OPEN

CASE REPORT

Perioperative Management of a Patient With Severe Cold Agglutinin Disease Undergoing Total Hip Arthroplasty With a Cemented Stem: A Case Report

Takumi Yamaguchi, MD,* Hiroyuki Hirate, MD,* Taiki Kusano, MD,† and Yukiko Inagaki, MD*

Patients with cold agglutinin disease who undergo total hip arthroplasty (THA) are rarely encountered. Patients with cold agglutinin disease are very sensitive to cold ambient temperatures and require scrupulous perioperative body-temperature management. However, THA requires a cementing procedure that exposes patients to cold temperatures during surgery and may result in autoimmune hemolytic anemia in these patients. Thus, perioperative management of patients with cold agglutinin disease undergoing THA requires more than just scrupulous systemic temperature management. Here, we present the successful perioperative management of a patient with severe cold agglutinin disease who underwent THA with a cemented stem. (A&A Practice. 2022;16:e01647.)

GLOSSARY

AIHA = autoimmune hemolytic anemia; **IVIG** = intravenous immunoglobulin; **RBC** = red blood cell; **THA** = total hip arthroplasty

Cold agglutinin disease is a rare form of cold autoimmune hemolytic anemia (AIHA). It is characterized by the presence of IgM antibodies against red blood cells (RBCs),[1] and a compliment-mediated mechanism that leads to intravascular and extravascular hemolysis.[2] Exposure to cold ambient temperatures can lead to critical complications, including hemolysis, gangrene, and ulcerations in patients with cold agglutinin disease.[3] Especially, surgical management of patients with higher antibody titers or thermal amplitudes is difficult, since strict local and systemic temperature management is needed. Therefore, it is important to take measures to avoid a decrease in body temperature caused by anesthetic-induced impaired thermoregulation and the decrease in the temperature of the surgical field caused by the implant cement during total hip arthroplasty (THA).

Here, we present the successful perioperative management of a patient with severe cold agglutinin disease undergoing THA using multimodal warming strategies and by raising the temperature of the cement. We obtained written informed consent from the patient to present this case.

From the Departments of *Anesthesia and Intensive Care and †Orthopedic Surgery, Japanese Red Cross Aichi Medical Center Nagoya Daini Hospital, Aichi, Japan.

Accepted for publication October 11, 2022.

Funding: None.

The authors declare no conflicts of interest.

Address correspondence to Takumi Yamaguchi, MD, Department of Anesthesia and Intensive Care, Japanese Red Cross Aichi Medical Center Nagoya Daini Hospital, Myokencho, Showa-ku, Nagoya, Aichi 466-8650, Japan. Address e-mail to tynmu148945@gmail.com.

DOI: 10.1213/XAA.0000000000001647

REPORT

A 65-year-old woman diagnosed with hip osteoarthritis was scheduled for THA. She had been diagnosed with osteoporosis and AIHA due to cold agglutinin disease (cold agglutinin titer of 1:52,428 at 4 °C) and took prednisolone 10 mg per day. Her symptoms included purple discoloration of the fingertips, toes, and nose when exposed to cold ambient temperature. Additionally, in every winter, she had shortness of breath with a hemoglobin level of 5 g/dL.

Although we suggested that surgery should be performed when the temperature was warm enough, the patient had unbearable joint pain. Thus, surgery was performed in spring.

At the time of admission, she had not experienced symptoms of Raynaud's disease for >2 weeks. However, her hemoglobin level was 6.2 g/dL at 3 weeks before the surgery and 7.2 g/dL at 2 days before the surgery, which necessitated preoperative transfusion of 8 units of RBC that were warmed to 40 °C using a HOTLINE Warmer (Smiths Medical Japan Ltd). Her hemoglobin level increased to 11.6 g/dL at the operating room. No other strategies, including erythropoietin, plasmapheresis, intravenous immunoglobulin (IVIG), or immune modulators to increase hemoglobin level or prevent hemolysis, were performed before the surgery.

