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Anesthetic care of a patient with IGA deficiency for posterior spinal fusion

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Keypoints

1. Deficiency of immunoglobulin A (IgA), defined as low serum levels of IgA in the presence of normal serum levels of other immunoglobulins including IgG and IgM, is the most common primary immunodeficiency in patients more than 4 years of age.
2. While generally asymptomatic, patients with significantly depressed serum IgA levels are at risk for anaphylactic and anaphylactoid reactions during the administration of blood and blood products.
3. Perioperative considerations in patients with a positive anti-IgA antibody test include intraoperative techniques to limit the need for allogeneic blood products and preparation for the transfusion of saline-washed blood and blood products or those obtained from an IgA deficient donor.

Abstract

Immunoglobulin (Ig) A deficiency is characterized by undetectable levels of serum IgA and normal levels of other immunoglobulins (IgG, IgM) in patients more than 4 years of age. Although generally asymptomatic, patients are at risk for anaphylactic reactions when receiving allogeneic blood products from non-IgA deficient donors. We present a 35-year-old male with IgA deficiency who required anesthetic care during posterior spinal fusion. The basic principles of IgA deficiency are reviewed, general techniques to avoid allogeneic blood products presented, and specific care of the IgA deficient patient discussed including techniques to allow the use of allogeneic blood products if needed.

Keywords

IgA deficiency, posterior spinal fusion, pediatric anesthesiology

Introduction

Deficiency of immunoglobulin A (IgA), the most common primary antibody deficiency in patients greater than 4 years of age, is defined as low serum levels of IgA in the presence of normal serum levels of other immunoglobulins including IgG and IgM.[1] IgA has two subclasses (IgA1, IgA2) and is the most abundant antibody in the body, predominantly present in secretions and providing host immune defenses against bacterial infections in the pulmonary and digestive systems. Although generally asymptomatic, patients may be at higher risk for allergies, recurrent sinopulmonary infections, chronic diarrhea, and lymphoid malignancies.[1] Additionally, when serum levels are severely depressed, these patients may be at risk for anaphylactic and anaphylactoid reactions to allogeneic blood products.[2] Adult levels of IgA are reached in adolescence with serum concentrations ranging from 61 to 356 mg/dL. IgA deficiency is diagnosed by documentation of a serum concentration less

than 5-7 mg/dL (the lower limit of detection of most laboratory assays). We present a 35-year-old man with IgA deficiency who required anesthetic care during posterior spinal fusion. The basic principles of IgA deficiency are reviewed, general techniques to avoid allogeneic blood products presented, and specific care of the IgA deficient patient discussed including techniques to allow the use of allogeneic blood products if needed.

Case report

Review of this case and presentation in this format followed the guidelines of the Institutional Review Board of Nationwide Children's Hospital (Columbus, Ohio). The patient was a 36-year-old, 49.1-kilogram male with IgA deficiency who presented for anesthetic care during a posterior spinal fusion for the treatment of neuromuscular scoliosis. Additional comorbid conditions included spastic cerebral palsy, epilepsy well-controlled with levetiracetam, anxiety, and osteoporosis. Medications included baclofen, gabapentin, levetiracetam, and escitalopram. Preoperative laboratory evaluation included hemoglobin 10.4 g/dL, hematocrit 29.8% and platelet count 175,000/mm^3. Prothrombin time was 13.7 seconds (normal: 10-13.5 seconds), active partial thromboplastin time (aPTT) was 30 seconds (normal: 30-40 seconds) and the international normalized ratio (INR) was 1.1. Given the history of IgA deficiency, preoperative consultation was obtained with the hospital blood bank and the perfusion services from the cardiac surgery team. Two units of blood were acquired from an IgA deficient donor. Additionally, plans were made in conjunction with the perfusion team to perform acute normovolemic hemodilution (ANH) after the induction of anesthesia and prior to the start of the case, intraoperative washing of blood products as needed, and to use intraoperative cell saver. Preoperative evaluation revealed a Mallampati grade I view and a normal cardiovascular and respiratory examination. Vital signs were unremarkable. He was assigned an American Society of Anesthesiologists (ASA) physical classification 3. The patient was held *nil per os* for 6 hours and was transported into the operating room where routine ASA monitors were placed. General anesthesia was induced by the inhalation of incremental concentrations of sevoflurane in nitrous oxide and oxygen. After the induction of anesthesia, two large bore peripheral intravenous cannulas and a radial arterial cannula were placed. A single dose of rocuronium (0.5 mg/kg) was administered and endotracheal intubation performed with a 7.0 mm cuffed endotracheal tube. Maintenance anesthesia included total intravenous anesthesia with propofol (10-30 µg/kg/min) and remimazolam (10 µg/kg/min) to achieve a bispectral index of 50-60. Intraoperative opioids included methadone (bolus dose of 5 mg after the induction of anesthesia) and remifentanil (0.1-0.3 µg/kg/min). Neurophysiologic monitoring included somatosensory and motor evoked potentials. ANH was performed with the removal of 585 mL based on the starting hematocrit and the administration of 5% albumin in a 1:1 ratio. Antifibrinolytic therapy included tranexamic acid (bolus dose of 50 mg/kg followed by an infusion of 5 mg/kg/hour). The patient was turned prone and positioned for surgery. Prophylaxis against surgical site infection included cefazolin and gentamicin. Controlled hypotension was provided to minimize intraoperative blood loss with maintenance of the mean arterial pressure at 55-65 mmHg. The surgical procedure last approximately 10.5 hours. Intraoperative fluids included Normosol®-R (5400 mL), 5% albumin (1250 mL), ANH blood (585 mL), and cell saver (1160 mL). Estimated blood loss was 2500 mL. No intraoperative allogeneic blood products were required. Intraoperative hemodynamic stability was maintained with a phenylephrine infusion (0.2-0.5 µg/kg/min) during spinal instrumentation. At the completion of the case, residual neuromuscular blockade was reversed with sugammadex, the patient was turned supine, and his trachea extubated when he was awake. He was transported to the post-anesthesia care unit and then the inpatient orthopedic ward. Postoperative analgesia was provided by intravenous acetaminophen and nurse-controlled analgesia with hydromorphone. This was

