

Allergic reactions in arthroplasty: myth or serious problem?

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Received: 10 July 2015 / Accepted: 14 September 2015
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Abstract

Purpose The purpose of this study was to determine the prevalence of sensitisation to chromium, cobalt, nickel, or a cement component in patients who received endoprosthetic surgery at our institution. Also, we aimed to assess the portion related to allergic reactions in endoprosthetic revisions and to follow-up those patients after allergic reaction related revisions.

Methods We selected patients with a pre-operative known sensitisation to chromium, cobalt, nickel, or a cement component for a post-operative allergic reaction. All patients who received revision surgery because of a potential allergic reaction were followed up post revision surgery.

Results Eight hundred fifty-five patients were pre-operative known to have a sensitisation to chromium, cobalt, nickel, or a cement component. Six hundred eighty-two patients (79.8 %) received a primary arthroplasty, and 173 patients (20.2 %) received a revision surgery. Seventeen patients (2.0 %) were revised because of allergic reactions. Allergic reactions were the cause for approximately 0.2 % of all endoprosthetic revisions and for 9.8 % of revisions in patients with sensitisation to one of the reviewed components.

Potential allergens were strictly avoided in the replaced prosthesis. Outcome scores improved post-operatively.

Conclusions The allergic patient should be thoroughly informed about potential reactions resulting from implant choice. Our study can serve as risk assessments by quantifying the incidence of allergic reactions due to endoprosthetic treatment.

Keywords Allergy · Arthroplasty · Nickel · Immune reaction · Revision · Prosthesis

Introduction

Allergy in modern arthroplasty is a problem that is not yet evaluated sufficiently. Various case reports describe allergic reactions such as eczema, rash, persistent swelling, sterile osteomyelitis, or aseptic loosening of the implant after endoprosthetic treatment [1–3].

The prevalence of allergies to components used in arthroplasty in the general population is well known: 13.1 % (20.4 % female, 5.8 % male) suffering from an allergy to nickel, 2.4 to 3 % to cobalt and approximately 1 % to chromium [4]. Potential allergens contained in bone cements such as gentamicin, benzoyl peroxide, and hydroquinone can cause hypersensitivity reactions in patients with arthroplasties as well [5–7].

In the 1970s, a high incidence of unexpected metal sensitisation was found in patients with metal-to-metal hip arthroplasties. Patients with metal-to-plastic prostheses had no greater incidence of metal sensitisation compared to a control group prior to a surgical procedure. If metal sensitisation does occur, loosening of the prosthesis may be a complication [8, 9].

Modern research contributed to the finding that an elevated proliferation and production of interferon-gamma in vitro may

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be present in blood lymphocytes of patients with sensitisation after hip arthroplasty. That led to the conclusion that a T_H1 (vs. T_H2) type response is likely associated with a metal-induced reaction. Such a specific lymphocyte reaction suggests that an adaptive immune reaction to debris of the metallic implant is present as well as a nonspecific innate immune response [10].

In the last few years it became widespread clinical practice to consider an allergic reaction in patients suffering from persistent complaints after endoprosthetic treatment once common causes, such as infection or aseptic loosening, have been excluded [11, 12].

However, it is still a challenge for the surgeon to estimate the risk of an allergic reaction after endoprosthetic treatment in a patient with a known sensitisation to components of endoprosthetic treatment.

The goals of this study were (1) to determine the prevalence of sensitisation to chromium, cobalt, nickel, or a cement component in patients who received endoprosthetic surgery at our institution, (2) to assess the portion related to allergic reactions (AR) in endoprosthetic revisions and (3) to follow-up those patients after AR-related revisions.

Materials and methods

We determined patients with a pre-operative known sensitisation to chromium, cobalt, nickel, or a cement component (e.g., gentamicin, benzoylperoxide, hydroquinone) for a post-operative AR. All these patients were treated with endoprosthetic surgery in the period from January 2006 to October 2013 at our institution. Data was obtained from the patient's medical records.

Data collection included the Harris Hip score (HHS) for total hip arthroplasty, the Hospital for Special Surgery score (HSS) for total knee arthroplasty, the gender, the age, the type of implanted prosthesis, the reason for primary surgery or revision surgery, and the potential AR. All patients, who received revision surgery because of a potential AR, were followed up post revision surgery (mean time two years). The study was conducted according to the guidelines of the local ethics committee. Informed consent was obtained from all individual participants included in the study.

