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Postoperative Management of Acquired Hemophilia A in Two Children and Literature Review

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Case Report

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Abstract

Background

To report the clinical manifestations, diagnosis, and treatment of two pediatric cases of trauma/surgery-associated acquired hemophilia A (AHA) to improve the awareness of the postoperative management of pediatric AHA.

Methods

The clinical manifestations, laboratory test results, diagnosis, treatment processes, and therapeutic efficacy of two pediatric AHA patients admitted to our hospital between February 1, 2025, and December 1, 2025, were retrospectively analyzed, along with a literature review.

Results

Two cases of pediatric AHA both developed severe bleeding after surgery. One case was a 7-year-old girl who suffered from massive intra-abdominal hemorrhage complicated by gastrointestinal bleeding following surgery for a choledochal cyst. After a second exploratory laparotomy for hemostasis and hematoma evacuation, she developed severe complications including higher FVIII inhibitor levels biliary fistula and peritonitis. She was eventually cured through conservative treatment. The other case was a 13-year-old girl who presented with necrotizing fasciitis caused by a thigh muscle hematoma. She underwent an incision and decompression along with the debridement of necrotic tissue, but the surgical wound continued to ooze blood postoperatively. After changing the hemostasis plan, the bleeding stopped. Both cases demonstrated a good prognosis without any sequelae during follow-up.

Conclusions

Clinical bleeding in trauma- or surgery-associated AHA is severe and unresponsive to conventional hemostatic methods, easily leading to life-threatening hemorrhage. Timely multi-disciplinary collaborative diagnosis and treatment(MDT), early identification and diagnosis of AHA, and standardized treatment are of great significance in improving the cure rate of the disease and saving lives.

Background

Pediatric acquired hemophilia A (AHA) is an extremely rare and life-threatening autoimmune disorder with an incidence of approximately 0.045 per million per year, often resulting in severe and life-threatening hemorrhage with a mortality rate as high as 20-33%[1]. Trauma- or surgery-induced AHA is rarely reported in the literature. Masked by the underlying disease, its diagnosis is often delayed. Postoperative bleeding, in particular, is easily misdiagnosed as being caused by infection, surgical technique faults, disseminated intravascular coagulation (DIC), or vitamin K deficiency. Repeated surgical explorations increase the risk of fatal bleeding; therefore, raising awareness of pediatric surgery-associated AHA is conducive to rapid diagnosis and treatment, thereby reducing mortality.

Methods

I. Case Presentations

Case 1: A 7-year-old girl was admitted due to "abdominal pain for over 1 week." Admission examination: Magnetic resonance cholangiopancreatography (MRCP) revealed a giant choledochal cyst (1899 cm) with intrahepatic bile duct dilatation (Type IVa) and cholecystitis. Routine blood and coagulation function tests showed no abnormalities. On February 12, she underwent a laparoscopic resection of the choledochal lesion + cholecystectomy + Roux-en-Y hepaticojejunostomy + jejunojejunostomy + liver biopsy. On postoperative day (POD) 1, she developed a fever of 38°C. Laboratory tests showed white blood cells (WBC): 15.5 ´ 10^9/L, CRP: 71.6 mg/L, lipase: 221 U/L, and amylase: 207 U/L. After targeted treatments including anti-infective therapy with cefoperazone-sulbactam and somatostatin, her temperature returned to normal. On POD 3, an isolated prolonged aPTT and a drop in hemoglobin were noted. Despite multiple transfusions of red blood cells and fresh frozen plasma, the coagulation function did not significantly improve (Figure 1). The patient gradually developed symptoms including abdominal pain, distension, melena, and ecchymosis around the umbilical incision. A follow-up abdominal CT scan revealed an encapsulated low-density mass with patchy hemorrhage (7.6 ´ 5.9 ´ 10 cm) adjacent to the pancreatic head, compressing the descending duodenum and displacing surrounding tissues (Figure 2).

