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

Mark Schultzel, MD[1]; Christopher M Klein[2]; Marine Demirjian, MD[3]; Colin Blout[2]; John M Itamura, MD[2]

Perm J 2020;24:19.091

E-pub: 11/22/2019

https://doi.org/10.7812/TPP/19.091

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 al[7] 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.[8,9] 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.[10-14]

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 al[6] 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 to 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)

Keywords: allergy, hypersensitivity, implants, metal allergy, metal implants, metal in surgery, orthopaedic surgery, orthopedic surgery

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 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.[19] 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.[22]

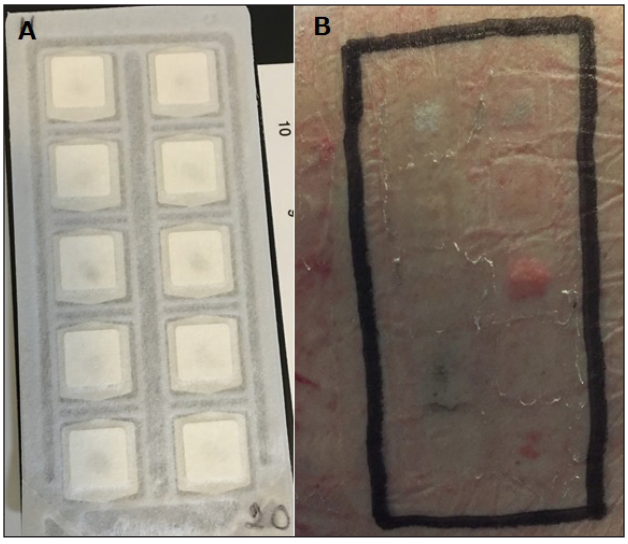

Figure 1. Patch tests for hypersensitivity to specific metals.

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.[15,19,22] In the study by Davis et al,[7] 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.[7] Despite the results of this study, our results found 1 patient with a titanium hypersensitivity, which has also been reported in another case report.[19]

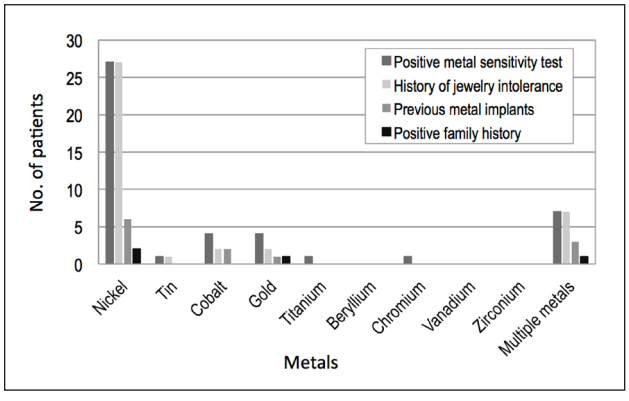

Figure 2. Frequency of positive results of patch testing, by type of metal.

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.[24] 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.[25] 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.[26] 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.[27]

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.[28] 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.[19]

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.[20] Blood tests and patch testing for acrylates have recently become commercially available.[29]

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.

Acknowledgment

The authors received research funding for this project from the Cedars-Sinai Kerlan Jobe Institute, Los Angeles, CA.

Kathleen Louden, ELS, of Louden Health Communications performed a primary copy edit.

How to Cite this Article

Schultzel M, Klein CM, Demirjian M, Blout C, Itamura JM. Incidence of metal hypersensitivity in orthopedic surgical patients who self-report hypersensitivity history. Perm J 2020;24:19.091. DOI: https://doi.org/10.7812/TPP/19.091

References

1. Jones CA, Beaupre LA, Johnston DW, Suarez-Almazor ME. Total joint arthroplasties: Current concepts of patient outcomes after surgery. Rheum Dis Clin North Am 2007 Feb;33(1):71-86.
2. Kurtz S, Ong KM, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am 2007 Apr;89(4):780-5.
3. Joint replacement registry [Internet]. Rosemont, IL: American Academy of Orthopaedic Surgeons; 1995-2019 [cited 2019 Jul 31]. Available from: www.ajrr.net.
4. Issa K, Pierce CM, Pierce TP, et al. Total shoulder arthroplasty demographics, incidence, and complications—A Nationwide Inpatient Sample Database study. Surg Technol Int 2016 Oct 26;29:240-6.
5. Jacobs JJ. Clinical manifestations of metal allergy. Adverse reactions to byproducts of joint replacements (AAOS/ORSI). Paper presented at: American Academy of Orthopaedic Surgeons Annual Meeting; 2012 Feb 7-11; San Francisco, CA.
6. Nam D, Li K, Riegler V, Barrack RL. Patient-reported metal allergy: A risk factor for poor outcomes after total joint arthroplasty? J Arthroplasty 2016 Sep;31(9):1910-15. DOI: https://doi.org/10.1016/j.arth.2016.02.016.
7. Davis MD, Wang MZ, Yiannias JA, et al. Patch testing with a large series of metal allergens: Findings from more than 1,000 patients in one decade at Mayo Clinic. Dermatitis 2011 Sep-Oct;22(5):256-71. DOI: https://doi.org/10.2310/6620.2011.11035.
8. Keegan GM, Learmonth ID, Case CP. Orthopaedic metals and their potential toxicity in the arthroplasty patient: A review of current knowledge and future strategies. J Bone Joint Surg Br 2007;89(5):567-73. DOI: https://doi.org/10.1302/0301-620X.89B5.18903.
9. Coleman RF, Herrington J, Scales JT. Concentration of wear products in hair, blood, and urine after total hip replacement. BMJ 1973 Mar 3;1(5852):527-9. DOI: https://doi.org/10.1136/bmj.1.5852.527.
10. Pizzoferrato A, Cenni E, Ciapetti G, et al. Inflammatory response to metals and ceramics. In: Barbucci R, editor. Integrated biomaterials science. New York, NY: Kluwer Academic/Plenum Publishers; 2002. p 735-91.
11. Holt G, Murnaghan C, Reilly J, Meek RM. The biology of aseptic osteolysis. Clin Orthop Relat Res 2007 Jul;460:240-52. DOI: https://doi.org/10.1097/BLO.0b013e31804b4147.
12. Hallab NJ, Jacobs JJ. Biologic effects of implant debris. Bull NYU Hosp Jt Dis 2009;67(2):182-8.
13. Davies AP, Willert HG, Campbell PA, Learmonth ID, Case CP. An unusual lymphocytic perivascular infiltration in tissues around contemporary metal-on-metal joint replacements. J Bone Joint Surg Am 2005 Jan;87(1):18-27. DOI: https://doi.org/10.2106/JBJS.C.00949.
14. Willert HG, Buchhorn GH, Fayyazi A, et al. Metal-on-metal bearings and hypersensitivity in patients with artificial hip joints: A clinical and histomorphological study. J Bone Joint Surg Am 2005 Jan;87(1):28-36. DOI: https://doi.org/10.2106/JBJS.A.02039pp.

