Complex total knee arthroplasty in a patient with bone cement allergy: A case report

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Abstract
Case: Total knee arthroplasty (TKA) is a common surgical procedure, with annually increasing numbers worldwide, and the great majority of TKAs utilize polymethyl methacrylate (PMMA) bone cement on a routine basis. However, there has been little awareness of hypersensitivity reactions to bone cement components which can potentially lead to serious adverse effects. We report the case of a 44-year-old female with severe knee arthritis and medically-warranted need for left TKA who had allergy to bone cement components. The allergy was fortuitously identified preoperatively, and the use of specialized implant components that removed the risk of exposure to the allergens helped to avoid potential complications.

Conclusion: Conscientious preoperative evaluation and planning will help to identify and manage patients with bone cement allergy. We report this case as it is an uncommon but yet medically significant case of complex primary TKA with multiple special requirements, each presenting a different learning point.

Keywords: Total knee arthroplasty, bone cement allergy, PMMA

Introduction
With aging populations and increasing physical expectations of individuals for healthy aging, osteoarthritis is becoming exceedingly common. In Singapore, osteoarthritis is estimated to affect up to 26% of the population by 2030 [1], with numerous numbers of TKA each year (2, 3). With the burgeoning numbers of TKA, complications following TKA and implant failure have consequently drawn more attention, as these can have significant and even devastating effects. Case reports and studies have evaluated the role of delayed hypersensitivity in failure of orthopedic implants, especially its metal components [4, 5]. On the other hand, much less attention has been paid to the possible allergic role of bone cement components, with the majority of these studies looking at this relationship from a postoperative and retrospective point of view in the setting of persistent postoperative pain, radiological aseptic loosening, and other manifestations [6-8]. To date, there has only been one other case report worldwide on the preoperative identification of allergy to methyl methacrylate, an acrylate component of bone cement, highlighting the difficulty and yet importance of such pre-operative detection [9]. We report a case of a 44-year old woman who needed a TKA but had preoperatively identified contact allergy to benzoyl peroxide and bone cement powder; the circumstances of the detection, and the subsequent protocols and decision making to ameliorate her risks.

Statement of Informed Consent
The patient was informed that and agreed to, her clinical data and images being used for submission as a case report for publication.

Case Report
A 44-year old lady with a history of previous arthroscopic lateral meniscectomy of her left knee at the age of 12 presented with progressively worsening left knee pain with stiffness, difficulty walking, as well as the sensation of ‘giving-way’ occasionally. Physical examination revealed a 20° valgus alignment and fixed flexion deformity of her left knee, with range of motion from 40-80° (Fig. 1).
Radiographic examination showed severe osteoarthritis of the left knee with obliteration of the lateral joint space and marked valgus deformity (Fig. 2). She was on conservative management for 5 years and was subsequently planned for left TKA despite her young age in view of severe arthritis, deformity and symptoms of pain and instability affecting her ambulation and daily activities.

Prior to knee surgery, it was noted that she had developed acute contact eczema over her hands and left ankle. In view of this history of allergy, she was referred to an allergist for testing. A basic series patch testing was conducted which included standard dermatological tests for allergies to preservatives, emollients, additives, rubber, glue and textile colors. A positive reaction to benzoyl peroxide, a standard active ingredient in topical acne solutions, was found (Fig. 3). This result was reviewed by the orthopaedic team during the preoperative assessment and it was then highlighted that benzoyl peroxide is also a key constituent of polymethyl methacrylate (PMMA) bone cement systems. As the planned surgery had included the use of standard PMMA bone cement, the patient subsequently underwent further patch testing with a specific test panel of bone-cement components, which again showed a positive reactions on day 2 and day 4 to cement powder in 1:10 dilution. The battery of tests confirmed contact allergy to both benzoyl peroxide and cement powder (Table I).