The data was processed and means and standard deviations were created using the statistical software package SPSS (version 20.0, SPSS Inc., Chicago, USA).

Results

Prevalence of sensitisation

Between January 2006 and October 2013, a total of 34,914 patients were treated with a hip or knee arthroplasty at our institution (24,763 primary arthroplasties and 10,151 revision

surgeries). Out of these, 855 (2.45 %) patients (792 female, 63 male) were pre-operative known to have a sensitisation to chromium, cobalt, nickel, or a cement component (e.g., gentamicin, benzoyl peroxide, hydroquinone). Table 1 shows the frequency of the particular sensitisation and the percentage of total arthroplasties during the survey period.

Portion related to allergic reactions in endoprosthetic revisions

These 855 patients with a pre-operative known sensitisation were divided in 682 patients (79.8 %) who received a primary arthroplasty, and 173 patients (20.2 %) who received a revision surgery. The revision surgeries could be divided into 31 patients (3.6 %) who were revised because of a periprosthetic infection, 125 patients (14.6 %) who were revised because of a late aseptic loosening of the implant or an implant component, malalignment of the implant or an implant component or trunionosis, and 17 patients (2.0 %) who offered AR such as malaise and nausea, itching, skin reactions and/or arthrofibrosis or early implant loosening, which could not be attributed to other reasons. Among these patients with AR were three hip and 14 knee replacements. All 17 patients with AR were female with a mean age of 58.2 ± 9.8 years. Thirteen of these patients had a positive patch test to nickel. Out of these, two patients had an additionally positive patch test to benzoylperoxide. Four patients were tested positive in LTT.

Post-operative periimplant histology was rated as AR (Krenn particle algorithm [13] type VII).

AR was the cause for approximately 0.2 % of all endoprosthetic revisions and for 9.8 % of revisions in patients with sensitisation to one of the reviewed components. Table 2 shows the implanted endoprosthetic systems and respective components.

Follow-up of patients after allergic reaction related revisions

The mean time of follow-up of these 17 patients post revision surgery was two years. In hip replacement, the pre-operative

Table 1 Frequency of the various sensitisations within the 855 patients and their respective proportion (%) as compared to all the arthroplasties during the survey period

Sensitisation to	Number of patients ^a	Percentage
Nickel	849	2.43
Cobalt	84	0.24
Chromium	39	0.11
Cement component	14	0.04

^a In part multiple allergies per patient

Table 2 Implanted endoprosthetic systems and the respective components in patients with allergic reactions (17 out of 855 patients)

Procedure	Amount	Material assembly
Total knee arthroplasty		
Bi-Condylar surface replacement (NexGen LPS Flex, Zimmer)	2	Cobalt-Chrome (Zimaloy), Tivanium, Ultra High Molecular Weight Polyethylen
Bi-Compartmental knee system (Journey DEUCE, Smith & Nephew)	1	OXINIUM™, Oxidized, Zirconium
Bi-Condylar surface replacement (Scorpio NRG, Stryker)	1	Cobalt-Chrome, Ultra High Molecular Weight Polyethylene
ROKNEP (LINK)	3	Cobalt-Chrome-Molybdenum, Ultra High Molecular Weight Polyethylen
Unknown bicondylar surface replacement (outside hospital)	7	
Total hip arthroplasty		
Allofit (Zimmer)	1	Pure titanium, Protasul™-Ti, Protasul-10
Unknown thrust plate prosthesis (outside hospital)	1	
Unknown arthroplasty (outside hospital)	1	

Harris Hip score (HHS) was 52.0 ± 3.6 . In knee replacement, the pre-operative Hospital for Special Surgery score (HSS) was 59.5 ± 10.2 . Potential allergens were strictly avoided in the replaced prosthesis. This was achieved by using prostheses containing titanium or prosthesis with anti allergic coating. In cases where a hypersensitisation against benzoylperoxid was present a cementless implantation was performed.

Post-operatively, the respective scores improved to 82.3 ± 23.2 for HHS and 73.1 ± 13.6 for HSS. However, two patients still had persistent skin reactions, such as itching and local redness. Figure 1 shows a representative eczematous reaction in a patient following total knee arthroplasty.

