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REVIEW ARTICLE

Shoulder arthroplasty in the patient with metal hypersensitivity

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Background: The in vivo effects of metal hypersensitivity remain a topic of much debate. At the core of this debate is the possible, although still hotly contested, link between metal hypersensitivity and poorly functioning or failing implants. There are multiple studies on this topic in the hip and knee arthroplasty literature, but the applicability of this experience to shoulder arthroplasty remains unclear. Although how often metal hypersensitivity affects shoulder arthroplasty patients remains uncertain, a multitude of case reports have implicated metallic implants as a source of local and systemic allergic reactions. We recommend a cautious approach to patients with a history of metal hypersensitivity, including a careful evaluation of suspected metal hypersensitivities in all patients undergoing shoulder arthroplasty. If available, we recommend a metallic implant with low to no nickel content in patients with metal hypersensitivity. Given the large and increasing, number of total shoulder arthroplasty procedures and the high percentage of the population having a known or suspected metal hypersensitivity, this review is intended to guide and educate the shoulder surgeon in the evaluation and treatment of this patient population and to point out the areas where evidence-based recommendations are lacking.

Level of evidence: Narrative Review.

Keywords: Shoulder arthroplasty; metal hypersensitivity; orthopedic metal composition; osteolysis; wear debris; hypoallergenic implant options

The incidence of total shoulder arthroplasty (TSA) is steadily increasing: approximately 10,000 such procedures were performed in the United States in 2002, increasing to nearly 27,000 in 2008.[27] Part of this recent increase can be attributed to expanded options for patients with a wide range of shoulder pathology. Specifically, the reverse shoulder prosthesis, which was approved by the U.S. Food and Drug Administration in 2003 for use in the United States, allows effective treatment of a broader range of shoulder pathology, including rotator cuff tear arthropathy, fracture sequelae, revision shoulder arthroplasty, tumor resection, acute fracture, and chronic fracture sequelae.[31,47]

Successful, long-lasting implantation of a metal and plastic joint replacement requires the surgeon to understand not only the mechanical effects on the prosthesis in vivo but also any potential biologic response. One such issue involves the patient with a suspected or known metal hypersensitivity. Dermal manifestations of metal hypersensitivity are relatively common, affecting approximately 10% to 15% the general population.[20] Specifically, sensitization to nickel alone is estimated at approximately 10% of the population. Other metals that are known to cause a reaction

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are beryllium, cobalt, and chromium.[20] Clinical findings in such hypersensitivity reactions include dermatitis, rash, and erythema. Rarely, systemic signs have been appreciated, including generalized pruritus and dyspnea.[14,23] In contrast to these topical metal reactions, the potential for hypersensitivity to metal implanted deeper in the body is not as well understood.

One of the first case reports of presumed in vivo hypersensitivity to metallic orthopedic implants was reported in the *Journal of the American Medical Association* in 1975. Barranco et al[2] described a 20-year-old woman seen with extensive eczematous dermatitis on the chest and back 5 months after stainless steel screws had been implanted to treat a chronic patellar dislocation. The patient's dermatologic condition persisted despite extensive topical steroid administration. The day after the screws were removed, the erythema and pruritus markedly subsided. The authors noted the composition of the stainless steel screws included significant amounts of chromium (20%), nickel (14%), and molybdenum (4%).

More recently, Gao et al[14] reported a case of systemic dermatitis after implantation of a cobalt-chromium-molybdenum total knee arthroplasty (TKA). The authors reported the patient developed eczema near the operative scar at 6 months postoperatively. During the next 3 months, the eczema spread and became chronic over a period of 1 year. The dermatitis was diffuse, with lesions at the neck, wrist, hand, ankle, and buttock, with corresponding severe pruritus. These lesions, as well as the pruritus, were refractory to antihistamines and corticosteroids, although whether these were oral or topical is unclear from the description. A skin biopsy specimen showed a nonspecific perivascular lymphocyte and eosinophil infiltration of the upper dermis, suggestive of a type IV delayed-type hypersensitivity (DTH) reaction. A patch test result was highly positive for chromium sensitivity (++++). Given these data, the patient was diagnosed with chromium hypersensitivity, and a revision TKA was performed with a zirconium-niobium (Smith and Nephew, London, United Kingdom) implant. The authors reported the resolution of pruritus at 3 days and eczema at 2 months postoperatively, with no recurrence of symptoms at the 1-year follow-up. Two other case reports of similar dermal manifestations of metal hypersensitivity after TKA have also been reported,[4,21] although the authors did not report whether the dermatitis resolved with removal of the offending implants.

Many orthopedic implants contain large percentages of nickel as well as other trace metals (Table I). Stainless steel is less commonly used in today's arthroplasty implants; however, most screws are made of this composite metal. As reported in Table I, most stainless steel alloys contain a large percentage of nickel.[11,20] Cobalt alloy, frequently used for total joint arthroplasty, has approximately 1% nickel content.[20] It is pertinent to note that titanium alloy has no appreciable nickel content, although there has been evidence to suggest even titanium ions can rarely provoke a relevant immunologic reaction.[28]

Given the large, and increasing, number of TSA procedures and the high percentage of the population having a known or suspected metal hypersensitivity, this review is intended to guide and educate the shoulder surgeon in the evaluation and treatment of this patient population and highlight the areas where evidence-based recommendations are lacking.

Basic science of metal ion hypersensitivity

All metals that come into contact with biologic systems corrode, thereby releasing ions.[20,24] These ions can then activate an immune response by forming a complex with native proteins. This metal-protein complex becomes the "allergen" because the combination of the metal with the patient's own protein is no longer recognizable by the immune system as "self," and an inflammatory reaction ensues.[20] Hypersensitivity can be an immediate (within minutes) humoral response initiated by an antibody or a delayed (within hours to days) cell-mediated response. Implant-related reactions are generally believed to be DTH reactions.[14,16,20] Cell-mediated DTH is characterized by activation of sensitized lymphocytes by an antigen, release of various cytokines, and finally, recruitment and activation of macrophages. In the dermis, the Langerhans cell, part of the monocyte cell line and similar in function to macrophages, is the primary antigen-presenting cell (APC) associated with dermal hypersensitivity.[15,41] In subcutaneous/periprosthetic tissue, the dominant APC responsible for mediating an implant-related hypersensitivity response remains unknown. There are several proposed candidate APCs in the periprosthetic region, however, including macrophages, endothelial cells, lymphocytes, Langerhans cells, and dendritic cells.[20,35,48]

Experience in hip and knee arthroplasty

No prospective or retrospective studies have evaluated the link between metal hypersensitivity and aseptic loosening of humeral or glenoid components in TSA, although an abundance of literature has been devoted to this topic in the hip and knee, which may give some insight into the care of TSA patients. In 2001, Hallab et al[20] reviewed multiple studies performed in the 1970s and 1980s that attempted to find a correlation between metal sensitivity and premature implant failure. Fifteen studies were included and summarized in their review. These reports found a weighted mean prevalence of sensitivity to nickel, cobalt, or chromium of 25% in patients with a well-functioning implant, which was approximately twice that of the general population.[3,20] When looking at patients with a "failed or poorly functioning" implant, the prevalence of metal