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Case Series of Silver Oxide–Containing Hydroxyapatite Coating in Antibacterial Cementless Total Hip Arthroplasty: Clinical Results of 50 Cases at 5-Year Follow-Up

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ABSTRACT

Background: Prosthetic joint infection, which is caused by implant treatment, is a severe complication. Consequently, silver-containing hydroxyapatite (Ag-HA)-coated implants have been developed to prevent prosthetic joint infection by combining Ag with HA. The Ag-HA-coated total hip prosthesis, which combines the antibacterial activity of Ag and the osteoconductivity of HA, is the first antibacterial cementless total hip prosthesis worldwide. This study aimed to evaluate the short-term outcomes of total hip arthroplasty (THA) with Ag-HA-coated implants.

Methods: Overall, 50 hips with various disabling hip diseases and postoperative infection risks that underwent a primary THA using an Ag-HA total hip prosthesis were enrolled. The patients included 37 women (41 hips) and 8 men (9 hips), and the mean age at the time of surgery was 77 years. The clinical outcomes and hip function before and at 5 years postoperatively were measured using the Japanese Orthopaedic Association hip score. Implant stability was assessed, and postoperative complications were also examined.

Results: The Japanese Orthopaedic Association score increased in all cases and improved from 41 to 86 points after the THA ($P < .001$). Radiography revealed no implant failure. Dislocation and deep vein thrombosis also occurred in 1 case each. However, there were no adverse reactions associated with Ag, and argyria was not observed in any case. Additionally, none of the patients experienced infection following the surgery.

Conclusions: Silver-containing hydroxyapatite–coated implants significantly enhanced patients' daily activities without any adverse effects on the human body attributed to Ag, and they are expected to reduce postoperative infections.

Introduction

The incidence of prosthetic joint infection, which is a severe complication caused by implant therapy, has been reported to be approximately 1% after primary total hip arthroplasty (THA) [1-3]. Although its incidence is relatively rare, infection is challenging to treat once it develops and tends to persist for a long duration. Recently, epidemiological studies suggested that the incidence and prevalence of prosthetic joint infection in the United States may be increasing [4]. Surgical resection and revision arthroplasty are required in severe cases, which impose heavy burden on patients and surgeons and generate high costs. Furthermore, it is projected that revision surgeries after THA will increase by 137% between 2005 and 2030, with the number of patients who are undergoing this procedure reaching 97,000 by 2030 [5]. Moreover, according to an estimate, health-care expenditure for revision surgeries will also increase, reaching $1.6 billion in 2020 [6]. Therefore, preventing these infections is becoming more important considering the recently growing number of patients at high risk of infection (eg, elderly patients and those with diabetes mellitus, chronic hepatitis,

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chronic renal dysfunction, immunosuppression due to collagen disease and malignant neoplasm, and previous hip surgery and infection) [7-9].

Numerous studies have reported using implants with antibacterial activity to prevent infection [10-14]. Silver (Ag) has been used as an additive in various medical devices. It is characterized by a broad antibacterial spectrum, potent antibacterial activity, and the low possibility of developing resistant bacterial strains. Notably, an Ag-coated mega-endoprosthesis prepared by coating the titanium surface with Ag has been applied clinically in orthopedic surgeries, resulting in reduced infection rates [15,16]. However, concentrated Ag is toxic to the osteoblasts and suppresses ossification; therefore, it cannot be applied in medical devices that are inserted into the bone marrow [17,18]. Therefore, to resolve this issue, Ag-containing hydroxyapatite (Ag-HA)-coated implants were developed by combining Ag with HA, which is recognized to possess high osteoconductivity [19]. Moreover, the Ag-HA total hip prosthesis (AG-PROTEX; KYOCERA Inc., Kyoto, Japan), which combined the antibacterial activity of Ag and the osteoconductivity of HA, is the first antibacterial cementless total hip prosthesis worldwide [20] (Fig. 1).

Remarkably, favorable THA outcomes with HA-coated implants have been reported [21,22]. However, it is yet to be determined whether Ag-containing HA yields outcomes as favorable as Ag-free HA and whether Ag results in adverse reactions or affects implant fixation. Therefore, in this study, we aimed to determine if Ag-HA-coated cementless THA has (1) good initial fixation and (2) good short-term clinical outcomes without complications (We hypothesize that Ag-HA-coated cementless THA would demonstrate excellent clinical result with implant stability).

Material and methods

In total, 50 hips of 45 patients with various disabling hip diseases and postoperative infection risk who underwent primary THA with an Ag-HA total hip prosthesis between April 2016 and March 2017 were enrolled in this study (Table 1). The patients included 37 women (41 hips) and 8 men (9 hips), and the average age at the time of surgery was 77.1 years (range, 46–90 years).

