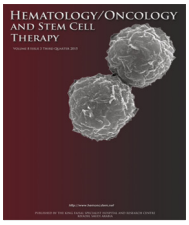
Hematol Oncol Stem Cell Ther (2016) xxx, xxx–xxx

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/hemonc



SPECIAL RESEARCH REPORT

Successful medical management of a neonate with spontaneous splenic rupture and severe hemophilia A

Sherif M. Badawy [a,b,e,*], Jenna Rossoff [a], Sushmita Yallapragada [a,c], Robert I. Liem [a,b], Anjali A. Sharathkumar [d]

[a] *Department of Pediatrics, Ann & Robert H. Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine, Chicago, IL, USA*
[b] *Division of Hematology, Oncology and Stem Cell Transplantation, Ann & Robert H. Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine, Chicago, IL, USA*
[c] *Division of Neonatology, Ann & Robert H. Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine, Chicago, IL, USA*
[d] *Department of Pediatrics, Division of Hematology, Oncology and Stem Cell Transplantation, University of Iowa Children's Hospital, Iowa City, IA, USA*
[e] *Division of Hematology and Oncology, Department of Pediatrics, Faculty of Medicine at Zagazig University, Zagazig, Egypt*

Received 17 March 2016; accepted 9 April 2016

KEYWORDS
Factor VIII deficiency;
Hemophilia A;
Neonate;
Splenic rupture

Abstract
Splenic rupture in neonates is a rare event, usually occurring in the setting of underlying predisposing conditions. Here, we present the case of a term neonate who presented with worsening anemia in the setting of known hemolytic disease during the newborn period and was later found to have a spontaneous splenic rupture. He was subsequently diagnosed with severe hemophilia A, and was managed medically with recombinant factor VIII replacement therapy without any surgical intervention. This is the first reported case of a neonate who had spontaneous splenic rupture and severe hemophilia A, and underwent successful medical treatment without any surgical intervention.

* Corresponding author at: Department of Pediatrics, Ann & Robert H. Lurie Children's Hospital of Chicago, 225 East Chicago Avenue, Box Number 30, Chicago, IL 60611, USA.
E-mail address: sbadawy@luriechildrens.org (S.M. Badawy).

http://dx.doi.org/10.1016/j.hemonc.2016.04.001
1658-3876/

Please cite this article in press as: Badawy SM et al., Successful medical management of a neonate with spontaneous splenic rupture and severe hemophilia A ..., *Hematol Oncol Stem Cell Ther* (2016), http://dx.doi.org/10.1016/j.hemonc.2016.04.001

Introduction

Spontaneous splenic rupture during the newborn period is extremely rare [1]. Spontaneous splenic rupture usually occurs secondary to an underlying coagulation disorder or splenic abnormalities [2]. It has been more commonly described with birth trauma, in the setting of macrosomia, shoulder dystocia, prematurity, prolonged labor, or breech presentation. Beyond trauma, abnormal splenic parenchyma (i.e., hemolytic disease of the newborn [HDN], leukemia, or congenital syphilis), abnormal coagulation (i.e., hemophilia), and maternal drug exposure (i.e., exposure to antiepileptic drugs) have also been identified as predisposing factors [3]. In the majority of cases, splenic rupture is thought to be secondary to increased intrathoracic pressure during labor and delivery, which pushes the spleen inferiorly into the abdominal cavity, exposing it to direct trauma through the birth canal during labor [4]. Upon rupture, the formation of a subcapsular hematoma usually occurs first, attempting to achieve hemostasis with local tamponade. Should this mechanism fail, the spleen ruptures hours to days later [5]. The classic triad of splenic rupture includes anemia, abdominal distension, and shock; however, this often occurs only at later stages, thus making prompt diagnosis of the utmost importance [2]. Herein, we report the first case of a neonate who had spontaneous splenic rupture and severe hemophilia A, and underwent successful medical treatment without any surgical intervention.

Case report

An infant weighing 2.95 kg was born at full term, 40 weeks' gestation, via normal spontaneous vaginal delivery to a 36-year-old gravida 2 para 2 Hispanic mother with negative serologies, negative antibody screen, and O-negative blood group. The mother had no medication exposures except for exposure to RhoGAM around 32 weeks. He was not circumcised and discharged home on Day of life 2 (DOL2) from the normal newborn nursery with no concerns. His family history was significant for a sister who had neonatal jaundice that required phototherapy, but was negative for liver disease, hemolytic anemia, or bleeding problems.