On the day of surgery, amino acids warmed to 40 °C using a HOTLINE warmer administered 2 hours before surgery. To avoid a decrease in the peripheral skin temperature, the operating-room temperature was maintained at 28 °C, and the patient was transferred from the ward to the operating room wearing gloves and socks and covered with blankets. Nevertheless, the axillary temperature was 35.8 °C when she entered the operating room. Therefore, anesthesia was induced after the axillary temperature reached 36.8 °C using a forced-air warming system (Bair Hugger, Augustine Medical Inc). During surgery, the gas administered through the ventilator was heated to 38 °C. In the operating room, the patient constantly wore the forced-air warming system,

gloves, and socks. Amino acids were continued during surgery, and all infusions were heated to 40 °C using a HOTLINE Warmer. In addition to these multimodal warming strategies, the bone cement (Simplex P Bone Cement; Stryker) was used at room temperature after advance simulation to confirm that it could be used at a higher temperature than usual (<25 °C). Figure 1 shows the intraoperative trends of the core (esophagus) and peripheral (hand interdigital) temperatures.

Due to the 1400-mL blood loss during surgery, the patient went into hemorrhagic shock and extracellular fluid as well as RBCs were rapidly administered during surgery. Her hemoglobin level did not drop because RBC transfusion was started as soon as bleeding occurred. However, her blood pressure remained temporarily unstable after admission to the ICU, and additional extracellular fluid and RBC transfusion were required. Finally, 8 units of RBC transfusions were required intraoperatively and postoperatively. Figure 2 shows the perioperative trend of the hemoglobin level and timing of RBC transfusion. During the course of treatment, the patient did not develop hypothermia, symptoms of Raynaud's disease, elevated lactate dehydrogenase or bilirubin levels, or hematuria due to hemolysis. The postoperative course was excellent, and the patient was discharged on postoperative day 11.

DISCUSSION

AIHA is a relatively rare disease, with an estimated incidence of 0.8 to 3 per 100,000, in which anemia is caused by autoantibodies against surface antigens of RBCs.[4] The causes of this disease are diverse, including infections and malignant tumors.[2] Cold agglutinin disease is an uncommon form of cold AIHA and accounts for approximately 15% to 25% of patients with AIHA, with an incidence of 1 per million people/y.[1] Cold agglutinins are found in a high percentage of the adult population without underlying disease, but usually at low titers (≤1:64).[5] Although high titers are quite rare, they are more likely to cause hemolysis. The severity depends on many factors, including the degree of complement activation, immunoglobulin classes and subclasses, titers, and thermal amplitude.[6] Cold agglutinins generally react at 0 °C to 4 °C, well below physiological temperatures and can cause symptoms of Raynaud's disease due to vasospasm in the nose, ears, and fingertips.[1,7]

Particular attention must be paid to temperature control in patients with high titers of cold agglutinins, since general anesthesia causes hypothermia due to exposure to a cold environment and anesthetic-induced impaired thermoregulation, which causes vasodilation, inhibits vasoconstriction, and reduces the metabolic rate by 20% to 30%.[8] In the present case, we set the ideal body temperature to >37 °C because the patient never reported symptoms of Raynaud's disease at 36.5 °C in her daily life. In previous reports, multimodal preoperative warming, including intraoperative forced-air warming, infusion warming, and intravenous amino acid infusion, was used to maintain the central and peripheral temperature above 37 °C.[9] Intravenous infusion of amino acids before and during anesthesia is known to prevent perioperative hypothermia by increasing heat production from enhanced metabolism.[10] In addition to these warming methods, the gas administered through the ventilator (Newport Ventilator Model e360) was warmed to 38 °C. The temperature of the gas administered from the anesthesia apparatus (Dräger Perseus A500) decreased to 28 °C, at the connection with the endotracheal tube, and there was no device to rewarm the gas in the anesthesia circuit. Therefore, we used a ventilator that could heat the gas in the middle of the circuit. This ensured the delivery of gas at 38 °C, even at the connection with the endotracheal tube. However, because condensation occurred in the circuit and endotracheal tube due to the large difference between the gas and room temperatures, it was necessary to monitor the ventilation volume and waveform of end-tidal CO_2.

