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ANESTESIOLOGIA

Official Publication of the Brazilian Society of Anesthesiology
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CLINICAL INFORMATION

Anesthesia for a patient with Fanconi anemia for developmental dislocation of the hip: a case report

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Abstract   Fanconi anemia is a rare autosomal recessive inherited bone marrow failure syndrome with congenital and hematological abnormalities. Literature regarding the anesthetic management in these patients is limited. A management of a developmental dislocation of the hip was described in a patient with fanconi anemia. Because of the heterogeneous nature, a patient with fanconi anemia should be established thorough preoperative evaluation in order to diagnose on clinical features. In conclusion, we preferred caudal anesthesia in this patient with fanconi anemia without thrombocytopenia, because of avoiding from N_2O, reducing amount of anesthetic, existing microcephaly, hypothyroidism and elevated liver enzymes, providing postoperative analgesia, and reducing amount of analgesic used postoperatively.

Introduction

Fanconi anemia (FA) is a rare autosomal recessive inherited bone marrow failure syndrome, characterized by increased chromosomal fragility, and generally associated with multiple congenital anomalies.[1]

Literature regarding the anesthetic management in these patients is limited. A management of a developmental dislocation of the hip was described in a patient with FA.

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Case report

A 2.5-year-old girl, born to first degree consanguineous parents presented with a failure to walking. She was delivered by spontaneous vaginal in time and small for gestational age, weighing 2.2 kg at birth. Physical examination revealed retarded growth (5.7 kg weight and 68 cm height) with absence of bilateral thumb (Fig. 1), café au lait spots at back, hypopigmentation at abdomen, generalized hyperpigmentation, and microcephaly.

Laboratory investigations did not reveal pancytopenia; hemoglobin, WBC and platelets were 11.4 g dl^{-1}, 7.4×10^3 dl^{-1} and 162×10^3 dl^{-1} respectively. ALP, GGT and

Figure 1   Absence of the thumb.

LDH levels were elevated and 564, 420 and 289 respectively. Ultrasound revealed hypoplastic horseshoe kidney.

The patient's medication included only levothyroxine because of hypothyroidism. No medication exist related FA.

Other investigations including electrolytes, BUN, creatinine, bilirubins, AST, ALT, prothrombin time, partial thromboplastin time, ECG, and echocardiogram were normal. The patient was euthyroidic.

Evaluation of the airway revealed no abnormalities, except microcephaly, and vital signs were normal. Adequate blood and blood products ordered depending on the procedure.

No medication was administered prior to the procedure apart from antibiotics. Anesthesia was induced with 8% sevoflurane in 100% oxygen. After peripheral i.v. access was secured, she was turned to the left lateral position. Caudal block was performed by using a 22-gauge short-bevel needle under aseptic conditions with bupivacaine 0.25% at $1\,ml\,kg^{-1}$. After caudal blockade inhalation anesthesia was lowered to 0.5–1% in 100% oxygen in order to obtain 4 or 5 point of Ramsay sedation scale. Peripheral oxygen saturation (SpO_2), heart rate, noninvasive blood pressure and end-tidal CO_2 ($ETCO_2$) were monitored throughout surgery. Ventilation was maintained via an oxygen mask with $2\,L\,dk^{-1}$ fresh flow spontaneously (Fig. 2).

Whole procedure including open reduction and putting the limb in a plaster cast from induction to recovery lasted 140 min and was uneventful. Recovery was fast and uneventful. Postoperative analgesia was not required for ten hours.

Figure 2   The patient with facemask during surgery.

Discussion

Fanconi anemia is an autosomal recessive disorder in over 99% of cases with 25% risk to siblings.[1] The incidence of FA is approximately three per million and the heterozygote frequency is estimated at one in 300 in Europe and the USA,[2] 1/100 in Ashkenazi Jews and South African Afrikaners due to ''founder effect''.[1,3] Consanguinity has been implicated in its incidence.[3]

Clinical features of FA can be broadly divided into two categories: congenital abnormalities and hematological abnormalities, which may include altered skin pigmentation and/or café au lait spots, short stature (impaired growth hormone secretion), thumb or thumb and radial anomalies, hip anomalies, vertebral scoliois, rib anomalies, male hypogenitalism, mental retardation, anorectal atresia, duodenal atresia, microcephaly, eye anomalies (microphthalmia, strabismus, ptosis, nystagmus), structural renal defects, low-birth weight, developmental delay, abnormal ears or hearing, and cardiopulmonary defects.[1–3] The most important clinical features of FA are hematological. Pancytopenia is the usual finding and typically presents between the ages of 5 and 10 years, the median age of onset being 7 years.[1] Clinically, the affected FA patient may present with bleeding, pallor and/or recurring infections.[2] The major cause of death in FA is bone marrow failure, followed in frequency by leukemia and solid tumors. The projected median survival from all causes for more than 1000 cases reported in the literature is age 20 years.[3] Of patients thirty or forty percent lack obvious physical abnormalities.[1–3] There is great clinical heterogeneity even within a genotype (sibling may be phenotypically different).[1] The gold-standard screening test for FA is based on the characteristic hypersensitivity of FA cells to the crosslinking agents, such as mitomycin C (MMC) or diepoxybutane (DEB).[5] FANCA is the most common complementation group, representing about 70% of cases.[1] Androgen therapy (oxymetholone), cytokines (G-CSF and GM-CSF), and supportive therapies such as blood and platelet transfusions form the mainstay of treatment prior to allogeneic hematopoietic stem cell transplantation. Gene therapy is experimental. E-amino caproic acid may be used for symptomatic bleeding. Steroids are occasionally used.[1–3] FA frequently terminates in myelodysplastic syndrome and/or leukemia.[1] Hematopoietic stem cell transplantation (bone marrow, cord blood, or peripheral blood stem cells) may cure aplastic anemia and prevent myelodysplastic syndrome or leukemia.[2,3]

