Incidence of Metal Hypersensitivity in Orthopedic Surgical Patients Who Self-Report Hypersensitivity History

Mark Schultzel, MD; Christopher M Klein; Marine Demirjian, MD; Colin Blout; John M Itamura, MD

ABSTRACT

Introduction: Metallic implants are integral to the practice of orthopedic surgery. Delayed-onset T-cell-mediated metal hypersensitivity (diagnosed by patch testing) is reported in 10% to 17% of the general population. Inconclusive evidence exists about the role of metal hypersensitivity in persistently painful or aseptic loosening of arthroplasties. Literature suggests that preoperative patch testing may influence surgical practice.

Objective: To determine the incidence of metal hypersensitivity in orthopedic surgical patients who self-report hypersensitivity and to characterize which metals are most commonly implicated.

Methods: A retrospective chart review of patients from a single surgeon's practice was conducted during a 1-year period. All patients were questioned about metal hypersensitivity history; all patients who responded affirmatively were sent for patch testing for specific metals.

Results: Only 41 (4.9%) of 840 patients self-reported any metal hypersensitivity. Of these, 34 (83%) were patch-test positive to 1 or more metals. There were 27 whose test results were positive for nickel, 4 each to cobalt or gold thiosulfate, and 1 each to tin or titanium. Seven patients had positive results to multiple metals, all of whom were also nickel hypersensitive. Six patients had metal orthopedic implants before patch testing, and 4 (67%) tested positively to a metal in their implant.

Conclusion: Metal hypersensitivity can be concerning for treating surgeons and patients. Greater awareness of a history to hypersensitivity may prevent patient exposure to implants containing metals that may cause hypersensitivity. Non-metal-containing or nonreactive metal implants are an option for patients in whom metal hypersensitivity is suspected or confirmed.

INTRODUCTION

Total joint replacement (TJR) has been a major advance in the treatment of joint arthritis, achieving predictably excellent results with relatively low perioperative morbidity.1 The incidence of TJR continues to increase, with more than 1 million total hip arthroplasties (THAs) and total knee arthroplasties (TKAs) being performed annually in the US.2,3 Total shoulder arthroplasty also is becoming more prevalent, with more than 39,000 cases performed in 2010.4

As the incidence of TJR continues to increase, the potential impact of implant corrosion and metal ion release on patients with metal hypersensitivity has become a concern. About 10% to 20% of the general population has metal hypersensitivity, as diagnosed by patch testing.5 Approximately 10% of the population is hypersensitive to nickel specifically, with the literature describing hypersensitivity to beryllium, cobalt, and chromium.6 A recent study by Davis et al7 of 1000 patients reported an even higher incidence, with positive patch test results in 57% of tested patients.

Metals with the highest hypersensitive patch-test reaction rates were nickel, gold, manganese, palladium, cobalt, nickel-chromium alloy (Ticonium), mercury, beryllium, chromium, and silver.

Metal debris from orthopedic implants has been found in synovial fluid and soft tissues of patients with metal prostheses, as well as isolated in both blood and lymph samples.5 Type IV hypersensitivity, mediated by T lymphocytes, has been described as the most common hypersensitivity type related to TJR, with infiltrates of both T and B lymphocytes being documented in soft tissue after explant of the hardware, suggestive of an immune response to the implant.8-14

Recently, the potential impact of metal hypersensitivity in the context of TJR has been reported. Multiple studies discuss patient-reported metal hypersensitivity to various metals and their effects on physical function, pain, systemic symptoms, and mental health for lower-extremity TJR.15 Patient reporting of metal hypersensitivity has also been studied extensively in lower-extremity TJR, but little literature exists on total shoulder arthroplasty. Nam et al16 reported a case series of 906 THAs and 589 TKAs, in which patients with self-reported metal allergies had lower overall Hip Society and Knee Society scores, as well as decreased postoperative Short Form 12 (SF-12) Mental Component scores. Clinical findings of hypersensitivity at the skin level may include contact dermatitis and general pruritis. The link between reported symptoms—particularly non-skin-related somatic symptoms and pain—and metal hypersensitivity in patients with metal implants is poorly understood.16,17

No consensus or standard exists on how to screen or what changes in treatment plans must be implemented when delayed-onset T-cell-mediated metal hypersensitivity is suspected or confirmed.18 There is inconclusive evidence as to the role of metal hypersensitivity in persistently painful or aseptic loosening of arthroplasties, yet findings of literature reviews suggest that preoperative testing may influence surgical practice.19-23 The purposes of this study are to determine the incidence of metal hypersensitivity in orthopedic surgical patients and to characterize which metals patients are most commonly hypersensitive.

