Case Report

Clinical Assessment of Severe Hemolysis in a 15-Month-Old Infant With Tetralogy of Fallot Undergoing Surgical Repair During Cardiopulmonary Bypass: A Case Report

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ABSTRACT

Some degrees of hemolysis are probable in pediatric patients receiving cardiopulmonary bypass. Nonetheless, severe hemolysis, even in premature infants undergoing cardiac surgeries, is rare. When hemolysis happens in a neonate or infant receiving cardiopulmonary bypass, numerous causes, including erythrocyte membrane defects, hemoglobinopathies, iso-immunization, undiagnosed enzyme abnormalities, and acquired conditions such as sepsis or drug interactions, should be considered. Urine discoloration may be considered a hemolytic reaction secondary to blood transfusion; still, in mild degrees of hemolysis due to mechanical trauma, this discoloration may not be noticed. One type of acute hemolytic reaction is immunological, which may happen secondary to the interaction between the recipient's antibodies and the donor's antigens, although most severe cases of hemolytic anemia are secondary to ABO incompatibility
In this case report, we describe a 15-month-old infant undergoing surgical repair for tetralogy of Fallot, who developed hemolysis during cardiopulmonary bypass. We also discuss the case's diagnostic workup and therapeutic management. ***(Iranian Heart Journal 2022; 23(3): 144-149)***

KEYWORDS: Hemolysis, Cardiac surgical procedures, Cardiopulmonary bypass

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The potential causes of hemolysis during heart surgeries are wide-ranging, including hemolytic reactions secondary to blood transfusion, cardiopulmonary pump circuits, mechanical trauma to red blood cells following suction, the production of oxygen-free radicals and the subsequent activation of the complement system and the inflammatory process, different types of inherited hemoglobinopathies, complications from the infusion of fluids, and other therapeutic measures during cardiopulmonary bypass (CPB).[1] Urine discoloration may be considered a hemolytic reaction secondary to blood transfusion; nevertheless, in mild degrees of hemolysis due to mechanical trauma, this discoloration may not be noticed, which can lead to significant mortality and morbidity.
In the case of severe hemolysis and in order to improve the prognosis, all clinical team

members of the patient should participate in its management.[2] In this case report, we describe a 15-month-old infant undergoing surgical repair for tetralogy of Fallot, who developed hemolysis during CPB. Additionally, we discuss the case's diagnostic workup and therapeutic management.

Case Report

The patient was a 15-month-old child, 9.5 kg in weight and 75 cm in height. The child was a known case of tetralogy of Fallot and a candidate for total surgical repair.

In the preliminary history taken from the parents, no disease was mentioned, except a heart abnormality that has been followed up on since birth. Preoperative clinical examinations were acceptable.

The results of preoperative lab studies, including biochemistry, coagulation, and U/A tests, were within the normal range. The patient's blood type was O+. Echocardiographic findings were in favor of tetralogy of Fallot. Upon the child's arrival at the operating room, standard monitoring, consisting of pulse oximetry, electrocardiography, and noninvasive blood pressure, was started. The patient had a blood pressure of 110/75 mm Hg, a pulse rate of 125 beats per minute, and an SaO_2 level of 85%.

Anesthesia was induced with inhaled sevoflurane because of the unavailability of a previously accessed peripheral vein. After a relative loss of consciousness, intravenous access with a 22G catheter was established in the right saphenous vein, and anesthesia induction was continued with cisatracurium (2 mg), fentanyl (50 µg), and midazolam (1 mg). The patient was intubated with a 4.5 mm uncuffed endotracheal tube. During anesthesia induction and intubation, no significant hemodynamic change was noted. The patient was connected to the anesthesia machine under pulse pressure variation (PPV), and capnography monitoring was commenced. An arterial line in the left radial artery and a central venous line in the right internal jugular vein were placed. Cerebral oximetry was established. The anesthesia level was maintained using a compound infusion of cisatracurium (2 µg/kg/min), fentanyl (0.2 µg/kg/min), and midazolam (0.25 µg/kg/min) during surgery. After a sternotomy, the heart was exposed by the surgeon. For the establishment of extracorporeal circulation, 400 IU/kg of intravenous heparin was infused, and the patient was supported by CPB. After about 15 minutes, urine discoloration in the urine bag, which was connected via an internal urinary catheter, was noticed. The discoloration was the only visible sign, while other clinical parameters such as blood pressure, heart rate, and arterial and cerebral O_2 saturation levels were within the normal range. As the first therapeutic step, priming with previously used blood was stopped, and the blood bag label was checked, which was consistent with the patient's demographic information and blood type. However, for the confirmation of this consistency, the blood bag and an arterial blood sample of the patient were sent to the central lab. No ABO or Rh inconsistency was reported.