Patients with FA may present for procedures such as Hickman catheter insertion for bone marrow transplantation, limb reconstructive surgeries, splenectomy, gastrointestinal anomalies, congenital heart defects, trauma or other related and/or non-related indications. The insufficiency of literature regarding anesthetic management of this condition makes it difficult to estimate the real impact of individual anomalies on the perioperative management.[6] It is important to emphasize that of patients thirty or forty percent have no abnormalities.[1–3]

Because of the heterogeneous nature of the condition, FA is difficult to diagnose on clinical features.[2] A thorough preoperative evaluation includes airway examination, and hematological, cardiopulmonary, hepatorenal

and endocrine evaluation for any component of the disease or any complication of the treatment of the disease. For example hyperbilirubinemia and hepatomegaly with fatty infiltrates could be attributed to therapy with androgen. All transfusions and any transfusion reactions must be documented.[6] Adequate blood and blood products should be ordered depending on the procedure. No family member should be used as a blood product donor until it has been determined that a transplant will not be performed.[3] Leukocyte-filtered blood products should be used to reduce reactions and HLA sensitization in case of future stem cell transplant. Similarly, single-donor platelets are preferred to reduce the frequency of antibody formation.[3]

Because thrombocytopenia usually develops initially,[4] particularly, thrombocyte count should be evaluated. Repeated respiratory tract infections and neutropenic sepsis may be present because of pancytopenia. Children with neutropenic sepsis may have subclinical coagulopathy that should be corrected preoperatively.[7] In case of neutropenia, it is mandatory to maintain strict aseptic precautions while handling these patients. Bacterial and viral filters should be used in the breathing circuits.[6]

Endocrinopathies are a common feature of FA. In a prospective study of 54 FA patients, it was found that hypothyroidism, impaired glucose tolerance, hyperinsulinemia, and subnormal response to growth hormone stimulation.[7] A complete endocrine assessment should be made to detect these aspects. Patients, who are on steroid therapy, must be documented regarding replacement therapy, glucose monitoring, edema, hypokalemia, myopathy, infection, and gastric prophylaxia.

Drug therapy for FA may also have anesthetic implications. Some of the serious adverse effects of androgen include hepatomegaly, cholestatic hepatitis, and elevated liver enzyme levels.[3] Androgens may increase the anticoagulant effect of oral anticoagulants (warfarin)[8] and may also increase insulin effects.[9] Adverse effects of G-CSF treatment relevant to anesthetic management include pericardial and pleural effusions and generalized capillary leak syndromes, which may result in interstitial pulmonary edema and arterial hypoxemia.[10]

Other drugs and chemicals causing acquired aplastic anemia should be avoided during the perioperative period. Medications interfere with platelet function should not be given to thrombocytopenic patients.[3] These include aspirin, antihistamines, and nonsteroidal anti-inflammatory drugs.[6]

Normal fasting regimes and minimal monitoring standards, if any indication exist, more monitorizations, should be applied throughout the perioperative period. Significant thrombocytopenia, if present, may preclude regional anesthesia. Infective endocarditis prophylaxis has to be considered for patients with cardiac involvement.[6]

A possible anesthetic consideration may include the avoidance of high inspired oxygen concentrations (FiO_2). There is sensitivity to oxygen-free radicals and to ionizing radiation.[1] Clarke et al. suggest that the sensitivity of FA group C cells to apoptosis induced by MMC is because of reactive oxygen species generation in the presence of high oxygen concentrations and not DNA cross-linking.[11] Low oxygen tension or antioxidants may be used to improve growth and decrease spontaneous or induced chromosome breaks in FA cells.[3]

In this case caudal anesthesia was preferred to avoid from N_2O, to reduce amount of anesthetic agent, to provide postoperative analgesia, and to reduce amount of nonsteroidal anti-inflammatory drugs and morphine.

Caudal epidural blockade is widely used to provide perioperative analgesia in pediatric practice. As a single injection, it offers a reliable and effective block for patients undergoing subumbilical surgery.[12]

Nitrous oxide-induced bone marrow depression is an additional concern. Some studies suggest that the use of nitrous oxide (N_2O) is harmful producing bone marrow suppression as it impairs methionine synthetase activity, disturbing folate metabolism and thus vitamin B12 metabolism.[13] On the other hand, we do not have any data in patient with FA.

In view of the hepatorenal derangement which can occur any time during the course of the disease, it is imperative to avoid anesthetic agents with potential hepatorenal toxicity. In this respect, it may be advisable to avoid halothane, long-acting muscle relaxants, nonsteroidal anti-inflammatory agents, and long-acting opioids such as morphine and pethidine.[6] Postoperative analgesia could be provided by caudal injection perfectly. Thus, amount of analgesic drug, such as nonsteroidal anti-inflammatory agents, morphine and pethidine, could be reduced. In this manner potential hepatorenal toxicity owing to analgesic agent could be avoided.

In conclusion, we preferred in the patient with FA without thrombocytopenia, because of avoiding from N_2O, reducing amount of anesthetic, existing microcephaly, hypothyroidism and elevated liver enzymes, providing postoperative analgesia, and reducing amount of analgesic used postoperatively.

Conflicts of interest

The authors declare no conflicts of interest.

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