On DOL4, he presented to our emergency room (ER) with jaundice and pallor with the following measurements: hemoglobin (Hb), 6.9 g/dL (14.5—22.5 g/dL); reticulocyte count (RC), 5.5% (0.5—2.5%); total bilirubin (TB), 15.1 mg/dL (4—12 mg/dL); and direct bilirubin (DB), 0.4 mg/dL (<0.3 mg/dL). His blood type was A+, Coombs+, and he was diagnosed with HDN secondary to ABO incompatibility, with antibodies against A antigen. Upon admission to the neonatal intensive care unit (NICU) he received a packed red blood cell (pRBC) transfusion (15 mL/kg) and was treated with one dose of intravenous immunoglobulins (500 mg/kg/dose) and received 2 days of phototherapy. Following treatment, his TB level showed a downward trend and the Hb level remained stable, so he was discharged on DOL6 with Hb of 13.1 g/dL and TB of 15.6 mg/dL.

On DOL11, he represented to our ER with abdominal distension, poor feeding, and worsening jaundice. His examination was significant for tachycardia, jaundice, a firm distended abdomen with a slightly enlarged liver, and palpable left flank mass. His Hb dropped to 8.1; at this point, his RC was 2.4%, TB was 15.6, and DB was 0.3 (<0.3 mg/dL).

After readmission to the NICU, pediatric hematology was consulted. Abdominal ultrasound showed an avascular heterogeneous solid mass in the left upper quadrant and ascites, and a subsequent computerized tomography scan showed an active perisplenic hematoma with moderate hemoperitoneum (Fig. 1). Pediatric surgery was consulted for further management. Coagulation studies showed a normal prothrombin time of 11.3 s (9.3—12 s), prolonged activated partial thromboplastin time of 76.5 s (29.5—36.8 s), which corrected on mixing studies, and coagulation factor VIII activity of <1% (45—150%).

The infant then received a pRBC transfusion and was started on recombinant factor VIII (rFVIII) concentrate at 50 IU/kg/dose every 8 h. He was continued on scheduled rFVIII infusions to maintain trough FVIII activity near 100% for 72 h and his FVIII and Hb levels were closely monitored.

On DOL12, he required a second pRBC transfusion due to the lack of appropriate Hb response to the initial transfusion, indicating ongoing bleeding, although he remained hemodynamically stable throughout this process. His Hb level then stabilized and slowly trended upward. Abdominal examination showed improved results with less distension and discomfort, and resolution of his left flank mass within a couple of days. On DOL13, enteral feedings were restarted, which he tolerated well. The frequency of rFVIII infusions was decreased to every 12 h for the next 48 h, and then to every 24 h for the next 3 days. The patient

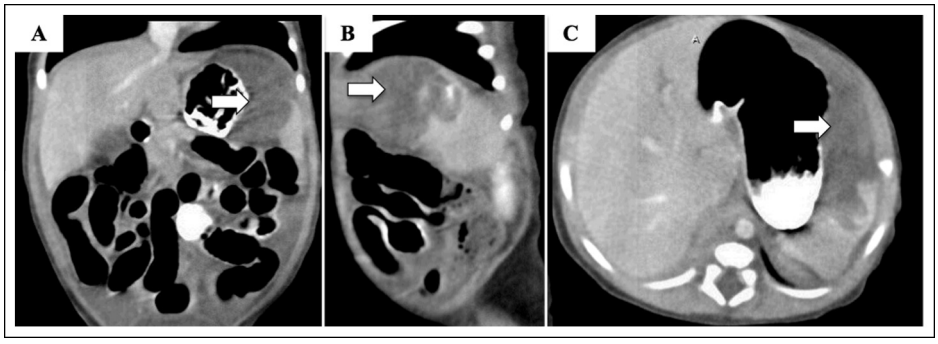


Figure 1 Computed tomography scan of the patient's abdomen and pelvis showing splenic rupture (white arrows): (A) coronal view; (B) sagittal view; (C) axial view.

Please cite this article in press as: Badawy SM et al., Successful medical management of a neonate with spontaneous splenic rupture and severe hemophilia A ..., *Hematol Oncol Stem Cell Ther* (2016), http://dx.doi.org/10.1016/j.hemonc.2016.04.001

Table 1 A summary of previously reported cases of splenic rupture in neonates with hemophilia.

Study	Presentation	Etiology	Treatment	Long-term outcome
Johnson-Robbins et al. [2]	DOL5: pallor, lethargy, distended abdomen, splenomegaly	Prematurity	Splenectomy	Unknown
Iannaccone & Pasquino [6]	DOL7: pallor, icterus, abdominal distension, left flank mass, hepatomegaly, cephalohematoma	Birth trauma	Unknown	Unknown
Tengsupakul et al. [7]	DOL3: poor feeding, lethargy, vomiting, pallor, abdominal distension	Unknown	pRBC & rFVIII transfusions, then splenectomy	High inhibitor levels at 6 weeks of age; soft-tissue bleeding at 9 months of age

Note. DOL = day of life; pRBC = packed red blood cells; rFVIII = recombinant factor VIII.

was discharged home on DOL18 with a stable Hb (13.2 g/dL), RC (1.2%), FVIII level (7%), and TB (9.7 mg/dL).