Table 1
Patient characteristics (diagnosis and risk of postoperative infection).

Characteristics	All hips (N = 50)
Diagnosis (number of joints)	
Osteoarthritis for acetabular dysplasia	27
Osteoarthritis for trauma	3
Rheumatoid arthritis	6
Osteonecrosis of the femoral head	6
Rapidly destructive coxarthropathy	4
Postpyogenic arthritis	1
Proximal femoral fracture	3
Risk of postoperative infection (partially duplicated)	
Old age (>75 y)	12
Diabetes mellitus	14
Chronic hepatitis	1
Chronic renal dysfunction (hemodialysis)	3 (1)
Collagen disease	16
Malignant neoplasm	6
Previous hip surgery	8
Previous hip infection	2

The Ag-HA total hip prosthesis is based on the SQRUM HA Cup and 910 PerFix Fullcoat D stem (KYOCERA Inc., Kyoto, Japan) currently used clinically. This implant has a porous structure on the bone-contact surface of the cup and the proximal third of the entire circumference of the stem and is coated with Ag-HA on the surface. This implant is a cementless THA implant with an uncoated cup surface facing the joint and neck. The implants contained 1.9–2.9 mg of Ag (mean, 2.28 mg). All patients included in this study who underwent a surgery at the same facility were placed in the decubitus position under spinal anesthesia, and their legs were left undraped. Additionally, the posterolateral technique was adopted in these cases. Prophylactic antibiotic therapy was administered 30

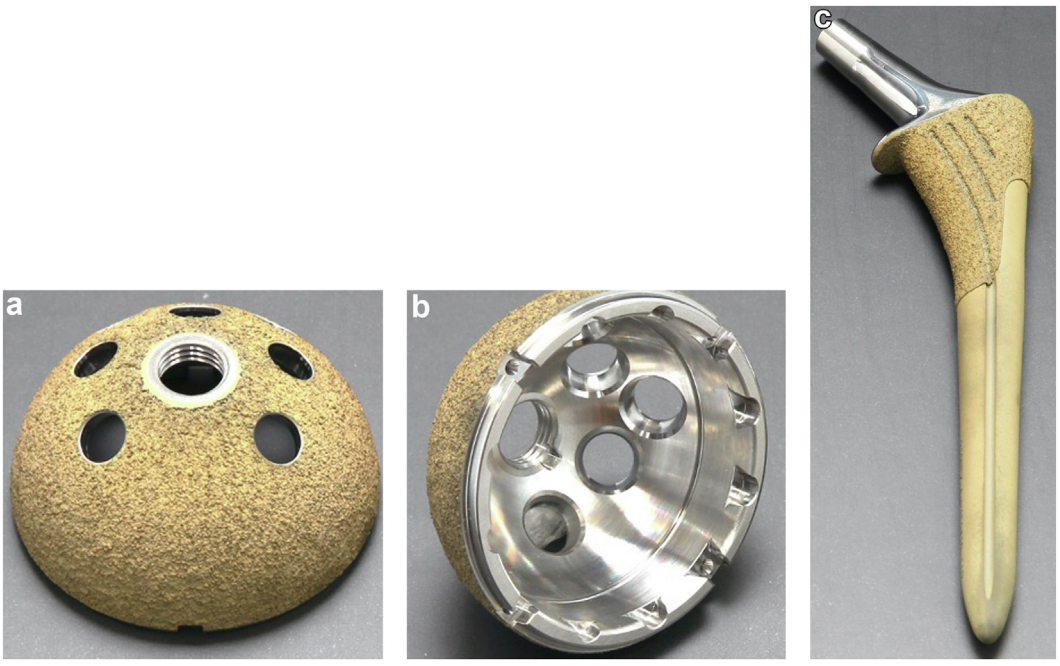

Figure 1. Photograph showing the silver-containing hydroxyapatite (Ag-HA)-coated total hip prosthesis. (a) This socket is a hemispheric titanium alloy socket that underwent porous processing by the arc spray of 0.5-mm titanium on the outer surface and with 2%–3% Ag-HA coating. (b) The cup surface facing the joint and stem neck is uncoated. (c) This stem is a fit-and-fill–type stem made of titanium alloy. The proximal part of the stem has porous processing by the arc spray of 0.5-mm titanium and is coated with 2%–3% Ag-HA on the entire surface.

minutes before the surgery and continued for 24 hours. Thromboembolic prophylaxis included early mobilization, active leg exercises, and antiembolic stockings. Finally, the patients were allowed to walk with full weight-bearing 1 day after the surgery and were followed up for 5 years.

