

Anesthetic Considerations of a Surgical Patient with Favism: A Case Report

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Abstract

Rationale: Favism is a genetic disease of Glucose 6 phosphatase dehydrogenase (G6PD) deficiency in human red blood cells. It is mainly due to the mutation of G6PD gene encoded on the X chromosome, which leads to the decrease of G6PD activity or deficiency. G6PD plays important roles in the metabolic process of human body. One of them is to protect the integrity of the erythrocyte membrane. When the body is lack of G6PD or its activity is reduced, the patient is prone to hemolysis after eating oxidant, such as fresh broad bean, or under strong stress.

Patient concerns and diagnoses: A 43 year old male patient diagnosed with lumbar intervertebral disc herniation was hospitalized and planned for a surgery of the lumbar spine under general anesthesia. The patient was diagnosed as favism at an early age, but in later growth and life there was no hemolysis due to the doctor's instructions.

Anesthesia: We chose total intravenous anesthesia and avoided some drugs which may induce hemolysis. During the operation, we monitored the heart rate, blood pressure, blood gas and urine indicators to determine whether the patient had hemolysis and actively deal with it.

Result: During the process, the patients' circulation and respiration was stable, the operation was smooth, and we followed up him the first-third 7th day after the surgery. The patients recovered well and had no acute hemolytic reaction. It can be seen that our treatment may provide some experience for postoperative anaesthesia of patients with broad bean disease.

Keywords: Favism; Glucose 6 phosphatase dehydrogenase (G6pd) deficiency; Anaesthesia; Hemolysis; Case report

Introduction

Favism (G6pd Deficiency) is the commonest enzymatic disorder of red blood cells (RBC) in humans, affecting about 400 million people all over the world [1,2]. It's a common complication is acute hemolysis.

Some drugs, surgical stimulation, postoperative infection, hyperglycemia, etc. are high risk factors for acute hemolysis in patient with G6PD deficiency [3].

Treatment of haemolytic reactions consists of discontinuation of the offending agent and maintenance of urine output by infusion of crystalloid solutions, diuretics and alkalization of urine.

However, general anaesthesia typically masks the immediate signs of hemolysis, proper management and monitoring are particularly important for anaesthesia.

Here, we report a possible anaesthesia management process of patients with favism in our case and hope to provide some experience.

Case Report

A 43 year old man (height 178 cm, weight 82 kg) recently had suffered a pain of right lower limb more than 2 months and felt worse a

week ago. After examined by CT and MRI, he was diagnosed with lumbar intervertebral disc herniation and spinal canal stenosis during hospitalization.

Then, our surgeon explained the condition to the patients and their family, and got informed consent of a posterior decompression of vertebral lamina. When he was six years old, he suffered from skin stasis due to eating broad beans.

His doctors diagnosed him as a favism patient through blood analysis (including a rapid fluorescent spot test detecting the generation of NADPH from NADP, Glucose-6-phosphate Dehydrogenase, erythrocyte fragility test, erythrocyte sedimentation rate and so on).

We learned despite of this illness, he still kept a normal life with the advice of his doctor and almost haven't suffered hemolysis from sixth.

Before the operation, we collected the patient's venous blood for a laboratory analysis (Table 1).

We found G6PD activity in our patient's red cell actually decreased, but the state of his blood still maintain stable.

Test item	Result	Notice	Normal range	Unit
G6PD activity	2.7	↓	8-15	U/gHb
The initial dissolution of red cell brittleness test	4.2	-	3.8-4.6	g/L
The total dissolution of red cell brittleness test	3	-	2.8-3.2	g/L
RBC	4.71	-	4.3-5.8	10 ¹² /L
Hb	137	-	130-175	g/L
HCT	42	-	40-50	%
Platelet	196	-	125-350	10 ⁹ /L