Simultaneously, another blood sample was sent to the laboratory for complementary tests, including aspartate transaminase, alanine transaminase, lactate dehydrogenase, haptoglobin, non-ABO blood groups, arterial blood gas, and biochemistry. The results are demonstrated in Table 1 and Table 2.

Table 1: Complementary lab tests performed during surgery

	Units	Results	Reference Values
Haptoglobin	g/L	0.1	0.3-2
LDH	IU/L	1576	Up to:480
AST	IU/L	99	5-40
ALT	IU/L	15	5-40

Table 2: Complementary lab tests performed during surgery

ABG							Electrolytes							
PH	PO_2	O_2 sat	PaO_2	HcO_3	TcO_2	BE	Na	K	Hb	Hct	BS	lactate	cl	Ca
7.44	459	100	27	18	19	-4	128	6.1	9.1	29	120	2.7	105	1.5

Table 3: Serial lab tests during 3 days of ICU admission

Parameters	Units	Normal Values	First 24 Hours of ICU Admission	Second 24 Hours of ICU Admission	Third 24 Hours of ICU Admission
Hb	g/dL	11-14	7.5	6.2	9.1
HCT	%	35-45	22.2	18.6	27.4
BUN	mg/dL	7-20	12	12	23
Cr	mg/dL	0/6-1/4	0.6	0.5	0.7
AST	IU/L	5-40	99	75	45
ALT	IU/L	5-40	15	20	18
LDH	IU/L	Up to 480	1576	995	570
PT	Second	14	21.3	20.5	21.4
PTT	Second	30-40	35	28	3.7
INR	-	1	1.6	1.5	1.57

A urine sample from the patient's urinary catheter was taken. The results were as follows:

- Appearance: semi-clear
- Color: red
- RBC: 0-1

The first K serum level after the initiation of CPB was 6.1 mg/L. Nonetheless, since there were no electrocardiographic changes or other clinical indications for treatment, no particular action was taken except for the administration of 1 mg/kg of bicarbonate, repeated twice for renal protection based on the ABG results and the urinalysis.

Further, according to the ABG results and the urinalysis and with the aim of renal protection and alkaline urine flow, 1 mg/kg of bicarbonate was administered, which was repeated twice. Additionally, fluid resuscitation with normal saline was continued until the urine output reached 2–3 mL/kg/h.

During CPB support and after disconnection from the circuit, arterial blood gas, biochemistry, pH, and hematocrit were measured every 1 hour and corrected in case of any abnormality. During the surgery and CPB support, the levels of hemoglobin and hematocrit were within the acceptable range. At the end of the surgery, the patient was disconnected from CPB with the aid of milrinone (0.5 µg/kg/min) and epinephrine (0.05 µg/kg/min). Heparin reversal was performed using protamine, and blood products (fresh frozen plasma: 2 units and platelets: 2 units) were transfused. The approach to unpredicted hemolysis during CPB is depicted in Figure 1.

Still intubated, the patient was transferred to the intensive care unit (ICU) and placed under the direct supervision of internal, pediatrics and cardiology services. The child was followed up by serial lab tests, including hemoglobin, hematocrit, blood urea nitrogen, creatinine, alanine transaminase, aspartate transaminase, the prothrombin time, the partial thromboplastin time, and the international normalized ratio (Table 3).