In view of this positive allergy test, it was decided to delay TKA while evaluating non-cemented implant options with particular considerations in view of the patient’s relatively young age and marked knee deformity and instability. The conflicting considerations were that cementless TKA systems generally do not provide the extra stability required for gross deformity corrections which was required in this case. Cementless TKA implants also have more concerns regarding their longevity and risk for earlier loosening which would be very relevant in patient’s age group[10,11]. An attempt to avoid TKA was made; as an interim management for her knee symptoms, our patient underwent left knee arthroscopic debridement, washout and removal of loose bodies. While her symptoms initially improved, they subsequently recurred with progressively worsening left knee pain, valgus deformity of her left knee and a valgus thrust painful gait. After considering and discussing with her the various options of management in view of her reported allergy to cement components, she finally underwent a complex cementless left TKA that was felt to afford sufficient stability and reduce (but not remove) the risk of future revision surgery.

Postoperatively, her recovery was uneventful as she started ambulating with walking frame and knee brace. Her knee ROM was 5-130° with neutral alignment (Fig. 4, 5, 6). At 2 weeks post-surgery, her wound healed well and left knee ROM was 5-90°. Postoperative radiographs at 2 and 4 weeks follow-up however revealed an incomplete fracture at the tip of tibial stem and so she was restricted from full weight bearing for further 4 weeks (Fig. 7, 8).

At 3 months follow-up, she was pain-free and walking independently without valgus thrust. Her left knee ROM was 15-90°, as the contralateral knee had a fixed flexion deformity of 10°. Repeat radiographs demonstrated healing of the incomplete fracture at the tibial stem tip (Fig. 9).

Currently at 6 months follow-up, she is pain free and back to routine lifestyle. Her knee ROM is 15-90°. Radiographs demonstrate implants in proper alignment without any subsidence (Fig. 10). She continues to be under regular follow-up.

**Discussion**

Benzoyl peroxide is well-known for its role in the treatment of acne. Besides its use as a medication, it is also a powerful bleaching agent and an integral component of bone cement used extensively in dental and orthopaedic implants as an interface between bone and metal to facilitate adherence. Bone cement is comprised of polymethyl methacrylate (PMMA), an acrylate that goes through a free radical polymerization process facilitated by additives, of which benzoyl peroxide plays an important role as an initiator, hence its relevance in cemented arthroplasties [12].

While there is currently scant awareness of benzoyl peroxide allergy in joint replacement surgery, it is a well-recognized entity in the field of contact allergy in dermatological products. It has been reported to cause skin reactions in the form of stinging/burning, itching, erythema, edema and even desquamation [13]. Although benzoyl peroxide is a known skin irritant that can make interpretation of weakly positive patch test reactions difficult [14], studies have shown that it does have a role in allergic sensitization, especially in high risk groups exposed to high concentrations of benzoyl peroxide, such as patients treated with 20% benzoyl peroxide for chronic venous ulcers in the 1980s and dental technicians who have repeated exposure to acrylates in the production of dentures [15,16]. This current report serves to highlight the importance of cross awareness amongst medical disciplines.

The possible role of benzoyl peroxide allergic sensitization in aseptic implant failure was brought to light recently. Fröschel et al. showed in their case series 6 patients with “painful endoprosthesis” who subsequently showed positive skin reactions to benzoyl peroxide and then underwent cementless revision knee arthroplasties. Histological examination of obtained tissue samples showed lymphocytic mediated perivascular infiltration with partly increased expression of CD3, suggestive of type IV mediated hypersensitivity reaction, and postoperative follow up after revision with cementless arthroplasties resulted in significant improvement of the Knee Society Functional Score [17].

Currently, the implant allergy working group of the German Association of Orthopaedics recommends allergy diagnostic patch testing with a standard metal and bone cement component series for persistent implant related pain/inflammation/loosening in the absence of infection or mechanical problems [18]. There are however no guidelines or recommendations pertaining to preoperative evaluation of implant allergy to our knowledge. It seems therefore difficult to defend a decision to proceed with an allergen in the cement in a patient with prior proven sensitivity to it, a view that is supported by Kaplan et al. who had similarly identified an allergy to PMMA preoperatively [9]. After extensive counselling, our patient underwent a cementless complex TKA as the only viable alternative given her incapacitating symptoms.

