

# Neuraxial Anesthesia for a Parturient With Hypogammaglobulinemia: A Case Report

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*Hypogammaglobulinemia is characterized as a deficiency in humoral immunity. Humoral immunity deficiencies include the absence of B cells and/or serum immunoglobulins. Common clinical features include a predisposition toward infections naturally defended against through antibody-mediated responses. Clinical manifestations of this condition, in the parturient, may contraindicate neuraxial anesthesia.*

*A 30-year-old parturient with hypogammaglobulinemia was admitted for repeated cesarean delivery and a bilateral tubal ligation. The pathophysiology and anesthetic management of the parturient with hypogammaglobulinemia is discussed.*

**Keywords:** Antibodies, humoral immunity, hypogammaglobulinemia, neuraxial anesthesia.

Specific immune responses in humans are based on humoral (B-cell) and cellular (T- and NK-cell) antigen recognition. B cells help the human body fight against extracellular infections through the production of antigen-specific immunoglobulins.<sup>1</sup> Immunoglobulins help to protect from bacterial, parasitic, and viral infections. Protection includes neutralization of bacterial toxins, activation of complement, and opsonization to enhance phagocytosis. Opsonization occurs when an immunoglobulin molecule labels the extracellular organism to inactivate and target the organism for destruction. This coating or opsonization enhances the efficiency of phagocytosis by mononuclear cells and neutrophils.<sup>2</sup> Immunoglobulins also capture antigen, foreign or self, for presentation and support of T-cell responses.<sup>1</sup> An example of efficient protective immunity to *Streptococcus pneumoniae* includes antibody and complement-mediated opsonization.<sup>3</sup>

There are 5 classes of immunoglobulins (Ig) produced by B cells. The classes include: IgG, IgM, IgA, IgD, and IgE. Immunoglobulins have multiple functions that are related to their structural diversity. B cells can produce up to 10<sup>9</sup> structurally different immunoglobulins.<sup>1</sup> There are 4 isotypes of IgG, designated IgG1 through IgG4. Most serum immunoglobulins consist of the IgG1 isotype.<sup>1</sup> Immunoglobulin G isotypes 1 + 3 exhibit specificity for protein antigens. The IgG3 isotype can recognize respiratory viruses.<sup>4</sup> The IgG isotypes 2 + 4 recognize polysaccharide antigens, which include the bacterial pneumococcal polysaccharide.<sup>2,4</sup> Usually IgG isotype deficiencies occur in pairs: IgG isotype 1 + 3 and/or IgG isotype 2 + 4.<sup>2</sup>

Defects in the immune system, hematopoietic or extrahematopoietic, are described as immunodeficiencies. Hypogammaglobulinemia is an immune deficiency that results in reduced or absent serum immunoglobulin.<sup>1</sup> Half of all diagnosed immunodeficiencies are B-cell deficiencies. This deficiency will be diagnosed in 1 in 700

people in the general population and in 1 in 50,000 persons of European ancestry.<sup>1</sup>

B-cell deficiency is classified as a primary (congenital) or secondary (acquired) immunodeficiency.<sup>2</sup> Patients presenting with primary immunodeficiencies usually have clinical manifestations in infancy or childhood.<sup>5</sup> More than 100 conditions have been associated with primary immunodeficiency disease, including allergies, autoimmune diseases, autoinflammation, hemophagocytosis, malignancies, and infectious diseases.<sup>5</sup> X-linked agammaglobulinemia (XLA) is the most common primary immunodeficiency. Of patients with XLA, 85% have profound hypogammaglobulinemia with reduced B-cell numbers and frequent infections.<sup>6</sup> The acquired immunodeficiency diseases include nephritic syndrome, enteropathy, catabolic disorders, and leukemia.<sup>2</sup> Symptom severity depends on the deficiencies of the specific immunoglobulin isotype.<sup>4</sup>

Hypogammaglobulinemic patients present clinically with recurrent upper and lower respiratory tract infections. Patients lacking IgG isotype 2 have the highest frequency of infectious complications, usually respiratory in nature.<sup>2</sup> These patients also appear to have an increased incidence of asthma or sinusitis.<sup>4</sup> The site of infection helps diagnose the type of immunoglobulin deficiency. Recurrent infections with encapsulated bacteria are usually associated with antibody and/or complement deficiency. Encapsulated bacteria most often seen include *Streptococcus pyogenes* and *S pneumoniae*, *Staphylococcus aureus*, and *Haemophilus influenzae*. Patients may also present with concomitant atopic disorders such as atopic dermatitis.<sup>2</sup>

