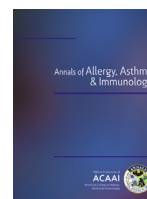




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Letter

Rash and a patch test result positive for cobalt in a patient with a hip replacement

Good biocompatibility is essential in materials used to develop orthopedic prostheses. Degradation, corrosion, and routine wear are expected with long-term use. However, in some cases, such routine use can release polymers and metals that compose the prostheses. Delayed-type hypersensitivity reaction can occur when metallic ions induce the immune system to react. Among the most common orthopedic metal sensitizers is cobalt.¹ We present a case of chronic urticaria in the setting of a hip transplantation and a patch test result positive for cobalt.

A 64-year-old woman with osteoarthritis underwent right total hip arthroplasty in September 2010. Postoperatively, the patient denied any difficulty with her hip. However, 5 months later, she reported having a pruritic rash. The patient was seen by her primary care physician and treated for eczema with triamcinolone. After medication failure, she was given prednisone and underwent autoimmune laboratory tests and an aeroallergen IgE specific panel. The results of both were negative and nonreactive. At the 1-year orthopedics follow-up, the patient inquired whether the hip replacement could cause the urticaria. By this time, the patient had tried a number of topical therapies targeted at treating the rash.

The patient was referred to the Allergy & Immunology Clinic in October 2011. Urticaria, circumscribed lesions of edema and erythema, was noted on all extremities, the trunk, and the face. A trigger for the patient's symptoms remained unknown. For 10 months, the patient was treated with cetirizine, hydroxyzine, dapson, and sulfasalazine with marginal success. In July 2012, the patient underwent a T.R.U.E Test panel of 36 allergens. Cobalt dichloride, a known metal ion in hip prosthesis, was the only allergen for which the test result was positive. The degree of positive responses to cobalt was 2+ (a strong positive).^{2,3} The relation between the positive patch test result and urticaria has been reviewed in previous reports, suggesting that an IgE-mediated reaction to metal can occur and cause urticaria.^{4,5}

Consideration must be given to other possible sources of cobalt, such as dietary cobalt, vitamin B₁₂, and light brown hair dyes.⁶ Our patient takes a multivitamin and uses hair dye, both of which may be contributing factors to the positive patch test result. The patient was treated with 300-mg subcutaneous monthly injections of omalizumab for 3 months without success. It took 2 months of oral tacrolimus before resolution of urticaria without residual skin changes occurred. Currently, the patient continues to take oral tacrolimus, 2 mg every morning and 1 mg at night. Although urticaria is often associated with IgE-mediated reactions, other mechanisms are possible as well. Future testing with an immediate 6-hour patch test with cobalt, a chronic idiopathic urticarial index, or autologous serum skin test is under consideration for this patient.⁷

Roughly 6.2% to 8.8% of symptomatic patch-tested patients with prior orthopedic implants tested positive for cobalt sensitization.⁸ However, the incidence and prevalence of hypersensitivity to implanted metals are unknown. Data suggest that approximately 5% of patients with positive patch test results developed metal-related cutaneous complications after implantation.^{1,9} Given the prevalence of cobalt sensitivity identified through patch testing, analysis of metallic implant-induced hypersensitivity is warranted.

Metallic debris from implants can trigger delayed-type hypersensitivity reactions. A recent prospective study analyzing metal sensitivity in patients with orthopedic implants noted an increase in the percentage of patients who have metal sensitivity 1 year after implantation. Among the most common sensitizing materials is cobalt.¹

Hypersensitivity as a factor in poor implant performance should be considered based on reports of patients with prosthesis loosening who also have delayed-type hypersensitivity to metals.¹ In a few cases, the debris generated by degradation of the implant may trigger a chronic inflammatory reaction caused by the release of proinflammatory cytokines (tumor necrosis factor α and interleukins 6, 1 α , and 1 β), leading to implant failure and macrophage-stimulated aseptic osteolysis.^{1,9}

In other cases, metallic debris is thought to alter bone homeostasis by stimulating T cells to generate pro-osteoclastogenic factors that further enhance osteolysis.¹ Analysis of patients with metallic hypersensitivity reveals that tissue adjacent to implanted metal has elevated levels of immune markers or cells, such as CD3 β T lymphocytes, CD4 β cells, and CD11c β dendritic cells or macrophages. In addition, an increased percentage of major histocompatibility complex class II expression was found.⁹

Thyssen et al⁸ found that 10% of hip implant components tested positive for cobalt. Further, the study by Thyssen et al⁸ noted that a linear correlation exists between serum ion levels after implantation and sensitization compared with controls.⁸ This took into account cobalt released from sources other than the implantation, such as dark and gold-plated jewelry.⁸

Despite the possibility of delayed-type hypersensitivity, implant failure, and cutaneous reactions, the decision to patch test every patient preoperatively for cobalt sensitization is generally not favored unless a known metal hypersensitivity exists. The decision to patch test patients with a known metal hypersensitivity resulting from watches, jewelry, or belt buckles before surgery may identify candidates for alternative prosthetic material, such as oxidized zirconium-niobium alloy in the case of conventional cobalt-chromium used in knee arthroplasty.¹⁰

A retrospective case-control study analyzed patients given a metal patch test before surgical implantation of a metal-containing hip prosthesis.¹ The study found that patients who tested positive

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and proceeded with the surgery had shorter prosthesis lifespans.¹ One study reported further that although a total hip arthroplasty generally has a mean lifespan of 120 months, this is shortened considerably to 78 months in patients with metal hypersensitivity.¹

In patients who have undergone surgical implantation of prosthesis and subsequently experience a cutaneous reaction (urticaria, pruritus, eczema, or vasculitis), joint pain after implantation, or implant loosening, an evaluation for hypersensitivity should be considered. The metals included in patch testing for patients with failed implants or dermatitis after implantation should be those metals most commonly found in the specific orthopedic prosthesis.⁹

The management options for patients with positive patch test results largely depend on whether clinical demonstration of hypersensitivity exists. That is, a positive patch test result alone should not dictate the management of patients with metallic prosthesis. However, in patients with contact dermatitis, joint loosening, and joint pain after implantation and patients who have undergone injectable corticosteroid therapy without success, perhaps removal of the offending agent and replacement with a less likely offending agent should be considered.⁹

Consideration must be given to the fact that few prospective data are available on the idea of patch testing patients before implantation. Given the retrospective data indicating a correlation between implantation failure and delayed-type hypersensitivity, it is arguable that such a study is warranted. However, what is clear is that a detailed history regarding whether a metal allergy existed before implantation is necessary. Perhaps by removing the offending agent, allergic symptoms may be alleviated; the management of patients with symptoms after implantation should reflect whether removal is a viable option; whether replacement of the implant with an alternative alloy, such as oxidized zirconium-niobium in the case of cobalt sensitivity, is possible; or whether the use of a nonallergenic coating is preferable.⁹

Capt Priya I. Nath, USAF, MC, JD, MD*
LtCol Christopher A. Coop, USAF, MD†

*Department of Pediatrics

San Antonio Military Medical Center

Joint Base San Antonio

Ft Sam Houston, Texas

†Department of Allergy and Immunology

Wilford Hall Ambulatory Surgical Center

San Antonio, Texas

priya.i.nath.mil@mail.mil

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