transitioned to oral medications when he was tolerating a clear liquid diet. The postoperative course was unremarkable and he was discharged home on postoperative day 6. Laboratory evaluation on postoperative day 1 included a hemoglobin of 6.8 gm/dL and hematocrit 19.3%. As the patient was hemodynamically stable without symptoms, no intervention was provided. At the time of discharge, the hemoglobin was 9.4 gm/dL with a hematocrit of 27.1%.

Discussion

IgA is the most abundant antibody in the body, participating primarily in host mucosal protection against infectious agents as it is found primarily in bodily fluids and secretions (breast milk, saliva, bronchial, and gastrointestinal fluids). IgA deficiency is the most common primary antibody deficiency (PAD).[3,4] The clinical diagnosis is confirmed by decreased or absent serum IgA levels with normal levels of IgG and IgM in a patient more than 4 years of age. The age cut-off is used to exclude transient deficiency due to delayed B-cell and IgA development in younger children. The primary etiology is postulated to be a maturation defect in B cells that produce IgA, although rarer acquired causes include drug-induced, congenital infections, and chromosomal abnormalities. The incidence of selective IgA deficiency varies among different ethnic groups with the highest prevalence in the Caucasian population. The incidence has been reported to vary from 1:143 to 1:965 in different geographic regions, with an equal distribution between the genders.[5]

Although the majority of patients are asymptomatic, recurrent infections including sinopulmonary and gastrointestinal infections as well as an increased incidence of inflammatory, autoimmune, and neoplastic diseases have been reported. The diagnosis was made in our patient when serum immunoglobulin levels were obtained during a work-up for possible celiac disease and chronic diarrhea. After the diagnosis, the patient and family were counselled and provided information regarding the potential for recurrent infections, the development of autoimmune diseases, and the risk of allogeneic transfusion therapy.

The primary concern during the perioperative care of patients with IgA deficiency is the risk of allergic or anaphylactoid reactions during the administration of blood or blood products.[6] IgA deficiency should be considered in the differential diagnosis of patients who have an allergic reaction or abrupt clinical deterioration following the administration of blood or blood products. The initial presentation may be similar to ABO incompatibility, hemolytic transfusion reaction, and anaphylactoid/anaphylactic responses to intraoperative products (latex) or medications.[7] Given these concerns, techniques to limit the need for allogeneic transfusion are frequently employed in this patient population.[8,9] These can be simply divided into techniques that can be used during the preoperative, intraoperative, and postoperative periods.

Preoperative care of a patient with IgA deficiency starts with a preliminary evaluation of baseline hemoglobin values and an evaluation of coagulation function. As feasible, medications that affect coagulation function should be discontinued or temporarily withheld. Although routinely obtained, preoperative laboratory evaluation of coagulation (platelet count, PT, and PTT) rarely reveals acquired or inherited disorders as the most common defect of coagulation function is platelet dysfunction related to von Willebrand's disease.[10] As such, the screening laboratory evaluation is complemented by a thorough family and patient history to identify bleeding concerns. This should include a thorough history to include herbal medications that may impact coagulation and platelet function.[11]

Preoperative anemia is a significant factor associated with the need for perioperative transfusion therapy.[12,13] A simple, safe, and inexpensive therapy is identification of the etiology of preoperative anemia, such as iron deficiency, with targeted therapy. When indicated, preoperative iron therapy may decrease or eliminate the need for allogeneic blood. Other preoperative therapies aimed at limiting the need for allogeneic transfusions include the

use of autologous donation and erythropoietin. Despite their efficacy, these techniques have generally fallen out of favor in most clinical situations due to their cost and the impact on the patient and families given the need for repeated hospital visits.