Table 1: The analysis of the patient's preoperative blood condition

Considering the patient's condition and operation needs, we decided to use total intravenous anaesthesia. After the admission, we performed central venous catheterization and radial artery catheterization under local anaesthesia in order to open central venous access and monitor ambulatory arterial blood pressure. At the same time, we also monitored electrocardiogram, oxygen saturation (SpO_2), pressure of end-tidal CO_2 (PETCO₂), airway pressure and BIS. In order to stabilize the patient's mood and anti-anxiety treatment, we used 40 ug Dexmedetomidine slowly for 20 min before the operation to calm the patient. 180 mg propofol, 25 mg sufentanil, 12 mg cisatracurium were used for anaesthesia induction and tracheal intubation under visual laryngoscope. Smoothly, we succeed in the process and control his breath by the anaesthesia machine with a moderate respiratory frequency (RF) and tidal volume (TV). Propofol, remifentanil and dexmedetomidine were maintained by target-controlled infusion (TCI) during the whole process.

The patient kept a prone position during the operation for the need of surgery. His airway pressure increased slightly but did not affect the respiration and circulation. The peak value of the airway pressure was lower than 30, and PETCO₂ was 35-45 mmHg. We timely deepened anaesthesia, when the surgeon began to scratch and other invasive operations. At the same time, a central venous pressure was measured every 30 min, and accordingly, intraoperative fluid infusion was guided.

After 30 min, we collected the patient's arterial blood and blood gas result. Also, we collected and recorded his urine, analyse its urine occult blood, urine protein, Urine Bilirubin and Urobilinogen, observed his skin and monitored his temperature. It is comforting that everything is normal. Since then, we did this every 30 min so as to master his whole condition and prepare for every possible emergency.

In view of the risk of acute haemolytic reaction in the patient's operation, we collected the blood of the patient by the surgeon's suction apparatus so as to maintain the stability of the blood circulation when the patient has an acute haemolytic reaction.

The amount of loss blood in the operation was 400-500 ml, the recovered blood was 100 ml, and the patients in the operation had a stable circulation and no haemolysis. Considering the risk of autologous blood transfusion for the patients with G6PD deficiency, there was a possibility of causing the rupture of red blood cells, so we recovered the patient's blood in the operation, but gave up transfusing to patients.

The surgeon's operation lasted 2 h, and the patient's state kept stable with our management. Finally, our patient gradually woke up, and then he was escorted back to the ward after 1 h in post anaesthesia care unit (PACU).

Besides, we went to the ward to follow up the patient on the first, third, seventh day after the operation. It was comforting that our patient was in a good condition without fatigue, fever, nausea, vomiting, dyspnoea, hypotension, skin bruises, bleeding, black urine and other acute haemolysis symptoms. And there was no obvious abnormality in laboratory tests such as Blood-RT, Urine-RT, and blood coagulation examination and so on.

Discussion

Although favism is an uncommon disease, but its complications are often urgent and serious, its clinical symptoms are often covered up in general anaesthesia and a lot of anaesthetic agents also induce paroxysm. During the perioperative management, it has brought some challenges for the anaesthesiologist, so it is particularly important to understand of its pathogenesis, treatment scheme in detail.

Favism is also called glucose 6 phosphatase dehydrogenase (G6PD) deficiency. This is a genetic disease. The gene encoding G6PD is located on the X chromosome [1,2]. Its mutation often affects G6PD, which is involved in series of biochemical reactions in the red cells [3].

There were two glucose metabolisms called the Embden-Meyerhof pathway and the hexose monophosphate shunt, while G6PD is the key enzyme [4]. During the process, nicotinamide adenine dinucleotide phosphate (NAPDH) is produced continuously. It is a hydrogen donor in the body, which can maintain the reduction of glutathione (GSH).

Reduced GSH is an important antioxidant *in vivo*, and it can protect the integrity of erythrocyte membrane for red blood cells. In the patients with G6PD deficiency, the pentose phosphate pathway is not normal and does not produce enough NADPH to maintain the reduction of GSH [1]. In this case, red cells are easily affected by oxidative stress and dissolve (Figure 1).