Besides temperature management, plasmapheresis before surgery has been reported to optimize patients with cold agglutinin disease for surgery, especially those who require hypothermic circulatory arrest; its effect, however, is transient.[4] Other treatments for cold agglutinin disease, including erythropoietin, IVIG, or immune modulators, were reported to be effective in some patients with cold

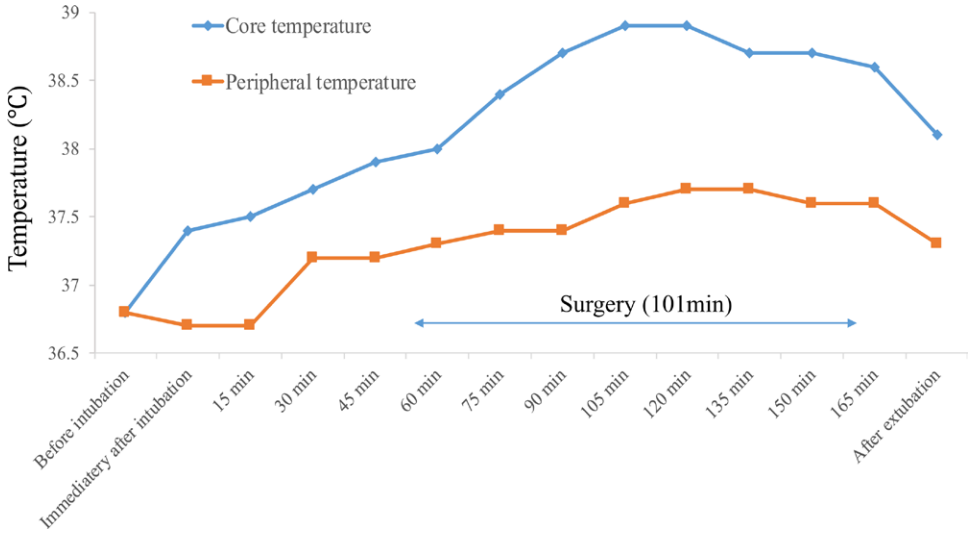

Figure 1. Changes in core (esophagus) and peripheral (hand interdigital) temperatures during surgical procedures.

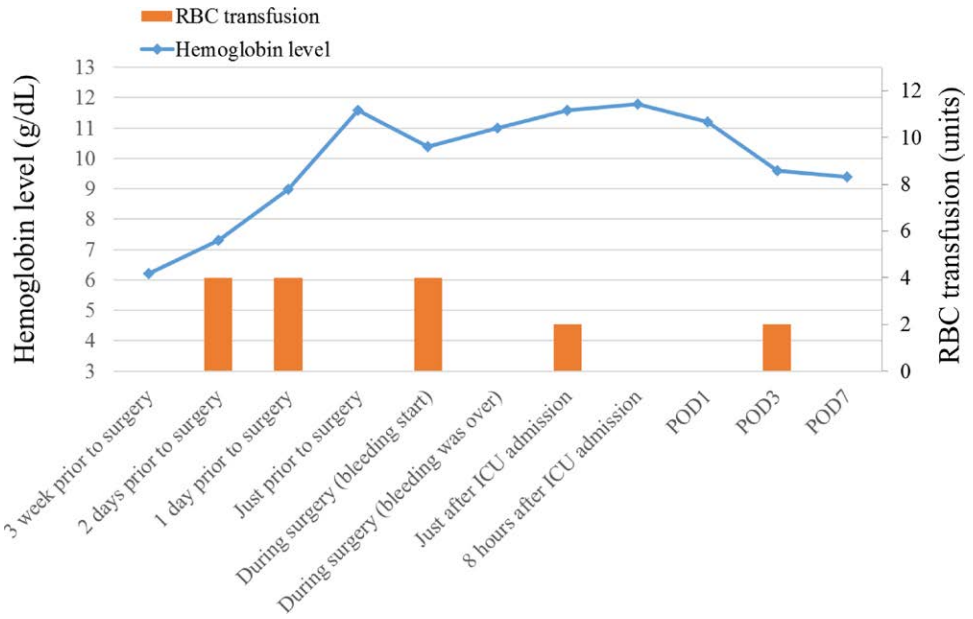

Figure 2. Perioperative change in hemoglobin level and amount of RBC transfusion.

agglutinin disease.[4] However, neither recommendation nor avoidance in perioperative period was discussed in the literature. Therefore, we believe that performing these treatments before surgery should be considered on case-by-case. In the present case, since the cause of hypothermia in surgery was anesthetic-induced impaired thermoregulation and local cooling with bone cement, and forced hypothermia as in cardiac surgery was not required, no additional preoperative treatment for cold agglutinin disease was performed.