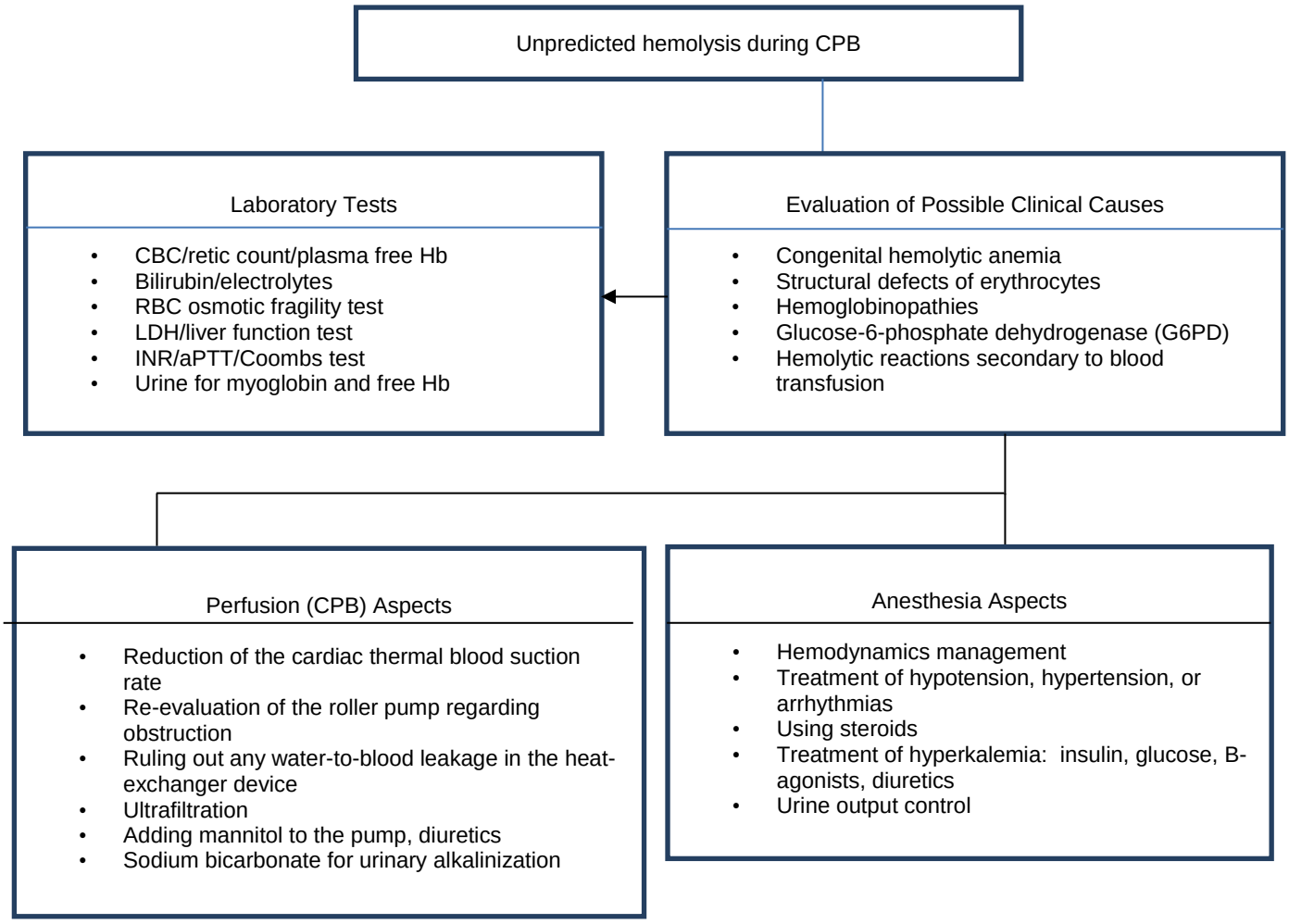

Figure 1: The approach to unpredicted hemolysis during CPB is presented herein.
CPB, Cardiopulmonary bypass

No pathologic factors such as hemoglobinopathies, enzyme abnormalities, or blood type abnormalities were detected. However, given the patient's hemoglobin and hematocrit abnormal levels, O− packed cell transfusion was suggested by the hematologist, and it was performed during the second day of ICU admission. Finally, on the fourth postoperative day, when urine discoloration was resolved, and the clinical and laboratory test results were stable, the patient was discharged from the ICU.