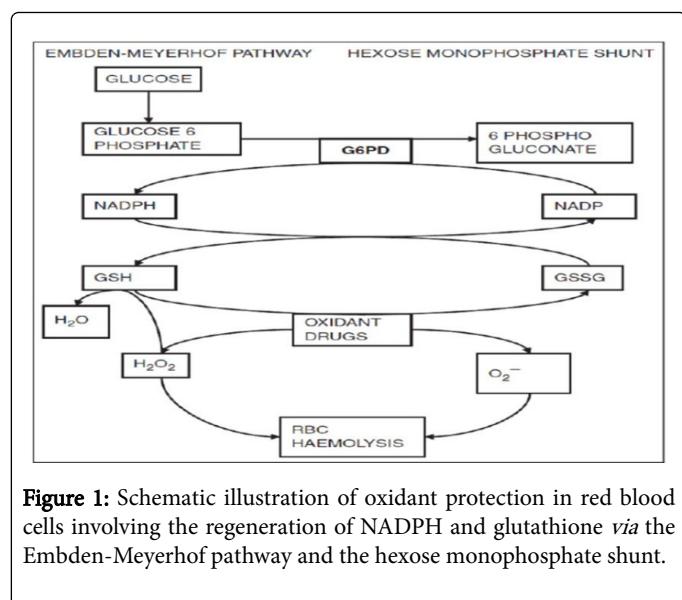


Figure 1: Schematic illustration of oxidant protection in red blood cells involving the regeneration of NADPH and glutathione *via* the Embden-Meyerhof pathway and the hexose monophosphate shunt.

G6PDd is found worldwide with varying frequencies depending on the region and ethnic group. The overall G6PDd allele frequency across malaria endemic countries is estimated to be 8%, corresponding to approximately 220 million males and 133 million females. The highest G6PDd prevalence has been found to occur in sub-Saharan Africa and the Arabian Peninsula, and the G6PD A- variant is the most predominant allele in the African continent, whereas the G6PD Mediterranean allele is more frequent in Western Asia [5]. Patients with favism often live a normal life, but they will suffer haemolysis after eating oxidant food and drugs, operation and infection [4-7]. The clinical manifestations include a sudden increase of temperature, yellow dye in the skin, hemoglobinuria, nausea, vomiting, pale face, irritability, respiratory urgency, weak pulse, and so on [8-10]. The main treatment for G6PD deficiency is avoidance of oxidative stressors. Rarely, anaemia may be severe enough to warrant a blood transfusion. Splenectomy generally is not recommended. Folic acid and iron potentially are useful in haemolysis, although G6PD deficiency usually is asymptomatic and the associated haemolysis usually is short-lived. Antioxidants such as vitamin E and selenium have no proven benefit for the treatment of G6PD deficiency. Research is being done to identify medications that may inhibit oxidative-induced haemolysis of G6PD-deficient red blood cells [11]. There are several implications for these favism patients in clinical work. First of all, a number of drugs (Table 2) can precipitate haemolysis in G6PD-deficient subjects. These drugs can interact with haemoglobin and oxygen, leading to the intracellular formation of hydrogen peroxide (H_2O_2) and other oxidizing radicals. As these oxidants accumulate within enzyme-deficient cells, haemoglobin and other proteins are oxidized, leading to loss of function and cell death. Then, infection is probably the most common factor inciting haemolysis in G6PD-deficient subjects [12,13]. The factors responsible for accelerated destruction of G6PD-deficient red cells during infection are not known. One possible explanation is that the red cells are damaged by oxidants generated by phagocytising macrophages-a mechanism similar to that seen with drug-induced haemolysis [14-16]. In addition, certain metabolic conditions, such as diabetic ketoacidosis, also appear to be capable of triggering destruction of G6PD-deficient red cells [12,13]. Both acidosis and hyperglycaemia are potential precipitating factors, and correction of the abnormalities is associated with reversal of the haemolytic process.

