Successful resuscitation of an extremely low birth weight neonate with massive, indomethacin induced gastrointestinal hemorrhage

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Citation

Abstract
We describe the first reported case of indomethacin induced massive gastrointestinal hemorrhage in a extremely low birth weight premature infant successfully treated by aggressive volume resuscitation.

CASE REPORT
A 20 year old primigravida was admitted for evaluation and management of preterm labor at 28 weeks gestation. Her pregnancy was complicated by fetal intrauterine growth retardation (IUGR) with absent end diastolic umbilical arterial blood flow and normal amniotic fluid index. She received betamethasone antenatally. Nonreassuring fetal heart tones with variable decelerations prompted an emergent cesarean section.

A female neonate (birth weight 692g) was born who was intubated, mechanically ventilated and received one dose of surfactant in the delivery room. Apgar scores were 2 and 8 at 1 min and 5 minutes of life, respectively. She received Vitamin K and was transferred to the neonatal intensive care unit.

During her first 24 hrs of life she was on low ventilator settings with normal arterial blood gases. She had an umbilical artery catheter placed with the tip at T9. On day of life (DOL) 2 she developed pulmonary hemorrhage. She developed a severe respiratory acidosis and was placed onto a high frequency oscillatory ventilator (HFOV). Respiratory acidosis was corrected and her hemorrhage ceased after placement on the HFOV. An echocardiogram revealed a moderate patent ductus arteriosus with L to R shunting, dilated left ventricle and atrium.

Indomethacin at 0.2mg/kg IV was started on DOL 3. On DOL 4 she received her second dose of indomethacin at 0.2mg/kg IV and was stable. She was inadvertently extubated but was immediately reintubated. Within 10 minutes of reintubation she had profuse amounts of bright red blood coming from her mouth and nares. No source of bleeding was evident on local examination of the oral and nasal cavity. Her ETT remained free of hemorrhage and gastrointestinal source of hemorrhage was confirmed after placing a nasogastric tube. The profuse bleeding from her NG tube, mouth and nares continued for the next 10 hours. During the first several hours the volume of blood loss was estimated at 30 ml every 30 minutes by weighing the gauze pieces soaked with blood.

Aggressive volume resuscitation with blood products with a goal to keep her hemodynamically stable was achieved with sequential and repeated transfusions of packed red cells, platelets and fresh frozen plasma through her umbilical arterial catheter. Over approximately 16 hours, she received 195 ml packed RBCs (281ml/kg), 36 ml single donor platelets (52 ml/kg), and 21 ml fresh frozen plasma (30 ml/kg). Her supplemental oxygen requirement was weaned during the volume resuscitation.

She had a grayish appearance at the beginning of the event which prompted dopamine infusion at 5 mcg/kg/min. This was discontinued at 38 hours. She also received intravenous ranitidine empirically for possible hemorrhagic gastritis. A pediatric surgical consultation was obtained to explore the unlikely feasibility (due to her size) for diagnostic and/or therapeutic upper gastrointestinal endoscopy and /or gastrectomy if the hemorrhage did not stop overnight. She survived this massive hemorrhage and subsequently had no bleeding episodes. A follow up echocardiogram showed closure of the patent ductus arteriosus. She remained
mechanically ventilated until DOL 31. She subsequently
developed BPD and was treated with diuretics and
supplemental oxygen and discharged home at two and a half
months of age. Cranial ultrasound images were normal. A
follow up MRI as an outpatient did not show any evidence
of white matter injury. Her ophthalmologic exam revealed
full vascularization. She has hypothyroidism that requires
ongoing thyroid hormone replacement therapy. Her von
Willebrand factor antigen and activity were within normal
limits. On follow up at 4 months she is growing along the
25th centile for weight, length, and OFC and achieved
appropriate milestones.

DISCUSSION

Volume resuscitation using blood products was the primary
focus in this baby's management. The volume of transfusions
administered equals two double volume exchange
transfusions. It was successful as the neonate had no
hemodynamic consequence through the entire episode and
survived. A MRI scan of the head at two and half months of
age did not reveal white matter injury. The hemorrhage
coincided with endotracheal intubation. Local trauma to the
oral mucosa, an important diagnostic consideration, was
ruled out by visual inspection of the oral cavity. Upper
gastrointestinal endoscopy was precluded by her size and the
profuse hemorrhage. Upper gastrointestinal endoscopy has
been performed in neonates treated with indomethacin.
Esophageal and gastric lesions diagnosed by endoscopy
correlate poorly with the gastrointestinal symptoms of
patients. Disseminated intravascular coagulation seemed
unlikely as she was otherwise well prior to onset of the
pulmonary hemorrhage, had no hemorrhage elsewhere with
normal platelet count. Since volume resuscitation was the
priority, interrupting the transfusions through the umbilical
arterial catheter, her sole vascular access, to collect blood for
diagnostic tests seemed unreasonable. The low platelet count
after the bleeding stopped probably is a reflection of dilution
of the platelets and other cellular components from the
multiple packed cell and fresh plasma transfusions.

Baby had compromised mesenteric vascular flow as
evidenced by intrauterine growth restriction with absent end
diastolic flow in the umbilical artery. The patent ductus
arteriosus further compromised the splanchnic circulation.

Treatment with indomethacin may have aggravated the
ischemia and precipitated the hemorrhage.

There is no case report of massive, postnatal, indomethacin
induced gastrointestinal hemorrhage in an extremely low
birth weight neonate in the literature. Gastrointestinal
bleeding has been reported due to indomethacin. Chirico et
al in their editorial correspondence describe a low birth
weight neonate who had massive gastrointestinal
hemorrhage following indomethacin therapy. They
performed a double volume exchange transfusion
successfully and postulate indomethacin induced platelet
dysfunction as a cause of the bleeding. Antenatal
indomethacin use in mother has been associated with
gastrointestinal hemorrhage, fetal anuria and neonatal
edema.

The dilemma of medical treatment versus surgery after
pulmonary hemorrhage due to a patent ductus arteriosus is
encountered frequently in clinical practice. There is no
evidence to support either decision. This case report
highlights one of the dangers of medical treatment as well as
the success of aggressive resuscitation and team work.

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