage. Emergence from anesthesia can be as dangerous as inducing anesthesia. Premature infants may experience cardiopulmonary compromise during the perioperative period, of which apnea, bradycardia, and cyanosis are the most common signs [7]. Cote et al. reported that the incidence of apnea was inversely related to both gestational age and postmenstrual age [8]. Infants who are 55 weeks in postmenstrual age or younger are at the greatest risk. Therefore, all such patients should probably be monitored for 24 h following surgery in order to detect apnea. In the present study, we monitored all patients undergoing the administration of oxygen or mechanical ventilation, and found that none of them experienced severe apnea postoperatively.

For premature infants, all fluid should be delivered through an infusion pump when possible. Maintenance fluid is 4 ml/kg per hour for the first 10 kg of body weight. We usually ensure that the drip chamber never contains more fluid than is safe to give in 1 h, in case the i.v. infusion accidentally remains wide open. During this study period, we had a case of an infant who developed an upper airway obstruction and pulmonary edema associated with laryngospasm or post-extubation laryngeal edema [9, 10]. The infant was injected with almost 30 ml/kg of Ringer's

acetate during induction. As a result, the patient was hypervolemic at the end of surgery. His hypervolemic status probably contributed to negative pressure pulmonary edema. Thus, it is important to ensure that the contents of the drip chamber are monitored carefully and that an infusion pump is always used for premature infants.

In summary, it is suggested that early vitrectomy for aggressive posterior ROP may be effective despite the associated perioperative risks. As aggressive posterior ROP progresses rapidly, prompt preoperative organization is required, including transfer and preoperative management in the NICU, timing of surgery and anesthetic planning. The anesthesiologist can play an important role in the perioperative management of such high-risk infants.

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