In some diabetic patients, occult infection may be a common trigger for inducing both acute haemolysis and ketoacidosis. General anaesthesia typically masks the immediate signs of haemolysis, making it difficult to identify a haemolytic crisis while the patient is asleep. Even hypotension, which could be a result of haemolysis, may be attributed to other causes in an anaesthetized patient. The appearance of free haemoglobin in plasma or urine is presumptive evidence of a haemolytic reaction. Treatment consists of discontinuation of the offending agent and maintenance of urine output by infusion of crystalloid solutions and diuretics such as mannitol and furosemide. As anaesthetists, we always need to focus on anaesthetic methods and anaesthetics when they meet a patient with favism. If possible, local infiltration anaesthesia, peripheral nerve block and spinal anaesthesia are much safer. But if we choose general anaesthesia, we must avoid some agents that can induce haemolysis. General anaesthetics are usually given by inhalation or by intravenous injection [17]. Several drugs are used intravenously, alone or with other drugs, to achieve anaesthesia or as components of balanced anaesthesia. There is a study shown that halothane has no effect on G6PD activity, but Isoflurane and Sevoflurane have [18]. However, halothane, which is no longer used in most countries, has strong side-effect and can easily lead to respiratory inhibition, bradycardia and arrhythmia due to excessive anaesthesia. In our case, we chose total intravenous anaesthesia without inhalation anaesthetics. Additionally, diazepam or midazolam, which have inhibitory effects on G6PD activity together with Isoflurane or Sevoflurane may increase severity of haemolysis [18]. Furthermore, Dexmedetomidine provides a largely natural induction of sleep, and thus is unlikely to cause respiratory suppression. Dexmedetomidine can also induce concurrent antioxidant, anti-inflammatory, and sedative effects [19,20]. Therefore, it is really a good choice for general anaesthesia. And also it is known that propofol and opioids can calm the sympathetic nervous system, relieve the pain and the stress of operation, so they are also the safe choice [21].

Drug category	List of name
Unsafe	
Antimalarial	Primaquine
	Chloroquine
	Quinine
Sulfonamides	Sulfapyridine
	Sulfapyridine
	Sulfamethoxypyridazine
	Sulfamethoxazole
	Acetanilide
Antipyretic analgesics	Aspirin
	Acetaminophen
	Aminopyrine
Antibacterials	Nitrofurans
	Chloramphenicol
	Aminosalicylic acid
	Nalidixic acid

Anthelmintic	Niridazole
	Stibophen
Chinese herb	Mint
	Camphor
	Naphthal
	Szechwan gentian
	Bear gall
Others	Vitamin K
	Probenecid
	Dimercaprol
	Broad bean
	Camphor ball
Anaesthetic agents	
Safe	Halothane
	Dexmedetomidine
	Ketamine
	Fentanyl
	Propofol
Unsafe	Diazepam
	Isoflurane
	Sevoflurane
	Procainamide
	Lidocaine

Table 2: Drugs and Chemicals Associated With Hemolysis in G6PD Deficiency

All of these, we would like to make four particular suggestions:

1. Exposure to oxidative drugs in the G6PD-deficient patient should be avoided.
2. Ketamine, fentanyl, propofol, midazolam, prilocaine and halothane are safe for perioperative use in the G6PD-deficient patient.
3. Use of isoflurane, sevoflurane and diazepam should be avoided in the G6PD-deficient patient.
4. Perioperative hypothermia, acidosis, hyperglycaemia and postoperative infection can precipitate haemolysis in the G6PD-deficient patient.

Conclusion

It can be seen that the complications of favism are often serious and urgent. And how to manage in perioperative period is of great importance. The most effective management strategy is to prevent haemolysis by avoiding oxidative stressors.

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