Intraoperative techniques to limit allogeneic transfusion requirements may include acute normovolemic hemodilution (ANH), controlled hypotension, blood salvage, and control of coagulation function including anti-fibrinolytic therapy.[14-17] These are combined with other general operating strategies including the maintenance of normothermia, appropriate patient positioning to avoid venous congestion, and use of topical hemostatic agents and electrocautery. In our patient, we chose ANH, controlled hypotension, intraoperative blood salvage, and the administration of tranexamic acid. In consultation with perfusion services, ANH was performed with blood removal after the induction of anesthesia and prior to the start of the surgical procedure. Blood was removed from the arterial cannula and replaced in a 1:1 ratio with 5% albumin to achieve a final hematocrit of 26-30%. The removed blood was stored in a standard blood bank bag with the addition of a citrate-dextrose solution as the anticoagulant. The collected blood was labeled and stored at room temperature. It was then reinfused when transfusion was needed, the benefit being that it provides not only red blood cells, but also active coagulation factors and platelets.

Despite the relative high incidence of IgA deficiency, there are a limited number of reports outlining the anesthetic or transfusion care of such patients with only 4 reports from the English language literature (Table 1).[18-22] In addition to standard preoperative and intraoperative procedures to limit the need for allogeneic transfusions, up to 40% of patients with IgA deficiency have anti-IgA antibodies that can cause anaphylactic reactions to IgA in transfused blood and blood products. Blood banks and centers generally maintain a list of IgA-deficient blood donors and with appropriate advanced notification, it may be feasible to obtain compatible blood components from these patients. These products should be screened for IgA levels and can be used if the IgA concentration is less than the detectable limit of the laboratory assay. When this preparation is not feasible, packed red blood cells and platelet concentrates can be washed (3 cycles) so that greater than 99% of the IgA in blood components can be removed. Although platelets can be washed, the process may result in platelet activation, making them less effective.[23]

Authors and reference	*Demographic information*	*Treatment and outcomes*
Alam A et al.[18]	49-year-old with COPD for lung transplantation.	Author noted that use of IgA-deficient components (blood or graft) may be challenging in emergent perioperative settings. A multidisciplinary coordinated approach is required to achieve transplantation in IgA deficient patients.
Steel C et al.[19]	33-year-old for emergency cesarean delivery.	Author mentions that IgA deficiency should prompt the measurement of anti-IgA antibodies to determine the risk of anaphylaxis.
Meena-Leist CE et al.[20]	46-year-old with stage IIB adenocarcinoma of the breast for autologous bone marrow transplant.	Author noted that most important factor in managing IgA deficient patients with anti-IgA antibodies is proper communication with all hospital staff to ensure only IgA-deficient components are transfused.
Jain R et al.[21]	Generic patient with IgA deficiency – no specific demographic details given.	Author noted that blood from IgA deficient donors is the gold standard. Also recommended washing of blood products and use of intraoperative autologous blood salvage.

Table 1. Anesthetic care of patients with IgA deficiency – reports from the English language literature

Other blood products including fresh frozen plasma and cryoprecipitate cannot be washed although it is feasible to keep these products frozen for up to 1 year, thereby increasing their shelf life and the potential of obtaining these from IgA deficient donors. Alternatively, when treatment of ongoing coagulation dysfunction is required, fibrinogen and other coagulation factors (factor VII, VIII, IV, and XIII) are available as recombinant single component products which eliminate the concerns of anaphylactic reactions to IgA in transfused blood products.[24,25] More recently, prothrombin complex concentrates (PCC) containing multiple vitamin-K dependent factors have seen increased use to treat coagulation defects of various etiologies.[26,27] PCCs are produced though ion-exchange chromatography using the cryoprecipitate supernatant of large plasma pools following the removal of anti-thrombin and factor XI. Variations in the ion-exchanger resins used for processing result in products with either three (factors II, IX and X) or four (factors II, VII, IX and X) factors. Although the specific components in the various four-factor PCCs vary somewhat depending on the manufacturer, these concentrates all contain therapeutic concentrations of the vitamin K-dependent coagulation factors (II, VII, IX, and X). To prevent activation of these factors, most PCCs contain varying concentrations of heparin in addition to varying concentrations of the naturally occurring anti-coagulant proteins (protein C, protein S, and AT-III). All PCCs undergo at least one step of viral reduction or elimination such as solvent detergent treatment or nanofiltration. To date, there are no reports regarding use of these agents in an IgA deficient patient although it is postulated that the processing steps would remove the majority of plasma and also the IgA immunoglobulin.

In summary, IgA is the most common primary immunodeficiency in children, adolescents, and adults. Although these patients may be at an increased risk of infections (sinopulmonary and gastrointestinal) as well as autoimmune diseases, during perioperative care, the primary concerns is the risk of allergic reactions during the administration of blood and blood products. Standard preoperative practices to limit the need for allogeneic transfusions include screening for preoperative anemia and assurance of normal coagulation function. Intraoperative techniques include ANH, intraoperative blood salvage, and controlled hypotension. Consultation with blood bank and hematology may help with the procurement of blood and blood products from IgA deficient donors. In the absence of such availability, packed red blood cells and platelet concentrates can be washed while selective coagulation factors or PCCs may be considered in the treatment of coagulation disturbances.

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