Clinical assessment of outcomes of THA

The hip joint status before and 5 years after the surgery was evaluated using the Japanese Orthopaedic Association (JOA) hip score, which is the proposed criterion for assessing hip joint function. The JOA hip score with a total of 100 points as full marks has the following 4 categories: pain (40 points), range of motion (ROM) (20 points), walking ability (20 points), and activities of daily living (ADLs) (20 points). In addition, the scores are presented as mean ± standard deviation. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 21 software (IBM Corp., Armonk, NY). The preoperative and postoperative JOA scores were compared using Wilcoxon rank-sum tests. Statistical significance was considered at $P < .05$.

Analysis of implant stability and complications

Implant status before and after the surgery was assessed using a standardized anteroposterior radiograph of the pelvis. Diagnostic imaging was performed 1 week and 5 years after the surgery. Additionally, the position of the socket, gap filling, and presence of radiolucent lines were evaluated on the pelvic side. The parameters examined on the femoral side included stem stability by Engh et al. [23] and collapsing of the stem.

During the postoperative follow-up, each patient was monitored for adverse reactions to Ag (local argyria, delayed wound healing, and neurological symptoms). An orthopedic surgeon assessed the neurological symptoms. Postoperative complications were also examined.

Results

The mean JOA score of the patients improved from 41.0 points (range, 14–79) preoperatively to 85.7 points (range, 68–100) postoperatively ($P = .001$). Pain, ROM, gait, and ADL improved significantly (Table 2).

Additionally, the implant did not shift, incline, or subside 5 years after the surgery, and the radiolucent line was not detected in all cases. All cases exhibited detectable spot welds on radiographs at the 5-year assessment, and all femoral components had bone ongrowth fixation (Figs. 2 and 3). Furthermore, five cases showed detectable stable pedestal formation, and 6 revealed noticeable cortical hypertrophy. Moreover, stress shielding of the proximal femur and calcar was discovered in 43 hips, of which 26, 14, and 3 had proximal femoral remodeling of grades 1, 2, and 3, respectively.

Furthermore, postoperative dislocation occurred in 1 case 2 weeks after the surgery, requiring a noninvasive reduction, although no failure was observed in the cup and stem fixation. However, this case did not exhibit recurrence after treatment. However, deep vein thrombosis (DVT) occurred in 1 patient, but peripheral DVT healed without treatment. Moreover, no patient showed any sign of adverse reactions to Ag (local argyria, delayed wound healing, or neurologic symptoms) or infection during the follow-up period.

Table 2
Preoperative and postoperative JOA hip score.

Score	Preoperation	5-y postoperation	*P* value
Pain (40 point)	13.0 ± 9.2	36.8 ± 2.4	<.001
ROM (20 point)	11.2 ± 5.0	17.2 ± 2.6	<.001
Gait (20 point)	7.2 ± 4.0	16.0 ± 4.6	<.001
ADL (20 point)	9.8 ± 3.4	15.6 ± 2.8	<.001
Total (100 point)	41.0 ± 14.7	85.7 ± 9.6	<.001

JOA, Japanese orthopaedic association.
Values are given as mean ± standard deviation.

Discussion

This study revealed the first short-term clinical outcome of the Ag-HA total hip prosthesis. Regarding the antibacterial activity of Ag, Ag-HA has been demonstrated in vitro to suppress the growth of *Escherichia coli*, *Staphylococcus aureus*, and methicillin-resistant *Staphylococcus aureus* and inhibit these bacteria from adhering to the metal surface [24,25]. Furthermore, Ag-HA significantly suppressed the proliferation and inflammation of methicillin-resistant *Staphylococcus aureus* in rat subcutaneous and tibial models in vivo [26,27]. Regarding implant stability, this prosthesis possesses an implant design for cementless THA with good long-term outcomes [28]. Moreover, the effectiveness of Ag-HA was similar to that of HA in rat tibial and femoral models, with no significant difference in fixation during a direct mechanical test of osteoconductivity [29,30]. Therefore, the Ag-HA total hip prosthesis is expected to have an anti-infection effect, good clinical outcomes, and bone fixation similar to those of HA-coated cementless THA.

A recent study reported a good clinical outcome and implant fixation with HA-coated cementless THA [21,22,28,31]. In this study, the JOA hip score at 5 years postoperatively significantly improved in all categories (pain, ROM, gait, and ADL). These findings reveal that THA with an Ag-HA-coated implant can significantly enhance patients' daily life activities.

