Case Report

Anesthetic management of a patient with hemophilia A with spontaneous acute subdural hematoma

Prakhar Gyanesh, Sanjay Dhiraaj

Department of Anaesthesiology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

Abstract

Intracranial hemorrhage in patients with hemophilia is associated with high mortality and sequelae. We report the case of 50-year-old man with Hemophilia A, who presented with spontaneous acute subdural hematoma and underwent craniotomy for clot evacuation. The patient received Factor VIII infusions perioperatively along with other measures to decrease blood loss. The patient presented with signs of high intracranial tension and received 3% saline intraoperatively and postoperatively to prevent brain edema. Recommendations for perioperative preparation and management of hemophilia, especially in the setting of emergency major surgery are reviewed.

Key words: Anesthesia, factor VIII, hemophilia, intracerebral hemorrhage

Introduction

Intracranial hemorrhage (ICH) is a life-threatening complication of Hemophilia. The site of bleeding is about equally distributed between subdural hematoma, intracerebral and subarachnoid hemorrhage.[1] Acute subdural hematoma (SDH) is one of the most lethal forms of intracranial injury. Prompt surgical evacuation, when indicated, has better prognosis.[2] Mortality from ICH in Hemophilia, however, is still high.[3]

Case Report

A 50-year-old, 70 kg, man presented with loss of consciousness for the last 12 hours. The patient was a known case of Hemophilia A, having previous history of spontaneous bleeding into joints, and had received Factor VIII twice. The patient was receiving analgesics for back pain. He was a hypertensive on irregular medications. There was no history of trauma or drug abuse or any other surgery in the past.

Address for correspondence: Dr. Prakhar Gyanesh,
Old PG Hostel, Room No. 2, SGPGI, Lucknow - 14, India.
E-mail: prakhargyan@gmail.com

Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/0970-9185.105819

The patient's heart rate was 56/min and blood pressure 118/78 mmHg. Glasgow Coma Scale (GCS) score was $E_1M_2V_1$ and pupils were bilaterally mid-dilated, not reacting to light. Patient's hemoglobin was 11.1 gm/dl, INR 1.61 and APTT 150 sec. Non-contrast computerized tomography (CT) scan showed an acute left temporoparietal sub-dural hematoma (SDH) with left frontal hematoma, with mass effect and a midline shift of 10 mm.

After shifting to the neurosurgery intensive care unit (ICU), patient was administered intravenous (IV) fentanyl 200 mcg, propofol 100 mg, vecuronium 8 mg and lignocaine 100 mg. Patients trachea was intubated and lungs mechanically ventilated. Neuroprotective measures in the form of mannitol (1 gm/kg, IV, TDS), dexamethasone (8 mg, IV, BD), seizure prophylaxis (phenytoin 100 mg, IV, TDS) and hyperventilation (to a PCO_2 of 32 mmHg) were initiated. The patient was scheduled for an emergency craniotomy and clot evacuation after stabilizing his coagulation parameters. Hematology consultation was taken and 11 vials (3000 units) of factor VIII concentrate (Hemofil M, Baxter) were transfused. His APTT was 26 sec two hours later and he was taken up for surgery.

Inside the operation theater, a 16G peripheral line was taken. His left radial artery was cannulated. Right internal jugular vein triple lumen catheter was put under ultrasound guidance for central venous pressure monitoring, and in anticipation of major blood loss. Monitoring included pulse-oximetry, electrocardiogram, end-tidal carbon dioxide, arterial blood gas (ABG) monitoring, temperature

monitoring (oropharyngeal) and urine output. Bilateral scalp block was given. Anesthesia was maintained with oxygen, air and isoflurane. The patient received fentanyl (200 mcg IV at the start of the surgery and another 100 mcg IV later, total dose 4 mcg/kg) for analgesia and vecuronium (0.1 mg/kg initially and the 0.01 mg/kg IV every 30 min) for muscle relaxation. 200 ml (3 ml/kg) of 3% saline was given over 30 minutes for brain relaxation at scalp incision.[4]