Discussion

Sensitisations to specific components, which are also an integral part of modern arthroplasties, are common in the general population. However, although confirmed AR in these patients after endoprosthetic treatment are rare, individual cases do occur.

The topic is still not well understood. In 1977, Deutman et al. reported outcome data for 212 patients undergoing total hip replacement who were tested pre-operatively for sensitisation to nickel, chromium, and cobalt. Fourteen patients showed AR. No sensitisation to the bone cement was recorded [14].

More recently, studies found that 0.6 % of patients with total knee arthroplasty and 1.2 % of patients with total hip arthroplasty may have a problem due to sensitisation to nickel or cobalt after implantation. However, only in one third of them revision surgery was performed [15]. The sensitisation to metal was reported as a possible cause of sterile loosening [16]. However, the rate of surgical revision was not increased in patients with metal allergies when compared to non-allergic controls from the Danish Hip Arthroplasty Registry [17].

If doubtful cases occur, a standardized diagnostic procedure is indispensable [18, 19]. We propose diagnostic steps as given in Fig. 2. The patient's history should be requested regarding potential allergic susceptibility, and the clinical presentation has to be well documented. Sometimes similar presentations can mimic an AR, such as an infectious cellulitis. Erysipelas after hip surgery is a distinctive form of cellulitis, which is characterized by the unusual topography, rapid onset, and the possibility of recurrence [20].

Prior to primary arthroplasty, allergy testing should be performed in patients in case of a history of metal AR similarly as