Author Affiliations
1 Southern California Permanente Medical Group, Orthopedic Medical Group of San Diego, Synergy Orthopedic Specialists Medical Group, San Diego
2 Kerlan-Jobe Orthopaedic Clinic, White Memorial Medical Center, Cedars-Sinai Medical Center, Keck School of Medicine, Los Angeles, CA
3 Department of Allergy and Immunology, University of California, Los Angeles

Corresponding Author
Mark Schultzel, MD (mschultzel@gmail.com)

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METHODS
This study is a retrospective chart review of patients from the orthopedic surgical practice of the senior author (JMI) during a 1-year period. All patients were routinely questioned about their history of metal hypersensitivity during an initial history taking and physical examination and during the planning paperwork for surgery. Patients were specifically asked about symptoms of rash, pruritus, or skin discoloration with jewelry or watch use; of symptoms with metal snaps, belt buckles, or buttons on clothing; of the earliest onset of symptoms; and of a family history of metal hypersensitivity. Patients were also asked about their surgical history and about receiving metal-containing orthopedic implants in previous surgeries.

All patients who admitted to metal hypersensitivity were sent for metal allergy patch testing for specific metals (Figure 1). The metals tested were nickel, cobalt, chromium, beryllium, gold, tin, silver, manganese, vanadium, zirconium, and titanium. All metal patch testing was performed by a single physician (MD) who was board certified by the American Board of Allergy and Immunology. The guidelines of the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) Statement were adopted for this manuscript (www.strobe-statement.org).

RESULTS
A total of 41 patients (4.9%) were sent for metal patch testing out of 840 new patients who were seen during the 1-year period. There were 34 patients (4.0%) whose patch-test results were positive to at least 1 metal. Of 32 patients (3.8%) who reported hypersensitivity when wearing metal costume jewelry or watches, 30 (3.6%) of these had positive patch-test results to at least 1 metal. Only 2 patients (0.2%) reported family members with suspected metal hypersensitivity.

On patch testing, 27 patients reacted positively to nickel; 4 each to cobalt and gold; and 1 each to tin, chromium, and titanium. Seven patients tested positive to multiple metals, and all of these cases were positive to at least nickel. Of the 32 patients with positive patch-test results, 6 (17.6%) had results positive to a metal in their existing orthopedic implant, which was placed before any patch testing (Figure 2). Four patients whose patch-test results were positive to a metal in their implant reported persistent edema, erythema, and postoperative joint pain. Three of these patients underwent revision operations because of suspected infections, all with cultures negative for infectious organisms. They all noted immediate alleviation of joint symptoms after receiving an implant replacement that contained no metals to which they were sensitive.

DISCUSSION
The majority of implants used in orthopedic operations are metal. Most of these implants are made from alloy metals, containing varied amounts of metals to which patients have displayed hypersensitivity, such as nickel, cobalt, and chromium. The pathophysiology of metal hypersensitivity–associated complications is incompletely understood and potentially complex. It is theorized to be related to a combination of the person’s T-cell immune status, reactivity of specific metal ions with HLA antigen and other proteins, and the corrosive and dispersal properties of the metals.