The use of cemented stems in THA provides good initial fixation, especially in patients aged >65 years or those with osteoporosis, and cemented stems are recommended to prevent intra and postoperative periprosthetic femoral fractures.[11] Moreover, cemented stems are advantageous in terms of bone density preservation because cementless stems are subject to further postoperative bone atrophy due to stress shielding.[12] The temperature of bone cement is usually maintained below 25 °C in a thermal chamber to ensure stable bone cementation, and the temperature in the operating room is often maintained at the same level. Although the patient was at risk for periprosthetic femoral fractures (age >65 years and osteoporosis), she had cold agglutinin disease, and procedures that exposed her to low temperatures had to be avoided. Therefore, we used the cement at as high a temperature as possible. Preoperative simulations were performed at 28 °C to confirm that bone cement could be used under this condition. By shortening the duration of mixing and stirring, the pliability of the cement was maintained within acceptable limits for the procedure. When the cement was implanted, good cement–bone and cement–implant interfaces were established without any complications, and no hypothermia or hemolysis was observed after cementation.

In conclusion, multimodal warming strategies and higher temperature of the cement allowed safe perioperative management of a patient with high cold agglutinin titer who underwent THA with cemented stems.

DISCLOSURES

Name: Takumi Yamaguchi, MD.
Contribution: This author treated the patient and wrote the first draft of the manuscript.
Name: Hiroyuki Hirate, MD.
Contribution: This author helped to edit the manuscript.
Name: Taiki Kusano, MD.
Contribution: This author treated the patient and helped to edit the manuscript.
Name: Yukiko Inagaki, MD.
Contribution: This author helped to edit the manuscript.
This manuscript was handled by: Kent H. Rehfeldt, MD.

REFERENCES

1. Swiecicki PL, Hegerova LT, Gertz MA. Cold agglutinin disease. *Blood*. 2013;122:1114–1121.
2. Gabbard AP, Booth GS. Cold agglutinin disease. *Clin Hematol Int*. 2020;2:95–100.
3. Berentsen S, Barcellini W, D'Sa S, et al. Cold agglutinin disease revisited: a multinational, observational study of 232 patients. *Blood*. 2020;136:480–488.
4. Zanella A, Barcellini W. Treatment of autoimmune hemolytic anemias. *Haematologica*. 2014;99:1547–1554.
5. Gertz MA. Management of cold haemolytic syndrome. *Br J Haematol*. 2007;138:422–429.
6. Petz LD. Cold antibody autoimmune hemolytic anemias. *Blood Rev*. 2008;22:1–15.
7. Temprano KK. A review of Raynaud's disease. *Mo Med*. 2016;113:123–126.
8. Bindu B, Bindra A, Rath G. Temperature management under general anesthesia: compulsion or option. *J Anaesthesiol Clin Pharmacol*. 2017;33:306–316.
9. Koyama Y, Asami Y, Nishikawa H, Ozaki M, Tsuzaki K. Perioperative management of a patient with severe cold agglutinin disease by using multimodal warming measures. *Korean J Anesthesiol*. 2021;74:358–360.
10. Aoki Y, Aoshima Y, Atsumi K, et al. Perioperative amino acid infusion for preventing hypothermia and improving clinical outcomes during surgery under general anesthesia: a systematic review and meta-analysis. *Anesth Analg*. 2017;125:793–802.
11. Abdel MP, Watts CD, Houdek MT, Lewallen DG, Berry DJ. Epidemiology of periprosthetic fracture of the femur in 32 644 primary total hip arthroplasties: a 40-year experience. *Bone Joint J*. 2016;98–B:461–467.
12. Morita D, Iwase T, Ito T. Bone restoration with cemented Exeter universal stem – Three-years longitudinal DEXA study in 165 hips for femur. *J Orthop Sci*. 2016;21:336–341.