Immunodeficiencies of the IgA class have been seen with patients who have a history of anaphylaxis following blood product transfusion. Deficiency of IgA is the most common Ig deficiency syndrome. In these patients an anti-IgA antibody of the IgE class can develop after transfusion of blood products containing IgA. Once sensitized, the patient is at risk of IgE-mediated anaphylaxis if blood

products are administered containing the IgA antigen.<sup>4</sup>

Therapy for immunoglobulin-deficient patients includes aggressive antibiotic treatment for acute infections, prophylaxis with intravenous immunoglobulin infusion (IVIG), and prevention or treatment of pulmonary diseases secondary to bronchitis or pneumonia.<sup>3</sup> Replacement of IVIG of 0.4 to 0.6 g/kg every 3 to 4 weeks is the therapy standard for all primary immunodeficiencies excluding IgA deficiencies.<sup>1</sup>

Patients presenting for neuraxial anesthetic management for cesarean delivery diagnosed with hypogammaglobulinemia can pose a challenge because of possible immunodeficiency and infection. Neuraxial anesthesia is generally a safe and preferred anesthetic for cesarean delivery. Absolute contraindications to neuraxial anesthetic include infection at the needle insertion site, including atopic dermatitis, which is often seen in hypogammaglobulinemia.<sup>4,7</sup> Neuraxial anesthesia is controversial in the febrile parturient. Fever and sepsis are classified as relative contraindications to regional anesthesia. Guidelines exist but do not offer clear standards for neuraxial anesthesia in the febrile patient. The most important clinical marker of infection is fever, but fever in the parturient lacks specificity and is common without sepsis.<sup>7</sup>

Complications of neuraxial anesthesia are rare but can result in serious adverse outcomes, which include but are not limited to infection, postpuncture headache, sequelae due to cardiovascular or respiratory instability, and lumbar puncture.<sup>4,7</sup> Neurologic injury resulting from spinal anesthesia has been documented in less than 0.07% of cases.<sup>8</sup> Injuries included paraplegia, monoparesis, cauda equina syndrome, pain, and sensory symptoms. These injuries are caused by trauma, ischemia, hemorrhage, arachnoiditis, abscess formation due to infection, and injection-agent toxicity.<sup>8</sup> Epidural or spinal anesthesia has been shown to decrease postoperative mortality of patients undergoing cesarean delivery compared with general anesthesia.<sup>7</sup> Spinal or epidural mortality and morbidity rates are less than those associated with general anesthesia.<sup>8</sup>

### Case Summary

A 30-year-old gravida 2, para 1, was hospitalized at term, 39 weeks' gestation, for her second cesarean delivery. She requested surgical sterilization. Her past medical history included insulin-dependent diabetes mellitus type 1, psoriasis, herpes simplex virus, group B streptococci positive, negative testing for hepatitis B antigen, and a diagnosis of hypogammaglobulinemia. The patient reported her father had a diagnosis of the same immunodeficiency. The patient said she did not smoke or drink alcohol. She had allergies to sulfamethoxazole, cephalixin, levofloxacin, and fluconazole.

The patient was a well-nourished, well-developed, pregnant white woman and had no pregnancy-related complications. Blood pressure readings were 130/65 mm

Hg, pulse was 60/min, respiratory rate was 18/min, and her temperature was 37.1°C. Chest auscultation was clear bilaterally. The cardiovascular system included a regular rate and rhythm without murmurs. Blood test results showed a hemoglobin level of 12.1 g/dL, hematocrit of 34.5%, and platelet count of  $161 \times 10^3/\mu\text{L}$ . Blood glucose level at 8 am was 156 g/dL, with no action taken. The parturient's blood type was B Rh-positive, with a negative antibody screen. Blood chemistry panel indexes were all within normal limits. The patient was normothermic with no outward signs or symptoms of infectious processes. An 18-gauge peripheral intravenous (IV) catheter access was established.

After the patient had an *S aureus* infection of the back and scalp in 2002, hypogammaglobulinemia of immunoglobulin isotypes IgG 1 through IgG 4 was diagnosed. Immunoglobulin deficiency of this type would predispose the parturient to infection. The patient was receiving IVIG every 4 months for her immunoglobulin deficit. The last dose was 2 months before admission. Fetal heart tones were recorded as 135 bpm. The fetal heart tracing was normal, indicating the fetus was in no distress.

Following a review of the patient's history and physical information, a plan of care, included elective spinal anesthesia, was developed by the anesthesiology team and the patient. General anesthesia would commence should the spinal anesthesia fail. The patient was transferred to the operating room, and standard monitors and alarms were applied. The patient was given 100% fractional concentration oxygen in inspired gas at 3 L/min through a nasal cannula. Prophylactic antibiotic, 1 g of vancomycin, was administered before the surgical incision.

