Case Report

Anaesthetic significance and management of a child with neonatal purpura fulminans

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ABSTRACT

Protein C deficiency is a rare autosomal-dominant disorder of varying severity. Patients with homozygous and compound heterozygous protein C deficiency present with neonatal purpura fulminans (NPF). Other presentations usually include disseminated intravascular coagulation and venous thromboembolism. This disorder usually poses a unique anaesthetic challenge to the anaesthesiologist, requiring special precautions to prevent various intra- and post-operative complications. We hereby report the successful anaesthetic management of a 1-month-old infant who presented with NPF.

Key words: Anaesthesia, disseminated intravascular coagulation, neonatal purpura fulminans, protein C

INTRODUCTION

Protein C deficiency is an autosomal-dominant[1] disorder presenting with recurrent thrombotic episodes like neonatal purpura fulminans (NPF), disseminated intravascular coagulation (DIC) and venous thromboembolism (VTE). Management of this entity requires long-term anticoagulation with or without protein C replacement.

We report the successful perioperative management of a premature neonate with protein C deficiency.

CASE REPORT

A 1-month-old female infant was brought by to us with complaints of decreased oral intake along with increasing hard woody swelling over her right upper cheek, with black discolouration of the cheek extending on to the right alae nasi for the last 2 days [Figure 1].

Detailed history revealed that the infant was born at 34 weeks gestation of a non-consanguinous marriage and weighed 2.6 kg at birth. Her Apgar score was 7 and 9 at 1 min and 5 min after birth. On the third day after birth, she developed a red lesion over the right elbow that developed into black eschar and rapidly grew in size. Detailed investigations revealed that D-dimer was elevated with an undetectable level of protein C.

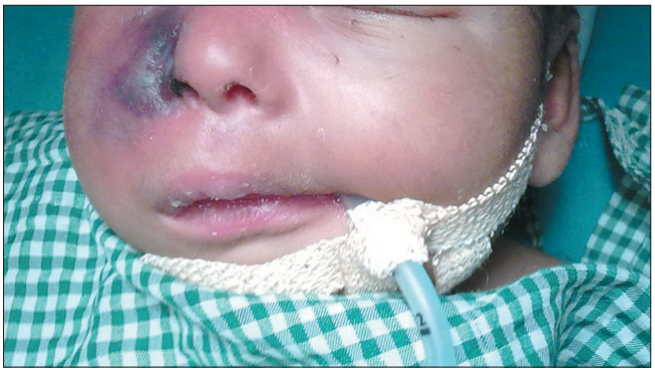

Figure 1: Image

On examination, the baby was lethargic and pale with a pulse rate of 160/min, respiratory rate of 70/min and temperature of 40°C, and weighed 3.0 kg. The abdomen was grossly distended. On auscultation, bowel sounds were decreased. Chest was normal with no other gross systemic abnormality. Local examination revealed tense woody swelling present over the right side of the cheek with overlying necrosis of the right side alae

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nasi. Investigations revealed haemoglobin of 6.8 gm%. Leukocyte count was 41,000 cells/cu mm. Prothrombin time showed an International Normalized Ratio (INR) of 1.05 with D-dimer of 1500. Total protein was reduced to 5.0 gm%. Kidney functions were within normal limits. The protein C activity level was grossly reduced to 10% (normal level – 80–130%). In view of the poor general condition, the patient was taken up for debridement of the necrosed tissue under general anaesthesia as an increased risk and the problems explained to the parents.

Pre-operatively, 10 mL/kg body weight of packed cells and 15 mL/kg of fresh frozen plasma (FFP) was transfused before shifting the patient to the operating room. She was also started on low molecular weight heparin therapy after admission with enoxaparin 0.9 mg to overcome the hypercoagulable state due to protein C deficiency.

After taking a valid informed consent, the patient was shifted to the operating room (OR) and was not premedicated as she was found to be lethargic. The OR was prepared to a temperature of 24°C, as paediatric patients are prone to hypothermia and, moreover, in this patient, hypothermia could have initiated further thrombosis. General anaesthesia was induced by inhalation of 8% sevoflurane in 100% oxygen. Tracheal intubation was successfully performed, without the use of neuromuscular blockade for laryngoscopy, with a 3.5-mm plain endotracheal tube. Laryngoscopy revealed palatal perforation that was attributed primarily to the underlying condition. However, it did not prove to be a difficult intubation. Anaesthesia was maintained with 5 μg fentanyl and 5 mg propofol intravenous and an inhalation mixture of oxygen, air and sevoflurane. Atracurium 2.0 mg intravenous in divided doses was administered for muscle relaxation. The palate was found to be necrosed and perforated, and the necrosed tissue was excised and corrective surgery was deferred considering the poor general condition of the patient. Intra-operatively oxygen saturation, electrocardiogram, non-invasive blood pressure, $EtCO_2$ and temperature were monitored. Temperature of the baby was maintained by using a forced air warmer. Intra-operatively, about 20 mL of isolyte P was insfused. Urine output was 5 mL, with the intra-operative course being uneventful. The entire procedure, which involved debridement of the necrosed tissue, lasted for about 30 min, with minimal blood loss.