DISCUSSION

Following trauma to the red blood cell membranes, hemoglobin is released into the plasma, and hemolysis occurs. Depending on the amount of free hemoglobin in the plasma, damage to the body organs may happen. Free hemoglobin reduces nitric oxide synthesis; as a result, thrombosis formation and vasoconstriction may ensue. This process can cause multiorgan damage, including damage to the heart, the gastrointestinal tract, lungs, and the genitourinary system.[1]

There have been several reports of some degrees of hemolysis during CPB in pediatric patients; however, severe hemolysis is rare even in premature infants undergoing heart surgeries. When hemolysis occurs in a neonatal or infant on CPB support, several causes such as abnormal erythrocyte wall

membranes, hemoglobinopathies, iso-immunization, undiagnosed enzyme abnormalities of erythrocytes, and acquired conditions (eg, sepsis and drug interactions) should be considered.[2]

Acute transfusion-induced hemolytic reactions occur following damage to the transfused erythrocytes or recipient erythrocytes. In patients under anesthesia, the presentation of hemolysis could be in the form of hypotension, hemoglobinuria, and bleeding conditions.[1]

One type of acute hemolytic reaction is immunological, which may occur secondary to the interaction between the recipient's antibodies and the donor's antigens or vice versa, or rarely due to the interaction between another antibody and antigen in the donor's blood. Although most severe cases of hemolytic anemia are secondary to ABO incompatibility, this type of hemolysis can be due to alloantibodies from previous transfusions or pregnancies, which act against antigens other than ABO.[2]

When the possibility of hereditary hemolytic anemia is considered, but no evidence for this diagnosis is detected in the peripheral blood smear, sickle-cell anemia and spherocytosis are ruled out. Additionally, when laboratory tests are negative for G6PD and nocturnal paroxysmal hemoglobinuria, investigations should be focused on hemolytic reactions induced by cardiopulmonary pumps.[2] In our patient, these findings, namely peripheral blood smear and enzyme tests, were negative.

Another significant factor in the case of hemolysis during CPB is osmotic and mechanical damage. Severe hyperthermia can be associated with an acute hemolytic reaction due to blood transfusion.[1] In our patient, neither the primed blood nor the patient's blood was exposed to high temperatures.

Mixing of blood and water at the level of the oxygenator during extracorporeal circulation (CPB) can be a cause of hemolysis, although this rarely happens because the installation of control systems in the field by manufacturers has been efficaciously done.

Using hyperosmolar fluids as the prime solution can be another possible cause of hemolysis in patients undergoing CPB, which is considered a mechanical trauma factor.[4]

However, recently and owing to the alterations made to the circuit used in the tubes such as the optimization of the size and length of the tube and the use of centrifugal pumps instead of roller pumps, such damage has been decreased. In addition to medical treatment, ultrafiltration can be drawn upon to reduce edema. It is also worth noting that alternative therapies for appropriate perfusion should be utilized.[5] Meanwhile, care must be taken to avoid injuries due to the obstruction of the tubes and the strong suction of the return pathways as much as possible.[6] Some tumoral lesions may contribute to hemolysis reactions.[7]

CONCLUSIONS

Several articles on hemolysis during CPB have suggested that it can be due to pro-inflammatory and pro-oxidant causes associated with CPB, inevitably producing numerous toxic substances. A significant point in this regard is designing an algorithm for the prevention, diagnosis, and treatment of globular damage and its complications.

Conflict of Interest

The authors declare that there are no conflicts of interest.

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