On POD 8, hematology consultation was requested. Detailed laboratory workups showed: Serum amyloid A >320.00 mg/L, full-range CRP 41.93 mg/L, WBC 11.93 ´ 10^9/L, hemoglobin 44 g/L, hematocrit 13.2%, neutrophils 82%, lymphocytes 12%; ALT 12 U/L, albumin 35.6 g/L, a-amylase 447 U/L, lipase 565 U/L. Coagulation profile: PT 15s, aPTT 109.70s, TT 16s, D-dimer 6.96 ug/mL. FVIII activity (FVIII:C) was 2%, and an aPTT mixing study showed poor correction. The factor VIII inhibitor (FVIII:Ab) titer was 2.6 BU/mL (Bethesda assay). Von Willebrand factor (VWF) antigen was 141%. Anti-β2 glycoprotein 1 antibody and anti-cardiolipin antibody IgG were positive, while an autoantibody 18-panel, lupus anticoagulant, autoimmune 3-panel, and rheumatology 2-panel were negative. The final diagnosis was acquired hemophilia A. The patient was treated with methylprednisolone 2 mg/kg and prothrombin complex concentrate (PCC) 50 IU/kg q12h. A follow-up abdominal ultrasound indicated an enlarging intra-abdominal hematoma. To further aid hemostasis and identify the bleeding site, the surgical team performed a second exploratory laparotomy on February 24 (POD 12) following clinical evaluation.

Perioperative hemostatic regimen: Recombinant activated factor VII (rFVIIa) 90 μg/kg was administered half an hour before surgery and every 3 hours postoperatively for a total of 4 doses. Once hemostasis was achieved, sequential bypassing therapy with PCC 50 IU/kg q8h was initiated. Intraoperative findings: Surgery-related blood loss was 100 ml, and 500 ml of old blood clots were evacuated from the pancreatic head area. The patient received a 4U RBC transfusion during surgery, and two drainage tubes were placed (one at the cyst bed and one in the pelvic cavity). Postoperatively, anti-infective therapy with cefoperazone-sulbactam was continued. Follow-up tests showed a gradual increase in FVIII:Ab, peaking at 5.6 BU/mL, with FVIII:C dropping to a minimum of 1%. The abdominal drain continuously output 250-500 ml of bloody fluid daily, and hemoglobin dropped to 65 g/L. Considering the inadequate hemostatic effect of PCC monotherapy, rFVIIa bypassing therapy was re-initiated postoperatively, combined with immunosuppressive therapy using rituximab (375 mg/m^2, qw × 4 doses) and immune tolerance induction (ITI) therapy with high-dose human FVIII (100 IU/kg/day). After 20 days of treatment, the FVIII inhibitor turned negative. The patient's bleeding symptoms gradually resolved, and the abdominal drainage volume significantly decreased to a minimal amount of bloody fluid (approximately 20-50 ml/day).

On POD 19 of the second surgery, the abdominal drain output dark green fluid, accompanied by fever and abdominal pain. An abdominal ultrasound revealed an encapsulated effusion with septations around the biliary loop (22 × 24 × 5 mm); a mixed echogenic mass in the lower medial aspect of the pancreatic head (55 × 47 × 35 mm), consistent with a hematoma; and an encapsulated effusion with septations adjacent to the sagittal portion of the portal vein (18× 26 × 6 mm). Intrahepatic bile duct dilatation and slight edema of the biliary loop were noted. Secondary anastomotic fistula, pancreatic fistula, biliary fistula, acute peritonitis, and infectious fever were suspected. Following a multidisciplinary consultation, it was concluded that a third surgery carried an extremely high risk and uncertain efficacy, potentially increasing the risk of hemorrhage and elevating inhibitor titers. Conservative treatment was recommended. Treatment plan: Considering the immunosuppressive effect of methylprednisolone could hinder wound healing and infection control, it was discontinued. Anti-infective therapy was switched to meropenem, while the original regimen of rituximab combined with high-dose recombinant FVIII was maintained. The surgical team performed an ultrasound-guided drainage tube placement into the encapsulated effusion cavity, extracting 130 ml of dark red ascites. Continuous abdominal lavage was performed daily. Finally, the biliary fistula healed spontaneously, and the patient was discharged in an improved condition. Subsequent follow-ups revealed no sequelae such as malnutrition, cholangitis, or jaundice.

