



Systemic Contact Dermatitis Possibly Related to Metal Implants

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Question:

I saw a patient with a knee replacement that resulted in prolonged swelling and a multiple macular, flat, almost violaceous rash of the tibial area that was nonpruritic. The procedure was done in 2009. In 2011, the patient had a laboratory test done in Chicago (orthopedic analysis) that amounted to a PHA test against several metals and bone cement. This test came back with numerous positive results, and the patient had the knee procedure corrected with a repeated replacement in 2011. He believes that the bone cement was cleared out and that none of the potentially incriminated metals, which included nickel and zirconium as well as any bone cement, were used in the new replacement. Since that time, he has had continued swelling in the knee with episodic recurrence of the described rash. I am unaware of the validity of this test for metals.

I would appreciate your comments and any further advice. The laboratory appears to be a "one-of-a-kind" in the Chicago area. The patient is 66 years old and basically has no other medical conditions with the exception of hypertension. He is on no other medications.

Response:

This question was posed to Luz Fonacier, MD, Head of Allergy Section, Division of Rheumatology and Immunology, Winthrop University Hospital, Mineola, NY, a nationally known expert in contact dermatitis. She responded as follows.

This is a complicated answer to a complicated question, so I will just present to you the literature and what we have written in the *Practice Parameters for Contact Dermatitis* that is in preparation.

Allergic contact dermatitis from bone cement components have been reported in 24.8% of patients (n = 239).¹ Bone cements of orthopedic implants are composed of methyl methacrylate, an N, N-dimethyl-p-toluidine reaction initiator, and a benzoyl peroxide activator. Hydroquinone is occasionally added as a stabilization agent for the methyl methacrylate. Antibiotic (eg, gentamicin) may be added as well. These agents are potential causes of contact allergy and joint loosening.² Positive patch test reactions are varied and have been reported to N,N-dimethyl-p-toluidine (10%), polymethyl methacrylate (2%-25%), benzoyl peroxide (8%-18%), hydroquinone (2%-5%), and gentamicin (17%-24%).^{1,3-5} Results of another series reported that 7 of 15 patients with early aseptic loosening of cemented total hip replacements had positive reactions to N, N-dimethyl-p-toluidine.³ Thus, it is important to consider reactions to cement in symptomatic patients after a procedure that used bone cement to allow for a more thorough evaluation. Other common

causes of implant failure are infection, recurrent dislocation, aseptic osteolysis, and fractures.

The proposed summary statement in the *Update on the Practice Parameters in Contact Dermatitis*, which is still under development, states the following: "The clinical relevance of commercially available blood tests to diagnose metal sensitization has not been determined. Most of these tests measure lymphocyte proliferation (stimulation index) after 7 days' incubation with or without allergen. There are limited allergens to test, and there tends to be a rapid decay of T cells; therefore, rapid transport is needed. Some orthopedic literature claim that the lymphocyte transformation test better reflects immune reactions within the body, whereas the patch test reflects cutaneous reactivity. At this time, both patch testing and LTT (lymphocyte transformation test) for orthopedic implant reactions still needs validation"

Having said that, your case is unique because the rash plus joint failure did not resolve with replacement. I would probably do this if this patient were referred to me:

1. I would still advise the need to rule out other causes of joint failure, such as infection, recurrent dislocation, aseptic osteolysis, and fractures. In this case, perhaps a second opinion may be helpful.
2. I would also look for other causes of the rash and possibly consult with a dermatologist.
3. Review of consultation notes and operative reports is important to a. confirm that the second replacement was done "cementless." b. identify as well as obtain the components of both the old and new prosthesis, including the metals and cement.
4. Do a patch test to a panel of metal salts and other implant components, including to bone cements in generally accepted and published concentrations if possible.
5. If there is no contraindication (ie, infection), then treat with oral corticosteroids for 3 weeks and see if the inflammation and rash resolve before even considering another surgery.

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