From the patients tested in this study, nearly all who had a history of metal hypersensitivity associated with skin contact to metal in clothing or jewelry had positive patch-test results to metals. Most patients with metal hypersensitivity were positive to nickel (n = 27), cobalt (n = 4), and gold (n = 4). This incidence is consistent with that reported in the published literature and suggests that routine questioning for history of anecdotal skin hypersensitivity may be an effective screening tool for true metal hypersensitivity. In the study by Davis et al, their results concluded that metals with the highest patch-test reaction rates are nickel, gold, manganese, palladium, cobalt, nickel-chromium alloy (Ticonium), mercury, beryllium, chromium, and silver. Metals causing no patch-test reactions include titanium, cobalt-chromium alloy (Vitallium), and aluminum powder. Metals with extremely low rates of allergic patch-test reactions include zinc, ferric chloride, and tin. Hypersensitivity to palladium and silver were determined to be cross-reactive with nickel. Despite the results of this study, our results found 1 patient with a titanium hypersensitivity, which has also been reported in another case report.
Nickel and cobalt are commonly used in metal alloys to confer stability and are present in most orthopedic implants available to surgeons. The amount of metal in these implants varies by company and product, but stainless steel plates and screws used for fracture contain high amounts of nickel, whereas high levels of cobalt are present in most arthroplasty implants, which are typically often cobalt-chrome. The most commonly used implants that are considered "low risk" are titanium and zirconium-niobium, which in arthroplasty can be used with polyethylene and ceramic-bearing surfaces in metal-hypersensitive patients. Zirconium-niobium does not contain nickel and has been associated with fewer wear particles, but it is significantly more expensive compared with other metal implants. Titanium alloy metals are marketed as "nickel-free" but often contain trace amounts of nickel and are also at risk for metal contamination during production.

A recent meta-analysis regarding metal hypersensitivity and TKA suggested that despite multiple case studies describing metal hypersensitivity reactions in patients who underwent TKA with a cobalt-chromium prosthesis, the lack of evidence-based medicine on metal hypersensitivity made it a diagnosis of exclusion, with patch testing or surgical intervention rarely indicated. In our series, 4 of the patients who tested positive for metal hypersensitivity already had metallic orthopedic implants from prior surgical procedures. All these patients had nickel hypersensitivity, and their implants were all made from nickel-containing stainless steel. Three of these patients underwent revision surgery because of suspected infection vs metal hypersensitivity, and their second implant was titanium (none of these 3 patients had patch-test-proven hypersensitivity to titanium). Two of these patients underwent revision arthroplasty, and the other patient underwent revision open reduction and internal fixation, with cultures negative for infectious organisms and no sign of implant loosening or failure. Their preoperative symptoms of edema and erythema over their incision sites and pain with use resolved within a month of their operations, suggesting that in the absence of loosening or infection, that metal hypersensitivity could have been the source of their symptoms. These anecdotal data are consistent with multiple case reports in which revision to a prosthesis made of a metal yielding patch-test negative results resulted in alleviation of symptoms, strengthening the argument for metal hypersensitivity testing and intervention.

With increasing concern regarding how metal hypersensitivity affects metallic implants used in orthopedic surgery, investigation into bone cement hypersensitivity may be of value. Bone cements are made of polymethyl methacrylate and contain additives such as dibenzoyl-peroxide, N,N-dimethyl-p-toluidine and 2-(4-[dimethylamino]-phenyl) ethanol, colorants (eg, copper-chlorophyll-complex), and antibiotics such as gentamicin. Blood tests and patch testing for acrylics have recently become commercially available.

CONCLUSION

T-cell-mediated delayed-onset metal hypersensitivity in orthopedic surgical patients can be a concern for treating surgeons and patients. More evidence is needed to establish a connection between metal hypersensitivity and risk of complications in procedures in which metallic implants are used. Greater awareness of metal hypersensitivity may prevent patient exposure to implants containing metals that they may react to. Non-metal-containing or nonreactive metal implants are an option for patients for whom metal hypersensitivity is either suspected or confirmed. Investigation of hypersensitivity to bone cement may also be of value to orthopedic surgeons.

Disclosure Statement
The author(s) have no conflicts of interest to disclose.

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The Patient's Own Words

In taking histories follow each line of thought; ask no leading questions; never suggest.

Give the patient's own words in the complaint.

— William Osler, MD, 1849-1919, physician, pathologist, teacher, diagnostician, bibliophile, historian, classicist, essayist, conservationist, organizer, manager, and author