Neostigmine 0.07 mg/kg and atropine 0.02 mg/kg were administered for reversal of neuromuscular blockade; however, the patient remained apnoeic. Naloxone 0.3 mg was administered but the apnoea persisted. The patient was shifted to the Intensive Care Unit for elective mechanical ventilation after waiting for a period of 90 min. However, the patient could not be reversed and had prolonged post-operative apnoea. It was then decided to electively ventilate the patient as post-operative apnoea is known to occur even 2–12 h after surgery. The infant was successfully weaned off mechanical ventilation and the trachea was extubated 8 h after surgery. Amphotericin therapy was initiated in the post-operative period as biopsy of the excised tissue revealed an active invasive fungal infiltration.

She was treated with warfarin potassium and FFP post-operatively, and the child remained clinically stable and was discharged on request, after being asked to come for regular follow-up in the paediatric, haematology and plastic surgery departments.

DISCUSSION

Protein C was first isolated by Johan Stenflo in 1976, and it was the third protein to be eluted by DEAE-Sepharose; hence, it was named as protein C.[2] The first case of protein C deficiency associated with venous thrombosis in a family was reported by Griffin *et al*.[3] in 1982.

Protein C is a Vitamin K-dependent glycoprotein circulating in the plasma in an inactive form (Zymogen), the activity of which is further augmented by Protein S, high-density lipoprotein and anionic phospholipids. Protein C acts on activated procoagulant factor V and VII and cleaves the critical sites, thereby activating these enzymes. Therefore, patients with protein C deficiency have decreased capacity to downregulate the thrombin generation once initiated by factor Va and VIIa.[4]

Activated protein C (APC) also plays a role in the regulation of inflammation.[5] APC binds to endothelial protein C receptor (EPCR) and cleaves the endothelial cell protease-activated receptor-1, resulting in downregulation of proinflammatory and proapoptotic mediators, upregulation of anti-inflammatory and antiapoptotic pathways and stabilization of endothelial cell barrier functions.

The disorder varies in severity, from mild

asymptomatic states with an incidence of 1 in 200–500 healthy individuals to a clinically significant state, the incidence of which has been reported to be around 1 in 20,000,[6] with no racial or ethnic predilection.[4] Patients with homozygous and compound heterozygous protein C deficiency present with neonatal purpura fulminans[7] (NPF).

Possible complications associated with protein C deficiency and of importance from an anaesthetic point of view are venous thromboembolism and increased risk of bleeding if the patient has been anticoagulated. Warfarin-induced skin necrosis and PF are serious life-threatening emergencies. PF is an acute disorder characterized by rapidly progressive haemorrhagic necrosis of skin due to dermal vascular thrombosis, which usually involves pressure points.[8] In this case, these manifestations were first noticed on the right elbow, which was initially managed conservatively and led us to the diagnosis of protein C deficiency. A similar lesion was then noticed over the right side of the cheek and ala nasi. Histopathological examination of excised tissue revealed dermal microvascular thrombosis along with active invasive fungal infection.

NPF is treated by protein C supplementation by administration of or human plasma-derived viral-inactivated protein C concentrate. A total of 1 IU/kg of protein C concentrate or 1 mL/kg of FFP will increase plasma concentration of protein C by 1 U/dL.[4] Considering the cost factor, difficulty in procurement of protein C concentrates along with urgency of the procedure, we used FFP and low molecular weight heparin (Enoxaparin).

Long-term replacement therapy in small infants requires placement of central venous access. Because of the inherent hypercoagulability of the affected patients, thrombotic and infectious complications of central venous access devices poses a limitation to continuous replacement therapy and hence must be accompanied by strict adherence to protein C replacement along with any concomitant low-dose anticoagulation. Instillation of fibrinolytic agent into the central venous access device may help to prevent catheter-related occlusion and infections, but there is no evidence to support this practice.[4]

In a retrospective study, Ingrid Pabinger[9] concluded that in children <14 years of age, thromboprophylaxis cannot be routinely recommended and, after the 14th year, the risk increases considerably. Warfarinization, whenever started, should always be preceded by several days of therapeutic heparin administration to warfarin-induced skin necrosis and other progressive or recurrent thrombotic complications, including venous thromboembolism, purpura fulminans or DIC. Patients in the paediatric age group can also be managed by a combination of two approaches (e.g., protein C replacement, approximately 50 U/kg, given every other day or three-times weekly in combination with less-intensive anticoagulation).