The patient received 1 vial (≈272 units) of Hemofil M every 2 h during surgery. 750 mg of tranexamic acid was also given. Blood loss was 900 ml. No PRBC transfusion was required. Serial ABG analysis showed no major acid-base imbalance. The patient remained hemodynamically stable throughout the surgery and was shifted back to ICU for postoperative elective ventilation. Post-operative analgesia was provided with IV fentanyl and paracetamol. Serum Na^+ levels were measured 4-6 hourly in the postoperative Day 1 and 2. In case Na^+ concentration was <155 mEq/L, we infused 200 ml of 3% saline. Our aim was to maintain Na^+ level between 150-160 mEq/L. A total of 7 doses were given in the next 48 hours. In general, an infusion of 1 mL/kg of 3% saline raises the serum Na^+ by approximately 1 mEq/L, regardless of baseline serum Na^+ concentration.[5]

One vial of Hemofil M was given 2 hourly to the patient in the 1st postoperative day and 3 hourly from the 2nd day. Tracheostomy was done on the 2nd postoperative day. Patient showed signs of neurological improvement on the 2nd day, with GCS improving to $E_2M_3V_T$, and was weaned off the ventilator on the 4th day. The factor VIII level was 64% on the 5th postoperative day and 46% on the 14th day. HEMOFIL M was continued till the 14th day. On the 21st postoperative day the factor VIII level was 39%. There was no postoperative hemorrhage. The GCS improved to $E_3M_5V_T$ by the 21st day but the patient had right hemiplegia.

Discussion

Hemophilia A, a recessive X-linked disorder involving lack of functional clotting factor VIII (FVIII), represents 80% of Hemophilia cases. Severe cases (<2% FVIII) have spontaneous bleeding, predominantly in joints and muscles. Moderate (2-10% FVIII) and mild (>10% FVIII) deficiency leads to excessive bleeding only after trauma or surgery. Delayed bleeding, after a period of apparent hemostasis, may occur from a weak clot being unable to maintain vascular integrity. Patients have high APTT but platelet count, bleeding time and prothrombin time are normal. Factor assay is diagnostic.

Intracranial hemorrhage, with incidence of 3-12%,[6] accounts for over 30% of deaths in Hemophiliacs.[7] Over 50% of the patients with ICH have psychoneurological sequelae. The mortality is more closely related to the bleeding site than to the severity of Hemophilia, with subdural hematoma and subarachnoid hemorrhage having better prognosis.[8]

Acute SDH with a thickness greater than 10 mm or midline shift greater than 5 mm should be surgically evacuated. In patients with acute SDH, surgical evacuation should be performed as soon as possible.[9] Our patient was a candidate for early surgery.

The recommended plasma factor level and duration of administration for major surgery are as shown as Table 1.[10]

Each FVIII unit per kilogram of body weight raises the plasma FVIII level by approximately 2%, with the half-life of 8-12 hours. FVIII should be infused by slow IV, at a rate not exceeding 3 ml/minute in adults and 100 units per minute in young children. Cryoprecipitates are the next choice and provide average 80 units FVIII content in a volume of 30-40 ml. Fresh frozen plasma may also be used if factor concentrates are unavailable. One ml of FFP contains 1 unit of factor activity.

Desmopressin, a synthetic analogue of antidiuretic hormone, boosts plasma levels of FVIII and vWF. A single IV infusion of 0.3 mg/kg increases the level of FVIII 3-6 times with peak response in 90 minutes. It is ineffective in patients with severe Hemophilia A and is of no value in Hemophilia B. Tranexamic acid is an antifibrinolytic agent that promotes clot stability and is useful as adjunctive therapy in Hemophilia. Factor VIIa has been used in hemophilic patients with inhibitors and also for early intervention following ICH.[11]

As FVIII assay was not available to us in emergency, we transfused 3000 units (70kg *90%*0.5) of FVIII before surgery. With the patient having significant midline shift with pupillary signs and impending brain herniation, we started neuroprotective measures and seizure prophylaxis after tracheal intubation. Guidelines suggest ICP monitoring in patients with SDH with a GCS less than 9.[9] Bleeding disorders are contraindications for intra-cranial pressure (ICP) monitoring and we did not monitor the ICP for this patient. The patient was taken up for surgery at the earliest, after the APTT normalized.