The patient was instructed on the proper sitting positioning for a subarachnoid block. Thoracic and lumbar landmarks were established. Strict aseptic procedures were followed. Povidone-iodine solution was used to prepare the back. A sterile plastic drape was then applied to the patient's back. A wheal was placed with a 25-gauge needle containing 1% lidocaine (Xylocaine) at the lumbar 2-3 (L2-3) interspace. A sterile 20-gauge introducer, followed by a 25-gauge Pencan needle with stylet (B. Braun, Bethlehem, Pennsylvania), was placed in the L2-3 interspace. Clear cerebral spinal fluid confirmed the subarachnoid space placement. No paresthesia was present. An anesthetic mixture of 1.6 mL of 0.75% bupivacaine with 8.5% dextrose was introduced into the subarachnoid space slowly. The Pencan needle and introducer were removed, and a sterile film dressing (Tegaderm, 3M, St Paul, Minnesota) was placed over the insertion site to ensure a closed sterile area. The parturient was positioned supine with left uterine displacement. Sensory loss was determined at the fifth thoracic dermatome, and surgical stimulation confirmed a successful block.

In a follow-up conversation with the patient postoperatively, she reported no signs and symptoms of infection and no headache.

## Discussion

The preoperative assessment of the patient provided the basis for an anesthetic plan. The presenting parturient was consulted on the risks and benefits of spinal anesthesia with specific reference to hypogammaglobulinemia. The risk for infection was stressed. The patient was afebrile with no presenting signs of infection. It was mutually decided that a subarachnoid block would proceed given the greater risks versus benefit of general anesthesia for her cesarean delivery. The patient was comfortable during the surgery and had no infectious sequelae resulting from the spinal block. Follow-up conversation with the patient confirmed aseptic conditions during the spinal block, as evidenced through the discussion of the lack of signs and symptoms of infection. Successful neuraxial anesthesia was evidenced by the patient's report of comfort and no postoperative puncture headache.

Prevention of postdural puncture infections is paramount in patients with known history of immunodeficiency. Strict aseptic technique can prevent the occurrence of a devastating outcome in an otherwise healthy patient.<sup>9</sup>

In a study of 179 reported cases of postdural puncture meningitis from 1952 to 2005, it was concluded that the most probable cause of infection was from aerosolized mouth and upper airway bacterial contamination from the provider of neuraxial anesthesia.<sup>9,10</sup> Three deaths discussed in this study occurred in healthy parturients with no risk of meningitis developing. This study provided evidence through bacterial DNA analysis that one parturient's bacterial meningitis isolate matched the nose and throat bacteria from the provider performing the neuraxial anesthesia.<sup>9</sup> Second to airway flora as a contaminate was contamination from skin flora or spread of infection from another infected site.<sup>10</sup>

Controversy exists concerning which antiseptic solution is best for skin preparation before neuraxial procedures. In the United States at present, povidone-iodine is the solution of choice. It takes at least 2 minutes for povidone-iodine to reach its peak bactericidal effect.<sup>9</sup> It is questionable whether providers should wait 2 minutes before initiation of the procedure. The duration of action is limited, and effectiveness is lessened by organic compounds such as the presence of blood and proteinaceous material in the area of use.<sup>11</sup>

Practitioners differ in their definition of essential components of strict aseptic technique. The US Agency for Healthcare Research and Quality recommends the following: thorough hand washing before performing any regional anesthetic technique, use of surgical masks, and the use of alcohol-based chlorhexidine antiseptic solution.<sup>11</sup> These guidelines are essential when providing care to an immunodeficient patient.

A good surgical mask prevents aerosolization of mouth and airway flora. A study focused on surgical mask protection found that a large soft, pleated, pliable mask was superior to a simple cloth or paper mask at filtering bac-

teria. This filtration was found to last only 8 hours. The study found that changing masks between cases improved protection from bacterial contamination.<sup>10</sup>

Chlorhexidine gluconate is a broad-spectrum potent germicide. Study results indicate that a solution of chlorhexidine is more effective as an antiseptic than povidone-iodine.<sup>9,11</sup> The addition of isopropyl alcohol to chlorhexidine gluconate enhances the bactericidal action.<sup>11</sup> Chlorhexidine solutions are currently approved by the US Food and Drug Administration (FDA) only for skin preparations before surgery. Their use for regional anesthesia has not been approved because of the lack of clinical efficacy data.<sup>11</sup> Studies in animals contradict the use of chlorhexidine solutions owing to neural toxicity. These findings have not been duplicated in humans during neuraxial procedures.<sup>9</sup> Chlorhexidine solutions are not currently available in neuraxial kits because of FDA labeling, which contraindicates their use for these applications. Discussions abound in reference to the manufacturer's recommendations and published guidelines endorsing this product for peridural anesthesia.<sup>12</sup>

In conclusion, patients presenting for neuraxial anesthesia with a history of immunodeficiency qualify for the most stringent aseptic techniques by the provider. Hypogammaglobulinemia, an immunodeficiency, predisposes one to infection. The parturient in this case report did well under subarachnoid block. Aseptic technique was adhered to in this case.

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