Case 2: A 13-year-old adolescent girl was admitted due to "swelling and pain in the right thigh for half a month." She developed right thigh muscle swelling following a collision during a physical education class half a month prior. On September 15, she visited a local hospital where tests showed an aPTT of 56s and a hemoglobin (Hb) of 56 g/L. An MRI of the thigh revealed an abnormal signal in the posterior muscle group of the upper right thigh, suggestive of infection complicated by an abscess. She was diagnosed with necrotizing fasciitis. An emergency incision and decompression of the right thigh muscle along with the debridement of necrotic tissue were performed that same day. Postoperative coagulation profiles remained abnormal. Further tests revealed an FVIII:C of 4.2% and an FVIII:Ab of 4.3 BU/ml, leading to a diagnosis of acquired hemophilia A. After symptomatic treatments including cryoprecipitate, fresh frozen plasma, and human coagulation factor VIII, the wound continued to ooze blood. She was transferred to our hospital on September 28. She had no previous history of bleeding or family history of bleeding disorders. Admission examination: A 15-cm surgical incision was visible on the right thigh, with dark red blood oozing from the distal end. Laboratory tests: aPTT 63.7s, PT 13.9s, FVIII:C 1.42%, FVIII:Ab 3.68 BU/ml. A lupus anticoagulant was suspected to be present, while the autoantibody 18-panel and phospholipid antibodies were negative. Inhibitor eradication therapy with rituximab (375 mg/m^2) combined with methylprednisolone (2 mg/kg) was initiated, alongside hemostatic treatment with human coagulation factor VIII (100 IU/kg/day) for 4 days, the wound continued to bleed. Therefore, the treatment was changed to recombinant human coagulation factor VIII. Hemostasis of the wound was achieved after 2 days. Two months later, follow-up tests showed the FVIII inhibitor had turned negative.

Results

II. Literature Review

Literature search was conducted in the PubMed, Embase, and Web of Science databases using the terms "acquired hemophilia A," "surgery," "children," and "pediatric." Five cases of surgery- or trauma-induced pediatric AHA were identified and synthesized with the two cases reported herein for a pooled clinical analysis(Table 1). Among the 7 AHA cases, 2 were male and 5 were female, with a median age of 12 years (range: 5–18 years). The median time from bleeding onset to diagnosis was 8 days (range: 2–23 days). Four patients developed severe infections, peritonitis, or hemorrhagic manifestations postoperatively, and two patients had elevated inhibitor titers compared to preoperative levels. After an AHA diagnosis, 3 cases received monotherapy with corticosteroids for immunosuppression (2 achieved remission, 1 failed to eradicate inhibitors); 3 cases were treated with corticosteroids combined with rituximab, achieving complete remission (CR); and 1 case resulted in death.

Discussion

Pediatric AHA is a rare acquired severe bleeding disorder. Approximately 56% of cases are idiopathic, while the rest are commonly associated with autoimmune diseases, infections, drugs, or malignancies leading to the production of FVIII autoantibodies[6]. Trauma- or surgery-associated pediatric AHA is rarely reported in the literature. Khan UZ reviewed 25 cases of surgery-associated AHA, finding that the majority were elderly, and 12 cases (48%) underwent digestive tract surgeries, of which 9 underwent hepatopancreatobiliary surgery[3]. In our report, 3 children developed FVIII inhibitors following choledochal cyst surgery. Therefore, certain surgical procedures—such as digestive tract surgeries, especially hepatopancreatobiliary surgery—may carry a higher risk for inhibitor formation [3–4].