Table 1: Recommended FVIII levels and duration of FVIII administration for major surgery

Major surgery	No resource constraints		Significant resource constraints	
	Desired level (%)	Duration (days)	Desired level (%)	Duration (days)
Pre-op	80-100		60-80	
Post-op	60-80	1-3	30-40	1-3
	40-60	4-6	20-30	4-6
	30-50	7-14	10-20	7-14

We used 3% saline to decrease the cerebral edema as hypertonic saline provides better brain relaxation than 20% mannitol.[4,5] Although coagulopathy has been described with hypertonic saline, it is a concern when >10% of blood volume is replaced with hypertonic saline, and is not a concern in the doses used in neurosurgery.[12] Recent studies also suggest that use of 3% saline in the neurosurgical patients has lesser derogatory effects on the clotting factors and platelets than the use of mannitol.[13]

Hemophiliacs undergoing elective surgery should be evaluated for the status of joints, spontaneous hematomas, airway and the presence of oral injuries. Induction of anesthesia should be smooth and drugs like succinylcholine are avoided to prevent muscle shakes, which may worsen muscle and joints hemorrhagic state.[14] Peripheral lines generally do not tend to bleed excessively.[15] Intramuscular injections, difficult phlebotomy, and arterial punctures should be avoided. Central venous access, if required, should be secured under ultrasound guidance.[16] We inserted both arterial and central line for better monitoring and patient safety.

Shifting the patient from ICU to operation theatre and back was done very carefully. Tracheal intubation and airway manipulation in these patients can lead to life threatening submucosal hemorrhages.[17] Early tracheostomy has been found to provide significant benefits in critically ill neurosurgical patients. It reduces the ICU stay, duration of ventilatory support and antibiotic dose requirement in these patients.[18] Early tracheostomy should be considered in patients with acute severe brain injury.[19]

Care is also needed with insertion of probes and thermometers, preventing trauma injuries because tongue and airway muscles bleeding may rapidly lead to airway obstruction. Pharyngeal aspiration should be extremely delicate. Extremities and pressure points should be padded to prevent intramuscular hematomas and hemarthrosis. Analgesia was provided with scalp block and fentanyl. Non-steroidal analgesics were not used. Temperature was monitored and hypothermia avoided.

Hypertension and tachycardia during surgery in Hemophiliacs can lead to increased surgical bleeding. Controlled hypotension techniques prevent hemostasis of small vessels but are not recommended. Hemodynamic conditions should be maintained near normal. Surgeon should give special attention to small vessel hemostasis rather than trusting on hemostatic physiological mechanisms.[14]

FVIII concentrates were continued in the intraoperative and postoperative period. In Hemophilia, major surgery should take place in a center with adequate laboratory support for monitoring of clotting factor level and preoperative assessment should include inhibitor screening. Elective surgery should be scheduled early in the week and early in the day for optimal laboratory and blood bank support. Availability of sufficient quantities of clotting factor concentrates should be ensured before undertaking major surgery.[9] As our patient needed emergent surgery, FVIII assay and inhibitor screening were not feasible preoperatively. Postoperative monitoring for bleeding was done with hemoglobin and APTT levels along with FVIII assay.

To conclude, we successfully managed a patient of Hemophilia A with ICH. Prompt surgery, neuroprotection, bleeding prophylaxis and early tracheostomy in this patient possibly lead to good outcome in this patient.

