

Bullous Pemphigoid Triggered by a Titanium-Containing Knee Implant

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A 75-year-old woman with a history of type 2 diabetes mellitus, hyperlipidemia, and severe degenerative joint disease of her knees underwent a total knee replacement of her left knee with a Zimmer titanium alloy tibial component and a cobalt-chromium-molybdenum femoral component. There was no history of skin disease and metal implants, and the surgery was performed without complications. However, within 2 months, she developed pruritic blisters around the implanted knee (Fig. 1). Predominant blistering was localized around her implanted knee, with rare blisters on her chest. She was afebrile and did not exhibit leukocytosis, and her bacterial cultures from blisters did not yield pathogenic organisms. Imaging was negative for malalignment and signs of infection. She was treated by her surgeon with oral antibiotics without resolution of the blisters and referred to dermatology.

Histologic analysis of a biopsy specimen from the edge of a blister revealed a subepidermal split with mononuclear infiltrate and numerous eosinophils. Direct immunofluorescence of a biopsy specimen of perilesional skin revealed linear deposits of C3 and immunoglobulin G along the basement membrane (not shown), supporting a diagnosis of bullous pemphigoid (BP). She was patch tested with cobalt, potassium dichromate, nickel, titanium (III) nitride, titanium dioxide, titanium (IV) oxalate hydrate, titanium, molybdenum, and acrylates from the dental series. At 48 and 96 hours, she exhibited a 1+ reaction to titanium (IV) oxalate hydrate only (Fig. 2). The blistering was managed successfully using topical clobetasol propionate 0.05% and doxycycline 100 mg by mouth, twice daily. Despite the positive patch test to titanium, there are no plans to remove her knee implant.

The differential diagnosis for pruritic blisters after this procedure includes edema bullae, bullous cellulitis, and allergic contact dermatitis.¹ Bullous pemphigoid is a rare complication of total knee replacements, and only 5 cases have been reported in the literature.

In all but one of these cases, generalized spread of bullae occurred.¹ This seems to be more common than localized disease around the surgical site and typically occurs within 3 to 7 days.^{1,2} Given the localized presentation of our case, the positive patch test result, and treatment outcomes, the underlying trigger for BP favors an implant-related titanium hypersensitivity.

Positive patch testing for titanium alloys with postoperative onset of BP has only been reported in a case of hip replacement.³ This was treated unsuccessfully with oral and topical antihistamines. Because of the recurrent, generalized, and severe presence of blisters, high-dose intravenous methylprednisolone, intravenous immunoglobulin, and subsequent oral prednisone were required for resolution. Methacrylates have also been described in a recent case as a contact allergen trigger of BP postoperatively, because they can be components of bone cement in the implant.⁴ Here, the BP was resistant to local corticosteroids, and the rash spontaneously resolved without any systemic intervention approximately 6 months later.

Our report adds a unique case to the literature that calls for future investigation and consideration of alternate implant materials to be studied for these patients.



Figure 1. Clinical presentation of bullous pemphigoid. Tense bullae with erosions were present around the implanted left knee surgical site.

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Figure 2. Seventy-two-hour reading of patch test. A 1+ reaction to titanium (IV) oxalate hydrate (bottom left). There were no reactions to the other 4 titanium derivatives or to nickel, cobalt, potassium dichromate, molybdenum, or acrylates tested.

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