A tailored atraumatic anaesthetic technique is the method of choice in these patients. Tissue compression and dehydration usually increase the risk of thrombosis. Use of a cuffed endotracheal tube may increase the risk of tracheal compression, submucosal thrombosis and necrosis.[9] Necrosis resulting from the underlying condition was attributed as the cause of palatal perforation, which was detected intra-operatively. To prevent pressure-related complications, our patient was positioned on a water mattress and all the pressure points were padded with soft cotton, and padding was also provided under a non-invasive blood pressure cuff as these could further lead to tissue compression and complicate the entire picture.[10] The infant was adequately hydrated with crystalloids and FFP. Administration of FFP also provided us with protein supplementation and protein C and also helped us to overcome dehydration as it leads to increased risk of thromboembolic phenomenon. A small-sized uncuffed endotracheal tube was used to decrease the possible risk of tracheal compression, submucosal thrombosis and necrosis. Prevention of hypothermia is also of utmost importance in patients suffering from protein C deficiency, as hypothermia may trigger thrombosis.

We report the perioperative management of a neonate with protein C deficiency, presenting in sepsis resulting from paralytic ileus and haemorrhagic dermal necrosis, with perioperative administration of FFP and low molecular weight heparin (LMWH). The patient however succumbed on the fifth post-operative day due to his co-existing co-morbidities like sepsis and paralytic ileus, which had further complicated the management of our case.

ACKNOWLEDGMENT

The child's parent were informed about the publication of the manuscript and the use of image in the journal.

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Conference Calendar Details

Name of the conference: 60th Annual National Conference of the Indian Society of Anaesthesiologists, ISACON 2012
Date: 26th to 29th December 2012
Venue: Labh-Ganga Convention Centre, MR 10-Bypass Junction, Indore, M. P., India
Organizing Secretary: Dr. Kishore Arora, Associate Professor of Anaesthesiology, M. G. M. Medical College & M. Y. Hospital, Indore 452 001, Madhya Pradesh, India
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Email: secretaryisacon2012@gmail.com, kkarora25@gmail.com
Website: www.isacon2012.com

Name of the conference: Indian Association of Cardiovascular Thoracic Anaesthesiologists (IACTA) 6th Perioperative Transoesophageal Echocardiography (TEE) Workshop Conducted by Indian Academy of Echocariography (IAE) & University of Minnesota, USA
Date: 4th to 6nd August, 2012
Venue: Narayana Hrudayalaya Hospitals, Bangalore
Organising Secretary: Dr. Muralidhar K, Director (Academic), Consultant & Professor, Anaesthesia & Intensive Care, Narayana Hrudayalaya Hospitals # 258/A, Bommasandra Industrial Area, Anekal Taluk, Bangalore – 560 099, Karnataka, India
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Name of the conference: CGSACON 2012, 9th Chhattisgerh Society of Anaesthesiologist Conferance
Date: 19th August, 2012
Venue: Hotel Intersity, Bilaspur
Organising Secretary: Dr. Mukesh Valecha
Contact: 9893081826
E-mail: cgsacon2012@gmail.com

Name of the conference: ISA South Zone conference 2012 – CASCO 2012 (Coimbatore Anaesthesia South Zone Conference 2012)
Date: 10th, 11th & 12th August, 2012 (Friday, Saturday & Sunday)
Venue: Codissia Trade Fare Centre, Avinashi Road, Coimbatore
Organising Secretary: Dr. K Sudarshan, Organising Secretary, CASCO 2012, 110/1, Sivaram Nagar West, Sungam, Coimbatore 641 045, Tamil Nadu, India
Contact: +91 09842262457
E-mail: casco2012@yahoo.com, doctorsudarshan@gmail.com

Name of the conference: 18th Annual Conference of Railway Forum of ISA 2012
Dates: 24th & 25th August, 2012
Venue: Kolkata
Organising Secretary: Dr. S Dasgupta, Flat No. B1-203, Mangalam Park, 14-Ho Chi Minh Sarani, Kolkata - 700 034, West Bengal, India
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E-mail: drsumanta@gmail.com

Name of the conference: I. S. A. Sponsored CME 2012
Dates: 2nd September, 2012 (Sunday)
Venue: Jindal South West (JSW) Steel Plant Township, Hosted by ISA, Bellary Branch & Department of Anaesthesiology and Critical Care, (VIMS), Bellary, India
Organising Chairman: Dr. D Srinivasalu
Organising Secretary: Dr. B P Mallanna
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Name of the conference: BAPU 2012, Sri Padmavathi Auditorium
Dates: 1st & 2nd September, 2012
Venue: Tirupati
Organising Secretary: Dr. M Hanumantha Rao, Department of Anaesthesiology & Critical Care, Sri Venkateswara Institute of Medical Sciences, Tirupati – 517507, Andhra Pradesh, India
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Name of the conference: AOA - 2012, 5th National Conference of Association of Obstetric Anaesthesiologists
Dates: 7th, 8th & 9th September, 2012
Venue: India Habitat Center, New Delhi
Organising Secretary: Dr. Anjeleena Kumar Gupta, Department of Anaesthesiology, Pain & Perioperative Medicine, 5th Floor, Super Speciality Block, Sir Gangaram Hospital, New Delhi – 110 060, India
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