Prior to diagnosis, trauma/surgery-associated AHA presents with wound oozing, severe surgical site hemorrhage, intra-abdominal bleeding, extensive subcutaneous ecchymosis, muscle hematomas, and soft tissue hematomas; hematuria and gastrointestinal bleeding are occasionally seen. Massive intra-articular bleeding (hemarthrosis) is generally absent (a key distinguishing feature from congenital hemophilia A). The severity of bleeding is disproportionate to the extent of surgical hemostasis, and the timing of the hemorrhage shows no clear correlation with the time of surgery or trauma. Studies indicate a

median time from surgery to bleeding of 2 days (range 0–8 days) [3], though reports exist of FVIII antibodies developing up to 30 days postoperatively [7]. Consequently, comprehensive coagulation tests should always be performed preoperatively. If an isolated prolonged aPTT of unknown etiology is identified, coagulation factor activity assays are recommended to maintain vigilance for AHA.

Due to the fact that the initial symptoms of bleeding in children with traumatic/surgical-associated AHA mostly occur in the surgical department, it is prone to cause delays in diagnosis[8]. The EACH2 registry indicated that one-third of patients experience a significant diagnostic delay, with 22% diagnosed 1 month after the initial bleed, and 11.1% taking more than 1 month to be diagnosed [9]. The CARE study showed that the median time from bleeding to definitive diagnosis for AHA patients in China is 30 days, with 46.5% of patients failing to receive a timely diagnosis [10]. Delaying the diagnosis for more than a month prolongs the bleeding period, necessitates higher doses of hemostatic factors, and significantly affects the duration of hemostatic therapy and the efficacy of immunosuppression [9–10]

Many patients undergo one or multiple surgical interventions to manage the bleeding, which increases the risk of transfusion, infection, and death with each subsequent procedure[3]. The article summarizes 5 cases that underwent surgical treatment due to severe bleeding. 3 cases underwent 2 or more surgeries, and the postoperative inhibitory substances were even higher. Moreover, more serious complications such as peritonitis, bile fistula, and DIC occurred. Therefore, when it is not life-threatening, conservative treatment should be considered as much as possible, and repeated surgical exploration should be avoided to prevent aggravating bleeding, increasing the risk of infection and elevated inhibitory substances. If the patient requires surgical intervention (such as decompression or hematoma removal), the preoperative coagulation status, age, underlying diseases, and comorbidities of the patient should be fully evaluated. After a multidisciplinary consultation and discussion, a detailed perioperative treatment plan should be formulated before proceeding with the surgery.

The management of AHA requires a two-pronged approach[11]: controlling acute bleeding and eradicating the inhibitor. Bypassing agents, such as recombinant activated factor VII (rFVIIa) and activated prothrombin complex concentrates (aPCC), are the first-line hemostatic treatments for AHA[12]. When monotherapy is insufficient, sequential therapy with rFVIIa and aPCC can be used, with careful attention paid to the dosing interval to prevent thrombotic events. High-dose rFVIII concentrates can also be used in conjunction with immunosuppressive agents. Aemisuzumab has shown good efficacy in preventing AHA bleeding. 87.1% of the patients had no external bleeding after using it [13]. However, since the equivalent FVIII activity of Aemisuzumab is only about 20%, it cannot meet the requirements for postoperative hemostasis. It can be used for the prevention of bleeding in outpatient AHA children.

Immunosuppressive therapy (IST) (corticosteroids, cyclophosphamide, rituximab, etc.) aims to eradicate the inhibitors, though it typically takes several weeks to become effective, and the risk of secondary infections must be monitored. The remission rate in pediatric patients is similar to adults, around 80.6%, but the spontaneous remission rate can reach 66%, significantly higher than the 12%-31% observed in adults [14]. It is necessary to pay attention to the risk of secondary infection caused by immunosuppression. In this article, 4 cases (4/7) of the children developed severe infection symptoms such as fever and peritonitis after the operation. When using immunosuppressants, broad-spectrum antibiotics should be used promptly to control the infection, and the therapeutic effect should be closely monitored and evaluated. The anti-infection plan should be adjusted in time, and the immunosuppressants should be discontinued if necessary [15].Plasmapheresis or immunoadsorption can rapidly remove circulating inhibitors and supplement FVIII to achieve effective hemostasis. While they cannot persistently eradicate inhibitors, they are useful in life-saving scenarios such as refractory bleeding or when emergency surgical intervention is required[12].