References

1. Nuss R, Soucie JM, Evatt B, Hemophilia Surveillance System Project Investigators. Changes in the occurrence of and risk factors for hemophilia-associated intracranial hemorrhage. Am J Hematol 2001;68:37-42.
2. Martinowitz U, Heim M, Tadmor R, Eldor A, Rider I, Findler G, *et al*. Intracranial hemorrhage in patients with hemophilia. Neurosurgery 1986;18:538-41.
3. Philip C. The Aging Patient with Hemophilia: Complications, Comorbidities, and Management Issues. Hematology Am Soc Hematol Educ Program 2010;2010:191-6.
4. Wu CT, Chen LC, Kuo CP, Ju DT, Borel CO, Cherng CH, *et al*. A comparison of 3% hypertonic saline and mannitol for brain relaxation during elective supratentorial brain tumor surgery. Anesth Analg 2010;110:903-7.
5. Hinson HE, Stein D, Sheth KN. Hypertonic Saline and Mannitol Therapy in Critical Care Neurology. J Intensive Care Med 2011 [Epub ahead of print].
6. Ghosh K, Nair AP, Jijina F, Madkaikar M, Shetty S, Mohanty D. Intracranial haemorrhage in severe haemophilia: Prevalence and outcome in a developing country. Haemophilia 2005;11:459-62.
7. Darby SC, Kan SW, Spooner RJ, Giangrande PL, Hill FG, Hay CR, *et al*. Mortality rates, life expectancy, and causes of death in people with hemophilia A or B in the United Kingdom who were not infected with HIV. Blood 2007;110:815-25.
8. De Tezanos Pinto M, Fernandez J, Perez Bianco PR. Update of 156 episodes of central nervous system bleeding in hemophiliacs. Haemostasis 1992;22:259-67.
9. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R; Surgical Management of Traumatic Brain Injury Author Group, *et al*. Surgical management of acute subdural hematomas. Neurosurgery 2006;58:S16-24.
10. Srivastava A, Brewer AK, Mauser-Bunschoten EP, Key NS, Kitchen S, Llinas A *et al*. Guidelines for the management of hemophilia. Haemophilia. 2013 Jan;19(1):e1-e47.[http://www1.wfh.org/publications/files/pdf-1472.pdf].
11. Roberts HR, Monroe DM, White GC. The use of recombinant factor VIIa in the treatment of bleeding disorders. Blood 2004;104:3858-64.
12. White H, Cook D, Venkatesh B. The use of hypertonic saline for treating intracranial hypertension after traumatic brain injury. Anesth Analg 2006;102:1836-46.
13. Luostarinen T, Niiya T, Schramko A, Rosenberg P, Niemi T. Comparison of hypertonic saline and mannitol on whole blood coagulation *in vitro* assessed by thromboelastometry. Neurocrit

Care 2011;14:238-43.
14. Flores RP, Bagatini A, dos Santos AT, Gomes CR, Fernandes MS, Molon RP. Hemophilia and Anesthesia. Rev Bras Anestesiol 2004;54:865-71.
15. Mallya P, Kaimar P, Jithesh R, Ranjan RK, Ambareesha M. Anaesthetic management of a patient with haemophilia. Indian J Anaesth 2007;51:145-7.
16. Parmet JL, Horrow JC. Hematological Diseases. In: Benumof JL, editor. Anesthesia and Uncommon Diseases. 4th ed. Philadelphia: W B Saunders; 1998. p. 299-301.
17. Hirshoren N, Varon D, Weinberger JM, Gross M. Airway Obstruction and Hemophilia-A: Epiglottis Hematoma. Laryngoscope 2010;120:1428-9.
18. Gandía-Martínez F, Martínez-Gil I, Andaluz-Ojeda D, Bobillo de Lamo F, Parra-Morais L, Díez-Gutiérrez F. Analysis of early tracheostomy and its impact on development of pneumonia, use of resources and mortality in neurocritically ill patients. Neurocirugia (Astur) 2010;21:211-21.
19. Pinheiro Bdo V, Tostes Rde O, Brum CI, Carvalho EV, Pinto SP, Oliveira JC. Early versus late tracheostomy in patients with acute severe brain injury. J Bras Pneumol 2010;36:84-91.

How to cite this article: Gyanesh P, Dhiraaj S. Anesthetic management of a patient with hemophilia A with spontaneous acute subdural hematoma. J Anaesthesiol Clin Pharmacol 2013;29:117-20.
Source of Support: Nil, **Conflict of Interest:** None declared.