

Case Report

Hypersensitivity to Benzoyl Peroxide in a Cemented Total Knee Arthroplasty

Cement Allergy

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Abstract: A small but significant proportion of cemented total knee arthroplasties develop aseptic loosening. Polyethylene debris is unlikely to be the cause in the small subgroup that experiences early loosening. Allergy to polymethylmethacrylate bone cement or its constituents has been reported in several different industries and in dentistry, dermatology, and joint arthroplasty. Although allergy to polymethylmethacrylate bone cement or its constituents is unusual, the possibility of a systemic inflammatory response and consequent pain and loosening must be considered. We report a case history of a patient who developed a systemic reaction and intractable pain after a total knee arthroplasty who was subsequently shown to be hypersensitive to the benzoyl peroxide component of bone cement. **Key words:** total joint arthroplasty, cement allergy, benzoyl peroxide.

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Aseptic loosening is the leading cause of arthroplasty failure. Several etiologic factors leading to aseptic loosening have been proposed, which include technical errors, unfavorable mechanical factors, and biological reaction to the implanted foreign material, particularly polyethylene debris. Polyethylene debris is unlikely to be the cause in the small subgroup that experience early loosening [1].

Allergy to polymethylmethacrylate (PMMA) bone cement or its constituents has been reported in several different situations including the cosmetic and printing industries, dentistry, and dermatology [2-6].

Hypersensitivity to the metallic components and bone cement used in total joint arthroplasty has also been described. Although allergy to PMMA bone cement or its constituents is unusual, the potential for a systemic inflammatory response and the possibility of pain and loosening must be considered [7-11].

Case History

Total knee arthroplasty, without patellar resurfacing, was performed in a 48-year-old woman with end-stage osteoarthritis of the knee. The

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patient had an uncomplicated early postoperative recovery. However, at 6 weeks, the patient was complaining of generalized knee pain; and clinical examination revealed a swollen knee and skin rash over the right lower limb and anterior abdominal wall. The patient was also systemically unwell. At this stage, she was referred to the medical team for evaluation. At a follow-up 3 months later, the patient continued to complain of knee pain; and examination still revealed a swollen and tender knee. Serological tests were found to be slightly elevated, with C-reactive protein at 12 mg/L (reference range, 0-10) and erythrocyte sedimentation rate at 30 mm/h (reference value, <20). White blood cell count at $12 \times 10^9/\text{L}$ was normal/slightly elevated, with the eosinophil count being normal. The radiographs revealed well-positioned and well-fixed components (Fig. 1). No organisms were iso-



Fig. 1. A, Postoperative anteroposterior radiograph of initial cemented total knee arthroplasty. B, Postoperative lateral radiograph of initial cemented total knee arthroplasty.

lated from the joint aspirate. The bone scan had a slightly increased uptake at the patellofemoral joint and raised the possibility that arthritis at this joint was partly responsible for the continued knee pain. The decision was therefore made to proceed with isolated patellofemoral resurfacing. At the time of resurfacing arthroplasty, at 11 months after the index procedure, moderate synovitis was encountered (nonspecific picture of synovitis with scanty macrophages and lymphocytes). There was no macroscopic or microscopic evidence of infection.

Despite the resurfacing, the patient's symptoms continued to persist. Further investigations were carried out to investigate a possible allergy. She was found to have a severe allergy to benzoyl peroxide, an initiating agent that initiates the polymerization process, in the PMMA cement. The allergy was so severe that an ulcer developed under the test skin patch.

Following this, the patient recounted that she had been previously diagnosed as being allergic to this agent. This was once a constituent of flour; and until it was removed, the patient could not work as a baker.

Because of continuing symptoms and the confirmation of the allergy, a decision was made to perform revision surgery. The cemented tibial and femoral components and the methylmethacrylate cement were removed. Reimplantation using uncemented components was performed. The intraoperative tissue cultures taken during revision surgery were negative for infection. The patient made an excellent recovery after the revision arthroplasty. At the latest follow-up of 3 months since the revision arthroplasty, the patient had minimal pain, the skin rash had resolved, and the swelling in the knee had disappeared completely.

Discussion

Benzoyl peroxide is an essential component of bone cement. Its function is to initiate the polymerization of methylmethacrylate monomer. Direct evidence for allergic reactions to benzoyl peroxide has been reported in dental and dermatological literature [5,6]. There has been only one case report of allergy to benzoyl peroxide in bone cement used for a total hip arthroplasty in 1979 [9]. Other hypersensitivity reactions to bone cements or their constituents have been reported, but this has largely been attributed to the *N,N*-dimethyl-*para*-toluidine component [11].

Studies of the cement bone interface of total hip arthroplasties have shown that a synovium-like

membrane forms that has the capacity to produce prostaglandin E2, collagenase, and other osteolytic products. The macrophage/giant cell reaction has been likened to a type IV hypersensitivity reaction (delayed hypersensitivity reaction that may explain delayed presentation of systemic symptoms). It is also not clear whether this is a primary or secondary phenomenon [12,13].

The currently accepted model for this delayed hypersensitivity is that a hapten such as benzoyl peroxide conjugates with a body protein, which creates a neoantigen capable of stimulating an immune response [14,15].

Our case report suggests that benzoyl peroxide hypersensitivity places the patient at risk of developing insidious pain, a systemic inflammatory response, and possibly aseptic loosening. After revision to uncemented femoral and tibial components, the patient's symptoms vastly improved. The cemented patella component was not revised principally for 2 reasons. Firstly, the authors felt that the volume of cement associated with the patella component was minimal and postulated that there would be a sufficient reduction in the volume or load/response just revising the femoral and tibial components. Secondly, we have little experience in uncemented patella resurfacing; and as the patella was well fixed and tracked optimally, we decided to leave it in situ.

We believe that a full allergy and occupational history should be taken to try to identify potentially sensitized individuals. These can then be patch-tested to determine those with definite allergies. In these groups of patients, careful consideration should be given to using an uncemented prosthesis.

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