Although the long-term impact of the HA coating on the hip prosthesis is still controversial, early bone ingrowth of the prosthesis and good long-term clinical outcomes have been confirmed in the HA-coated prosthesis [32,33]. In this study, bone-ongrowth fixation of the Ag-HA total hip prosthesis was observed in all cases, and no loosening was observed. Additionally, the toxicity of Ag increases with density, and bone ingrowth may be obstructed by the high concentration of Ag [19,34,35]. However, Ag-Ha coatings have been reported to possess good osteoconductivity and facilitate new bone formation in vitro and in vivo [29,30]. In a clinical study, we reported that the Ag-Ha-coated socket presented early bone ongrowth histologically [36], and Eto et al. stated that Ag-HA-coated total hip prosthesis of 1 year has good initial stability in clinical trials [20]. In this study, no inhibition of osteogenesis or early loosening was observed 5 years after the surgery due to the addition of Ag. However, there was slight excessive stress shielding. Therefore, the short-term implant fixation of the Ag-HA total hip prosthesis was considered satisfactory.

Additionally, postoperative dislocation and DVT occurred in 1 case each in this study. Nevertheless, no infection or argyria development/other adverse reactions due to Ag developed in the patients.

Although Ag possesses antibacterial activity, it can also induce adverse reactions. Hepatopathy, nephropathy, neuropathy, and leukopenia because of high levels of Ag have been reported [34,35,37]. Argyria is a typical adverse reaction to Ag. Specifically, argyria involves blue-gray skin discoloration originating from the precipitation of Ag, which occasionally causes an intense disturbance of the external appearance [37]. Notably, no patient developed any of these adverse reactions to Ag or wound complications in this study. The maximum concentration of Ag contained in the Ag-HA implant was 2.9 mg, which was significantly lower than that in a silver-coated mega-endoprosthesis [16,38]. Furthermore, the

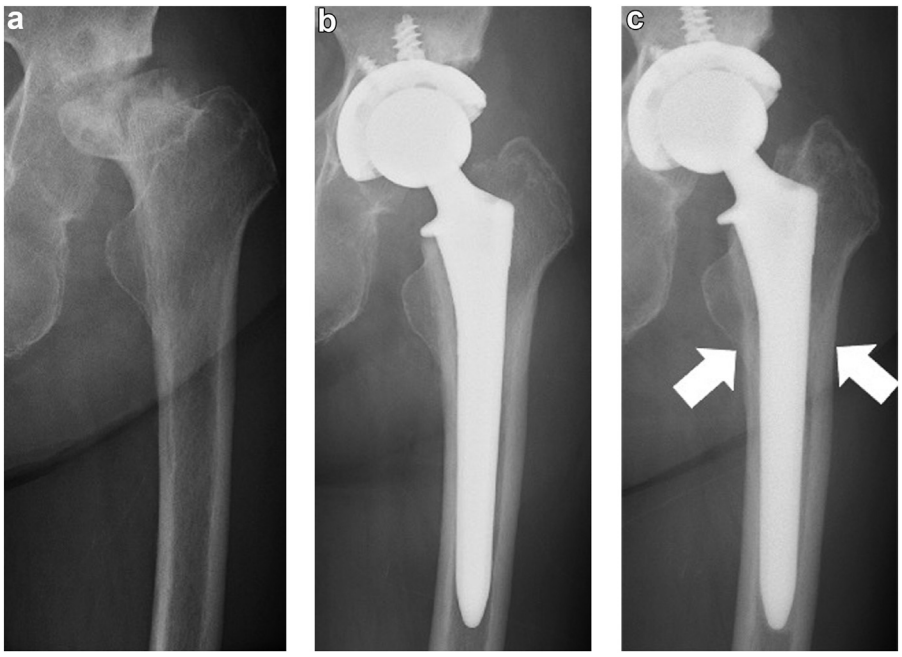

Figure 2. Photograph showing a case. (a) Case of a 74-year-old woman. Preoperative left hip anteroposterior radiograph of the pelvis. (b) She was on medication for rheumatoid arthritis and underwent left THA with an Ag-HA total hip prosthesis because of rapidly destructive coxarthropathy. (c) Five years after the THA. There was no movement, inclination, or subsidence of the acetabular or femoral implants. Spot welds are detected in Gruen zones 2 and 6 (white arrows). Stable pedestal formation, cortical hypertrophy, and radiolucent lines were not detected. The stress shielding was observed as grade 2.

concentration of Ag in the Ag-HA implant is also low since a total dose of 4 g of Ag is required to develop argyria [39-43]. Eto et al. reported that the blood Ag level peaked at 2 weeks, decreased subsequently, and was within the normal range after the Ag-HA implant was inserted [20]. Therefore, we believe that this implant's likelihood of developing argyria or other adverse reactions is minimal.