**Fig. 1** Eczematous reaction in a patient following total hip arthroplasty

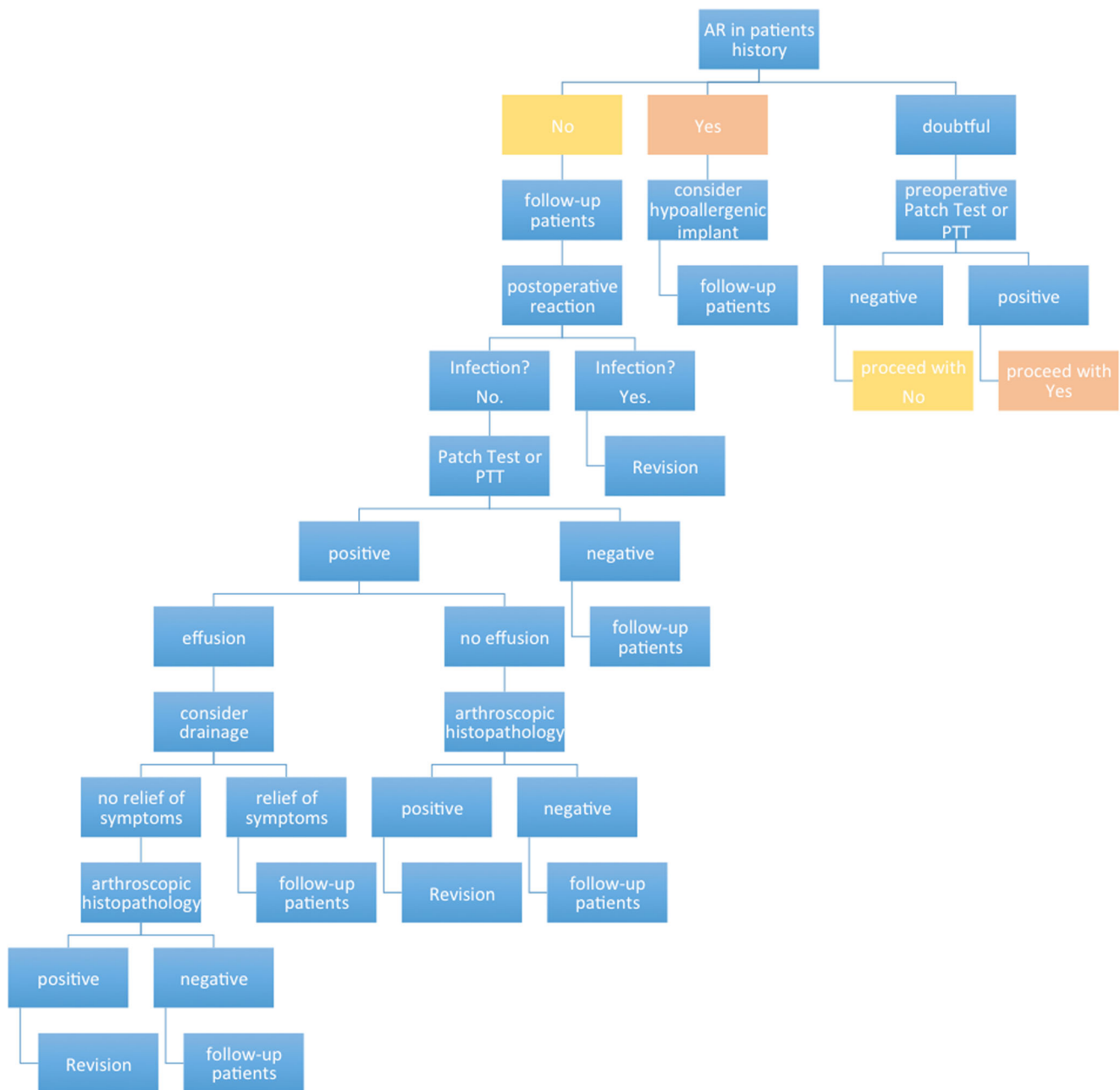


Fig. 2 Diagnostic and therapeutic pathway for patients with allergic reactions (AR) in endoprosthetic treatment

in failed arthroplasties, especially with metal-on-metal implants and when the cause of the loosening is doubtful [21]. In such cases a patch test including implant-metal and bone cement series should be performed for allergy testing [22]. In patients with a total knee arthroplasty, the frequency of positive patch testing is higher than in the normal population, although no predictive value is attributable to the sensitisation, because according to Granchi et al. patch testing was not able to discriminate between stable and loose implants [23, 24]. In addition, the LTT is helpful. Advantages include quantitative results and the facilitation of multichallenge agents and dose

testing [25]. However, the authors feel that a general routine pre-operative allergy testing is not indicated.

If post-operative problems occur, infection should be excluded immediately [26, 27]. In some cases with persistent effusion found to be not due to infection, wound drainage is reported to relieve symptoms [3].

Before an exchange of the prosthesis is performed it is recommended to perform knee arthroscopy to obtain tissue for microbiological and histopathological investigations. Particles should be characterized according to the Krenn particle algorithm. In cases of severe lymphocyte/macrophage

infiltration, necrosis, abrasion particle detection, and granuloma formation, a toxic or allergic reaction to implant material should be considered [13].

Recently, it was shown that the choice of a modern hypoallergenic implant may prevent potential reactions [28]. However, this is still a subject of current controversy [29]. A survey calculated that 84 % of surgeons would prefer to use such a coated allergy implant for their patients [15]. It is important to mention that until now, no long-term results were available for these types of prostheses. However, case reports and small patient series describe symptom relief upon revision with hypoallergenic implants [30]. The choice of the implant type has to be critically discussed with the patients.

We conclude that the allergic patient should be thoroughly informed about potential reactions resulting from implant choice. Our study can serve as risk assessments by quantifying the incidence of allergic reactions due to endoprosthetic treatment. It also provides a pathway on how to handle potential allergic cases in endoprosthetic joint replacement.

Compliance with ethical standards

Conflict of interest Thorsten Gehrke receives royalties from Link, as well as honoraria for speaking at symposia from Link, Zimmer, Hereaus, Biomet, and CD Diagnostics; he works as a consultant for Link, Zimmer, Biomet, CD Diagnostics, and holds stocks in CD Diagnostics. Carl Haasper receives honoraria for speaking at symposia from Link, Zimmer, Smith & Nephew, and receives research support from Link, AO/Synthes, and Arthrokinetics. Daniel Kendoff receives honoraria for speaking at symposia from Link and Biomet. Peter Thomas receives honoraria for speaking at symposia from Link, DePuy, Aesculap, and CeramTec, and works as a consultant for DePuy, and Biomet; he also receives research support from DePuy-Synthes, Aesculap, and CeramTec. This funding is not directly related to the findings presented in this article.

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