The hemophilia team followed the patient in the outpatient bleeding disorders clinic with further reduction in his rFVIII infusions to every 48 h for 7 days, and then transitioned him to an on-demand infusion regimen. Eight weeks later, abdominal ultrasound showed resolution of the left upper quadrant mass. He continued to be followed in our comprehensive hemophilia clinic every 6 months and currently receives on-demand rFVIII replacement therapy. He has received a total of 17 doses of rFVIII (3692 IU) with no evidence of inhibitors. He continues to show normal growth and development.

Discussion

We presented a rare case of a neonate who had spontaneous splenic rupture and severe hemophilia A and was successfully managed medically with preservation of his spleen and without any surgical intervention in the setting of HDN.

Effective hemostasis requires adequate levels of both factor VIII and factor IX, which are deficient in patients with hemophilia A and B, respectively, the most common coagulation disorders diagnosed in the newborn period. There are only a handful of reports of splenic rupture in newborns with hemophilia [2,6,7]. The majority of these patients are diagnosed in the setting of postcircumcision bleeding, intracranial bleeding, prolonged bleeding after venipuncture/heel stick, or a positive family history [8]. It is noteworthy that our patient did not exhibit bleeding symptoms after multiple blood draws during his prior hospitalization for HDN, so there was no clinical indication to perform coagulation screening tests. The underlying hemophilia contributed to poor local hemostasis in an already friable spleen, eventually leading to bleeding [2]. The timely initiation of further laboratory and radiological evaluation allowed for a prompt diagnosis of both hemophilia and splenic rupture.

Management of splenic rupture ranges from conservative treatment to emergent splenectomy [9]. It is difficult to estimate the proportion of splenic ruptures that are successfully managed medically for two reasons. First, those in the neonatal period are very rare and often discovered only at autopsy. Second, there is a wide spectrum of etiologies for the splenic rupture in the rest of the population. In newborns with severe hemophilia, replacement of appropriate factor concentrates and maintaining their levels within the hemostatic range are vital.

While there has been one case report of a subcapsular hematoma in a neonate with hemophilia who did not require surgical intervention [6], this is the first reported case of an overt splenic rupture in a newborn with severe hemophilia that did not result in emergent splenectomy. The two other cases of splenic ruptures reported in neonates with severe hemophilia required splenectomy (Table 1) [2,7]. Considering the severity of the bleeding, we maintained his FVIII levels over 100% until adequate hemostasis was achieved. Subsequently, we kept his trough levels between 1% and 10% until his splenic laceration had completely healed. Although he received short-term weekly secondary prophylaxis, he did not continue on it, based on his clinical phenotype of bleeding afterward.

Please cite this article in press as: Badawy SM et al., Successful medical management of a neonate with spontaneous splenic rupture and severe hemophilia A ..., *Hematol Oncol Stem Cell Ther* (2016), http://dx.doi.org/10.1016/j.hemonc.2016.04.001

Conclusion

Based on our literature review, we have reported on the case of the first neonate with spontaneous splenic rupture and severe hemophilia A who underwent successful medical treatment without surgical intervention. In newborns with hemophilia or other bleeding disorders, appropriate replacement of exogenous factor concentrates could prevent emergency splenectomy.

Conflicts of interest

The authors have no conflicts of interest to disclose.

References

[1] Hui CM, Tsui KY. Splenic rupture in a newborn. J Pediatr Surg 2002;37:E3.
[2] Johnson-Robbins LA, Porter JC, Horgan MJ. Splenic rupture in a newborn with hemophilia A: case report and review of the literature. Clin Pediatr (Phila) 1999;38:117—9.
[3] Acar K, Cinbis M. A neonatal death due to rupture of the normal spleen. Internet J Pediatr Neonatol 2001;2:1—4.
[4] Lloyd LG, Witt W. Splenic rupture in a neonate–a rare complication. SAJCH 2011;5:94—6.
[5] Van Praagh R. Causes of death in infants with hemolytic disease of the newborn (erythroblastosis fetalis). Pediatrics 1961;28:223—33.
[6] Iannaccone G, Pasquino AM. Calcifying splenic hematoma in a hemophilic newborn. Pediatr Radiol 1981;10:183—5.
[7] Tengsupakul S, Sedrak A, Freed J, Martinez-Carde L, Fireman F, Pierre L, et al. Splenic rupture in a newborn with severe hemophilia–case report and review. J Pediatr Hematol Oncol 2010;32:323—6.
[8] Conway JH, Hilgartner MW. Initial presentations of pediatric hemophiliacs. Arch Pediatr Adolesc Med 1994;148:589—94.
[9] Buess E, Illi OE, Soder C, Hanimann B. Ruptured spleen in children–15-year evolution in therapeutic concepts. Eur J Pediatr Surg 1992;2:157—61.

Please cite this article in press as: Badawy SM et al., Successful medical management of a neonate with spontaneous splenic rupture and severe hemophilia A ..., *Hematol Oncol Stem Cell Ther* (2016), http://dx.doi.org/10.1016/j.hemonc.2016.04.001