Preoperative planning involved accruing the armamentarium needed to achieve stable metaphyseal fixation of the implant in femur and tibia without the need of bone cement and the necessity of stem augmentation for diaphyseal fixation and weight transmission. In view of her 20° valgus and the possible collateral ligament imbalance, a constrained implant was planned with hinged implants as a backup. Metaphyseal sleeves were the near ideal implants in the current context as the surgery needed additional metaphyseal fixation in the setting of a constrained insert and the current available cementless implants do not offer metaphyseal fixation. Stem augmentation was planned.
for diaphyseal fixation, to offload the implant and thus facilitate immediate post-operative weight bearing. We used a TKA system for our patient that incorporated specific features in the design of the implant, namely – porous coated sleeves, rotating platform, constrained insert and variable stem options, that made this implant system most optimal for our patient.

Ligament balancing required extensive soft tissue release on the lateral side- popliteus, posterolateral capsule and the scarred LCL bands from lateral femoral epicondyle. Bone cuts were minimal to avoid joint line elevation. A femoral sleeve was used for metaphyseal fixation, to improve rotational stability and to promote osteo-integration. A tibial sleeve and a fluted uncemented stem were used for the reasons stated above.

Today, cemented total knee arthroplasties remain the gold standard owing to the evidence of good survivorship [10, 19, 20] across various registries. Previous cementless implants were associated with high early failure rates due to osteolysis at the tibial implant-bone interface [20] and aseptic loosening, with reasons including patch porous coating, poor tibial locking mechanisms, and use of first-generation polyethylene [21, 22]. However with advancements in implant design and biomaterials, cementless implants are now showing improvements in all cause and aseptic survivorship [23]. However, to our knowledge, there are no cementless revision or constrained knee implant systems available. Hence, in our patient, we opted for cemented implants with sleeve and stem augments to achieve the best possible result.

Although cemented TKA is the gold standard, cementless TKA is a considerable option in rare situations such as allergy to bone cement constituents. Long term survivability of the implant is also debatable as there is no literature to suggest otherwise. We report this case as it is a unique challenging situation of a young patient with documented allergy to bone cement constituents, requiring complex primary TKA with off-label usage of cemented implants without cement. This report also serves to highlight the importance of weighing up conflicting considerations in medical decision making when faced with a limiting medical conundrum.

Table 1: Specific test panel of bone-cement components – strong positive reactions to benzoyl peroxide, cement powder and cement powder in 1:10 dilution

| Substances                                    | Day 2 | Day 4 |
|----------------------------------------------|-------|-------|
| Benzoyl peroxide 1% from series in pet       | ++    | +++   |
| Cement liquid 1:10 in pet                    | -     | -     |
| Cement liquid 1:40 in NaCl                   | -     | -     |
| Cement powder as is                         | +     | +++   |
| Cement powder 1:10 in pet                    | -     | +++   |
| Cement hardened pieces in pet                | -     | -     |
| Methylmethacylate                            | -     | -     |
| Hydroquinone                                 | -     | -     |

Legend:
Pet Petrolatum
NaCl Sodium chloride
- Negative
(+) Erythema (E)
+ E + Infiltration (E/I)
++ E/I + Papulovesicle (E/I/P)
+++ E/I/P + Blister

Fig 1: Preoperative clinical photos – significant valgus and flexion deformities of the left knee

Fig 2: Preoperative left knee radiographs – severe tricompartmental osteoarthritis, worst in the lateral compartment

Fig 3: Basic series patch testing – positive skin reaction to bone cement and benzoyl peroxide
Fig 4: Postoperative clinical photos – neutral alignment of Left knee in coronal and sagittal plane.

Fig 5: Postoperative left knee radiographs – cement less constrained implant with metaphyseal sleeve in femur, metaphyseal sleeve and stem augment in Tibia.

Fig 6: Pre and postoperative full-length alignment radiographs – significant improvement of left lower limb alignment postoperatively.

Fig 7: Postoperative radiograph at 2 weeks showing incomplete fracture at the tip of tibial stem.

Fig 8: Postoperative radiograph at 4 weeks showing incomplete fracture at the tip of tibial stem.

Fig 9: Postoperative radiograph at 3 months showing callus formation and bone healing of the incomplete fracture at the tip of tibial stem.
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