In summary, the perioperative management of AHA: 1. Control acute bleeding and remove inhibitors; 2. Timely control infection; 3. Strictly adhere to surgical indications to avoid the risks of multiple surgeries that increase bleeding and the elevation of inhibitory factors; 4. Actively treat the underlying diseases; 5. Early multi-disciplinary collaboration to formulate appropriate diagnosis and treatment plans to reduce postoperative complications and improve prognosis.

Conclusions

Trauma/surgery-related AHA is rare and has a high mortality rate. Bleeding always occurs at the surgical/injured site and is often accompanied by multiple complications. The bleeding may be very severe and even life-threatening. For non-hematology clinicians, diagnosis and treatment pose great challenges. Multiple surgeries may increase the risk of bleeding and elevated inhibitors. Post-operative bleeding related to trauma or surgery requires the surgeon to more strictly adhere to surgical indications and through multidisciplinary collaboration to formulate an appropriate treatment plan to reduce postoperative complications and improve prognosis.

Abbreviations

acquired hemophilia A (AHA), FVIII activity (FVIII:C), The factor VIII inhibitor (FVIII:Ab),Magnetic resonance cholangiopancreatography (MRCP), On postoperative day (POD), Von Willebrand factor (VWF), Recombinant activated factor VII (rFVIIa), prothrombin complex concentrate (PCC), activated prothrombin complex concentrates (aPCC),immune tolerance induction (ITI), complete remission (CR), Immunosuppressive therapy (IST), disseminated intravascular coagulation (DIC)

Declarations

Clinical trial number

not applicable.

Ethics approval and consent to participate

The Institutional Review Board of Guangzhou Women and Children's Medical Center confirmed that formal ethical approval was not required for this single retrospective case report, as it involves no clinical trials or interventional procedures on human subjects. All procedures performed were in accordance with the ethical standards of our institution and with the 1964 Helsinki Declaration and its later amendments.

Consent for publication

Written informed consent for publication have been obtained from the patient’s guardians (father of the patients). The consent can be provided on request.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

LZ, JKL contributed to data collection, analysis, data interpretation and manuscript preparation. YHL supervised the study and contributed to data interpretation and manuscript preparation. All authors discussed the results and revised the manuscript.

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Authors' information

Not applicable

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Table

Tables1: Clinical data of 7 children with acquired hemophilia A

Case	Sex	Age	Trigger	Time from onset to diagnosis d	FVIII:C %	FVIII:Ab (BU/ml)	Surgical procedure	IST	Hemostatic therapy
1[2]	Female	11	Traumatic cerebral hemorrhage leads to bilateral orbital compartment syndrome	8	31	1.78	Emergency incision of both corneas	methylprednisolone	fresh frozen plasma
2[3]	Female	12	congenital choledochal cyst	23	3	-	Four times, laparotomy for hemostasis	NA	FVIII fresh frozen plasma
3[3]	Male	18	congenital choledochal cyst	11	11.2	16	Three times, laparotomy for hemostasis	methylprednisolone IVIG plasmapheresis for four times	PCC fresh frozen plasma cryoprecipitate\ FV is ineffective, use rFVII for rapid hemostas
4[4]	Female	5	Intussusception/intestinal perforation	3	<1	6-60	Partial small intestine resection	prednisone rituximab	rFVII
5[5]	Male	12	Forearm hematoma	2	5	33.6	NA	prednisone	aAPCC ineffective rFVIIfor rapid hemostas
	Female	7	congenital choledochal cyst	8	1	2.6-5.6	One time, laparotomy for hemostasis	methylprednisolone rituximab	aAPCC ineffective rFVIIfor rapid hemostas rFVIII
	Female	13	Forearm hematoma	2	1.42	4.3	Muscle incision and decompression, and removal of necrotic tissue	methylprednisolone rituximab	rFVIII