15. Hallab N, Merritt K, Jacobs JJ. Metal sensitivity in patients with orthopaedic implants. J Bone Joint Surg Am 2001 Mar;83(3):428-36. DOI: https://doi.org/10.2106/00004623-200103000-00017.
16. Innocenti M, Carulli C, Matassi F, Carossino AM, Brandi ML, Civinini R. Total knee arthroplasty in patients with hypersensitivity to metals. Int Orthop 2014 Feb;38(2):329-33. DOI: https://doi.org/10.1007/s00264-013-2229-2.
17. Gao X, He R-X, Yan S-G, Wu L-D. Dermatitis associated with chromium following total knee arthroplasty. J Arthroplasty 2011 Jun;26(4):665.e13-6. DOI: https://doi.org/10.1016/j.arth.2010.06.002.
18. Razak A, Ebinesan AD, Charalambous CP. Metal allergy screening prior to joint arthroplasty and its influence on implant choice: A Delphi consensus study amongst orthopaedic arthroplasty surgeons. Knee Surg Relat Res 2013 Dec;25(4):186-93. DOI: https://doi.org/10.5792/ksrr.2013.25.4.186.
19. Razak A, Ebinesan AD, Charalambous CP. Metal hypersensitivity in patients with conventional orthopaedic implants. JBJS Rev 2014 Feb;2(2):01874474-201402000-00004.
20. Thomas P. Clinical and diagnostic challenges of metal implant allergy using the example of orthopedic surgical implants. Allergo J Int 2014;23(6):179-85. DOI: https://doi.org/10.1007/s40629-014-0023-3.
21. Morwood MP, Garrigues GE. Shoulder arthroplasty in the patient with metal hypersensitivity. J Shoulder Elbow Surg 2015 Jul;24(7):1156-64. DOI: https://doi.org/10.1016/j.jse.2015.01.015.
22. Mesinkovska NA, Tellez A, Molina L, et al. The effect of patch testing on surgical practices and outcomes in orthopedic patients with metal implants. Arch Dermatol 2012 Jun;148(6):687-93. DOI: https://doi.org/10.1001/archdermatol.2011.2561.
23. Granchi D, Cenni E, Giunti A, Baldini N. Metal hypersensitivity testing in patients undergoing joint replacement: A systematic review. J Bone Joint Surg Br 2012;94:1126-34. DOI: https://doi.org/10.1302/0301-620X.94B8.28135.
24. Thomas P, Schuh A, Ring J, Thomsen M. Orthopedic surgical implants and allergies: Joint statement by the Implant Allergy Working Group (AK 20) of the DGOOC (German Association of Orthopedics and Orthopedic Surgery), DKG (German Contact Dermatitis Research Group) and DGAKI (German Society for Allergology and Clinical Immunology) [in German]. Orthopade 2008 Jan;37(1):75-88. DOI: https://doi.org/10.1007/s00105-007-1453-3.
25 Dearnley PA. A review of metallic, ceramic and surface-treated metals used for bearing surfaces in human joint replacements. Proc Inst Mech Eng H 1999;213(2):107-35. DOI: https://doi.org/10.1243/0954411991534843.
26. Bader R, Bergschmidt P, Fritsche A, Ansorge S, Thomas P, Mittelmeier W. Alternative materials and solutions in total knee arthroplasty for patients with metal allergy [in German]. Orthopade 2008 Feb;37(2):136-42. DOI: https://doi.org/10.1007/s00132-007-1189-x.
27. Thomas P, Thomas M, Summer B, et al. Impaired wound-healing, local eczema, and chronic inflammation following titanium osteosynthesis in a nickel and cobalt-allergic patient: A case report and review of the literature. J Bone Joint Surg Am 2011 Jun;93(11):e61.
28. Lachiewicz P, Watters T, Jacobs J. Metal hypersensitivity and total knee arthroplasty. J Am Acad Orthop Surg 2016 Feb;24(2):106-12. DOI: https://doi.org/10.5435/JAAOS-D-14-00290.
29. Goon AT, Bruze M, Zimerson E, Goh C-L, Soo-Quee Koh D, Isaksson M. Screening for acrylate/methacrylate allergy in the baseline series: Our experience in Sweden and Singapore. Contact Dermatitis 2008 Nov;59(5):307-13. DOI: https://doi.org/10.1111/j.1600-0536.2008.01440.x.

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, conservationalist, organizer, manager, and author