

Prolonged Severe Anemia and Transfusion Refusal Following Abdominal Surgery. A Case Report and Short Literature Review

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Introduction

Founded in late 1870, The Jehovah Witness Christian Movement counts more than five million members in over 230 countries [1]. Basing the stand on passages from the Bible, members of this sect refuse blood transfusions. Acceptance of blood by a Jehovah Witness would entail exclusion and excommunication from the church, resulting in social isolation by their own relatives and friends. It was estimated that the head quarter church group overseeing Jehovah Witnesses (the so-called Watchtower), banned from fellowship some 40,000 members or approximately 1% of its memberships annually [2].

Even if survival with extremely low hemoglobin concentrations has been reported in literature, in case reports, case series, and retrospective studies [3-6], very low level of hemoglobin and consequent reduction in O₂ delivery, are nearly unanimously considered detrimental for patient *quoad vitam* prognosis and, where sudden significant bleeding occurs, can be reached very quickly. In the case of Jehovah's Witnesses, alternatives to the transfusion of blood products as routine treatment must be sought. Lots of solutions have been proposed and studied over the years. They range from pharmacological management of preoperative anemia (administration of iron, B12 vitamin, folic acid and erythropoietin) when the clinical conditions of the patients permit sufficient delay to an elective surgery, as well as correction of pre existing nutritional deficits [7], acute normovolemic hemodilution [8,9], minimization of intra operative blood losses and optimization of tolerance of anemia [10].

Nevertheless, most of proposed techniques are difficult or impossible to implement in the setting of urgent surgery, especially when massive hemorrhage is not expected.

In this case report, we present a Jehovah Witness affected by liver failure with portal hypertension due to chronic alcohol abuse and chronic anemia, who developed hemorrhagic shock during urgent umbilical hernia repair for strangulation. Patient refusal to receive blood transfusion was respected throughout general anaesthesia and subsequent intensive care unit and ward stay.

Case Report

A 71 year old Caucasian man, with a three year history of inguinal and umbilical hernia, presented to the hospital due to worsening of symptoms, with distension, tenderness and pain of the umbilical bulge. In 2009 elective repair was not undertaken due to refusal by the patient to subscribe written informed consent for anesthesia, comprehensive of consent for eventual transfusion. Moreover, the patient suffered severe comorbidity due to previous alcohol addiction: hepatic cirrhosis with portal hypertension and esophageal varices, portal hypertensive

gastropathy, chronic pancreatitis, chronic anemia (preoperative values of 7.4 g/dl). General surgeon on duty set indication for urgent surgical repair, and the patient, asked by the anesthetist, confirmed and subscribed his absolute and unequivocal refusal to receive blood transfusion any time before, during or after the surgery. The patient was fasted since more than ten hours and presented contraindication (coagulopathy due to liver failure) to regional anesthesia, so general anesthesia was induced with Propofol, Cis-Atracurium and Remifentanyl and maintained with Sevoflurane in O₂ enriched air (inspiratory fraction 0.4). Orotracheal intubation was performed uneventfully. After midline incision, inadvertent lesion of a large vein in the context of periumbelical portosystemic shunt (caput medusae), resulted in sudden massive hemorrhage (estimated blood loss of 2 l) leading to shock. Infusion of large amounts of fluids was initiated, as well as dopamine infusion at a rate of 6 µg/kg/min and the hemorrhage was eventually stopped by the surgeon. By the end of the procedure, which lasted 60', 2500 ml of crystalloids (Ringer Lactated), 1000 ml of synthetic colloids (4% Hydroxyethyl starch) and 200 ml of natural colloids (20% Human Albumin), had been infused. Patient mean arterial pressure was 60 mmHg, hemoglobin concentration 3.6 g/dl (hematocrit 12.4%), prothrombin time (International Normalized Ratio) 2.15, activated thromboplastin time 46 seconds. The patient was then transferred to intensive care unit. His Acute Physiology and Chronic Health Evaluation score (APACHE II) score was 18. Mechanical ventilation and sedation (Midazolam) were not discontinued, in attempt to limit as much as possible oxygen consumption. Supportive therapeutic measures included: subcutaneous erythropoietin (60 µg on admission, then once a week), intravenous Fe Gluconate (ten 177 mg vials over eight day of Intensive Care Unit stay), folic acid (15 mg/die), Vitamin B12 (1mg/die), Vitamin K (100 mg every 2 days) as well as nutritional supplementation (total parenteral nutrition, followed by enteral nutrition from the fifth post-operative day), electrolyte and micronutrients supplementation as needed and Protromplex* (coagulation factors II, IX and X 600 UI each, intravenous on admission). Diagnostic phlebotomies were limited as much as possible. Hemoglobin reached a nadir of 2.9 g/dl on the fourth postoperative day, and then increased to 4.5 g/dl the seventh postoperative day (mechanical ventilation was then discontinued and orotracheal tube removed). Sedation had been discontinued since the second post-operative day to permit the psychiatric consultant to ascertain the patient ability to decide to persist in his refusal to transfusions, despite imminent danger for his life. The 9th postoperative day, the patient was dismissed to the surgical ward from which was discharged on the 24th post-operative day without major complications: his hemoglobin had reached 8.3 g/dl, hematocrit 27%. During all stay in the surgical ward, hemoglobin never fell below 6.7 g/dl and varied between 6.7 and 8.9 g/dl.