Figures

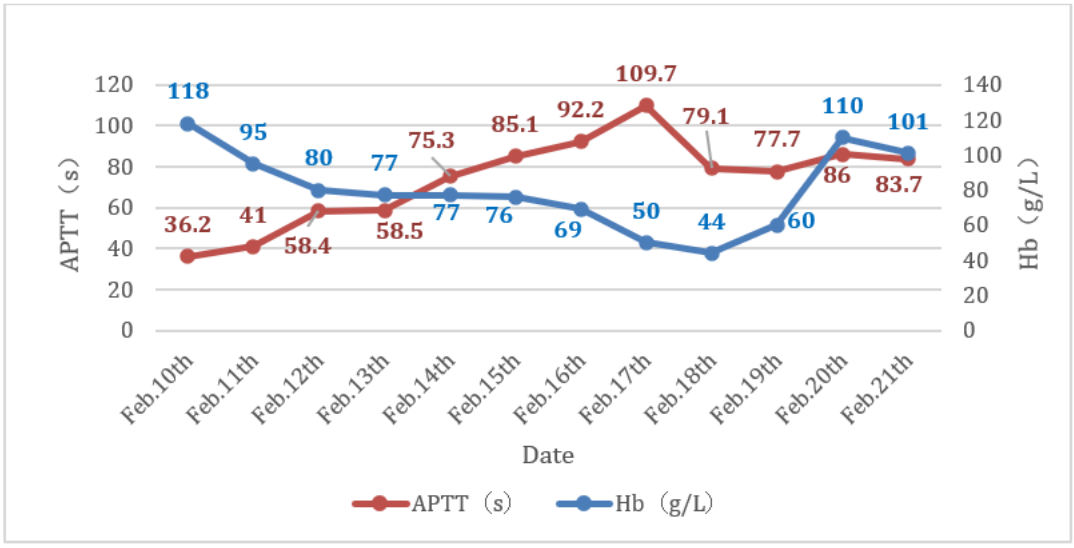


Figure 1

The changes in APTT and hemoglobin values after surgery

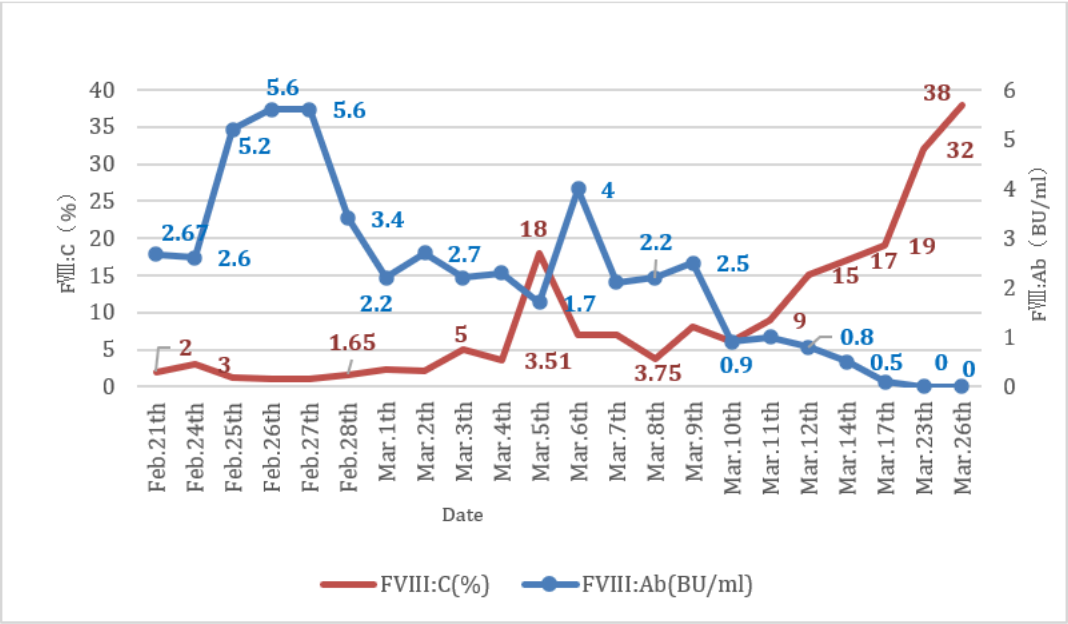


Figure 2

Changes of FⅧ:C and FⅧ:Ab during hospitalization