Although the infection was not observed in any case, whether an Ag-suppressed infection was present remains unknown because of the small sample size and short follow-up period. Moreover, in a previous study using a rat tibial model, the antibacterial activity was shown 4 weeks after implantation, suggesting that Ag-HA could sufficiently prevent acute and subacute infections [29]. Therefore, we believe this Ag-HA implant has antibacterial activity in patients at an elevated risk of infection (eg, more severely immunocompromised hosts and postpyogenic arthritis).

This study has some limitations, which included a small sample size and short follow-up period. Furthermore, it is crucial to

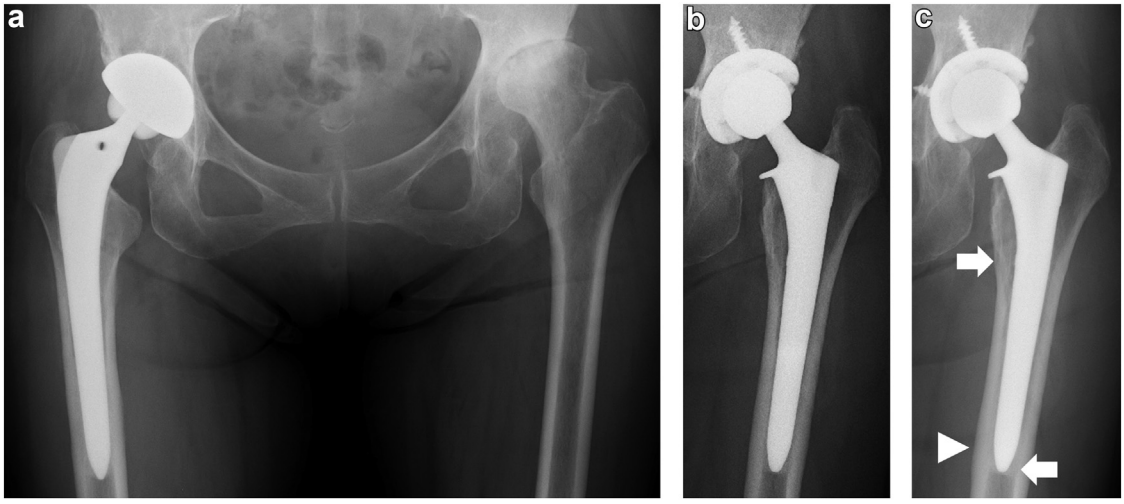

Figure 3. Photograph showing case 2. (a) Case of a 63-year-old woman. Preoperative left hip with anteroposterior radiograph of the pelvis. (b) She was undergoing right THA because of osteoarthritis for acetabular dysplasia and second debridement for prosthetic joint infection. She underwent left THA with an Ag-HA total hip prosthesis because of osteoarthritis for acetabular dysplasia. (c) Five years after the THA. There was no movement, inclination, or subsidence of the acetabular or femoral implants. Spot welds are detected in Gruen zones 2, 3, and 5 (white arrows) and cortical hypertrophy detected in Gruen zones 5 (white triangle). Stable pedestal formation and radiolucent lines were not detected. The stress shielding was observed as grade 2.

conduct long-term evaluations involving a larger number of participants and assess the antibacterial activity of Ag-HA total hip prostheses in patients who are at elevated risk of infection (eg, more severely immunocompromised hosts and patients undergoing a prosthesis revision surgery after infection).

Conclusions

The Ag-HA total hip prosthesis contains both Ag and HA and can alleviate or improve pain, ROM, walking capability, and ADL. No adverse reactions to Ag were observed in this study. Additionally, Ag-HA is expected to prevent infection in patients at a high risk of infection, considering the antibacterial activity of Ag. Therefore, it is a potential method for reducing postoperative infection, preventing declining quality of life, and obtaining favorable outcomes in patients undergoing prosthetic arthroplasty.

Institutional review board approval

The study protocol was in accordance with the ethical guidelines of the 1975 Declaration of Helsinki, and the institutional review board of our institution approved this study (2022-05-02). All patients provided informed consent for the publication of this study.

Conflicts of interest

M. Mawatari is a board member of the Japan Hip Society. All other authors declare no potential conflicts of interest.

For full disclosure statements refer to https://doi.org/10.1016/j.artd.2022.10.017.

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