Sixty days after the first operation, the patient was re-admitted to the hospital because of development of incisional strangulated hernia, ileal perforation, peritonitis and septic shock. Peritoneal lavage and surgical repair of perforation and incisional hernia were performed, and the patient was readmitted to Intensive Care Unit in extremely serious conditions (APACHE II score of 33). His hemoglobin was 7.3 g/dl (preoperative value 8.9 g/dl). Hepatic function had worsened to end stage since the first hospital stay two months before: Child Turcott Pugh score was 12 and the patient showed clear signs of hepatic encephalopathy as he was weaned from sedation. During the second Intensive Care Unit stay, hemoglobin levels never fell below 5 g/dl, nearly twice the lowest level reached during first episode. Despite high intensity care, he died 13 days later for multi-organ failure.

Discussion

The refusal of a Jehovah's witness patient to undergo blood transfusion constitutes an important ethical and legal problem. The need to adopt a life saving therapeutic measure clashes with the patient's right to choose based on one's system of values and religious beliefs. In the context of critical and perioperative medicine difficulties are increased by acute and unpredictable events that require a prompt intervention and hinder the adoption of measures made to optimize the patient's ability to face acute massive blood loss.

Our patient was severely chronically ill when he came to our attention. For the discussed matter, it is particularly interesting to examine his preexisting state of chronic anemia, which was one of the reasons that prevented the surgical team to correct electively his inguinal hernia in the first place. Both hepatic cirrhosis and alcohol abuse, even if the latter was not present since a couple of years in our patient (the patient quit drinking when he became a Jehovah Witness), are known causes of chronic anemia, with several mechanisms [11,12]. Dilutional pseudoanemia characterizes advanced liver disease [13]; moreover unapparent bleeding from several causes (portal or alcoholic gastropathy, hemorrhoids) can lead to profound anemization [14]. Compromised synthesis Vitamin K dependent coagulation factors (II,VII,IX,X), as well as alterations in number and function of platelets, are other known predisposing cause to chronic bleeding in these patients [14].

Several indications are reported in the literature to reduce the need of transfusion, especially in the context of election surgery with moderate to high hemorrhage risk [15]. A painstaking pre-operative assessment of the patient is essential, and ought to be carried out at least 4-8 weeks before surgery. Identifying the causes of a potential anemia allows to institute appropriate therapy, if there is proven iron deficiency, it must be corrected [16-18], by giving oral or intravenous iron. The administration of B12 vitamin and folic acid are described as definitely effective therapies in the case of documented deficit, or potentially useful in the context of a multimodal approach to erythropoietic support. Usage of erythropoietin is recommended in patients for whom iron deficiency anemia has been ruled out, several studies have highlighted its effectiveness in reducing the use of transfusions in different types of surgery [17-19]. In selected cases it was possible to manage Jehovah's witness patients without resorting to transfusions for major surgery operations with high hemorrhagic risk [20]. Suspension or correction of anticoagulant therapies, the correction of potential deficiencies in coagulation factors, the administration of procoagulant (such as tranexamic acid) [21,22] agents all represent additional viable strategies, the application of which has to be contextualized in the individual patient based on the

entity of hemorrhagic and thrombotic risk. In our case, these strategies were not taken into account before surgery, as massive blood loss was totally unexpected.

In the case of the patient undergoing urgent surgery, most of these measures cannot be applied. In this case the management of severe acute intraoperative bleeding, in itself a dramatic event even when all available resources can be drawn upon, becomes especially complex. In this context it is necessary to intervene on all factors conditioning the supply of oxygen to tissues in order to compensate, as much as possible, the severe reduction in hemoglobin. It is only possible to act on cardiac output by administering fluids, crystalloids and colloids, and inotropic and vasopressor drugs, therefore enhancing the compensation mechanisms that are naturally activated in the healthy subject to ensure continuous perfusion and tissue oxygenation.

The case we described allows for highlighting of part of these issues. In our patient surgery was an emergency procedure and therefore had to be carried out urgently. The patient had presented chronic anemia likely due to his basal pathology and previous alcohol abuse. This basal condition was made much worse when unexpected and massive acute intra-operative bleeding did occur. Support of cardiovascular function obtained with fluidotherapy and vasopressors, the optimization of respiratory exchanges and the unloading of work of breath determined by mechanical ventilation, allowed in the acute situation to keep the patient alive while waiting for erythropoietic support therapies to increase emoglobin levels. One possible advantage was that since his anemia was chronic, the patient was well adapted to it. Of course it is possible that on the long term, the anemia might have had a negative impact on the tissues repair mechanisms, thus causing further complications, which eventually proved irreversible. Anyway, it is possible to obtain a good outcome for a surgical wound even with very low hematocrit values given that a good perfusion is warranted [23], so in the last decades always more restrictive transfusion strategies were adopted. Several authors evaluated the correlation between anemia and wound healing, with conflicting results [24-26]. Minimal hemoglobin level that definitely compromises the process of wound healing is not clear. In animals, the effect of acute intraoperative anemia seems to determine an unfavourable outcome [27]. Even if our patient had other risk factors for a compromised healing (particularly hepatic failure), we think that prolonged extreme anemia in the postoperative period may have played an important role in his outcome.

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