INTRODUCTION

Biomaterial-related hypersensitivity is a well-documented phenomenon, although little is known about its clinical incidence and its impact on implant failure (1). Metals and acrylic cements represent the main components of orthopaedic implants. In contact with biological systems, they may undergo corrosion or degradation, therefore releasing ions and molecules. Per se, these do not have antigenic properties, although they can either act: (1) as haptons, binding to protein carriers, or (2) as adjuvants, that is, forming insoluble complexes with the antigen enhancing the activity of phagocytes. These novel material-protein complexes may therefore elicit a delayed-type hypersensitivity reaction (DTH). We used a panel of representative haptons to assess the incidence of DTH in a consecutive series of patients undergoing revision surgery due to aseptic loosening of hip or knee prostheses. The aim of the study was to evaluate the feasibility and the clinical value of the in vivo skin testing (i.e., patch testing) to predict host reactions to bioimplants.

PATIENTS AND METHODS

Patch testing was performed on a consecutive series of 35 patients that were being considered for revision surgery for aseptic total hip or knee prosthetic loosening. Of these, 12 were males and 23 females. Thirty patients had a hip implant, and 5 had a knee prosthesis. Twelve patients (34%) had an additional implant at another site. Five patients (14%) had a history of metal hypersensitivity, 26 (74%) denied any kind of previous allergy, and 4 (11%) reported non-specific symptoms. Hypersensitivity to metals was tested by using the following haptons: 5% nickel sulfate, 1% cobalt chloride, 2% chromium trichloride, 0.5% potassium dichromate, 2% ferric chloride, 2% molybdenum chloride, 2% manganese chloride, 2% titanium dioxide, 1% aluminium chloride, and 2% vanadium trichloride. Haptons for bone cements were: 5% methyl-methacrylate, 2% butyl-methacrylate, 2% triethylene glycol dimethacrylate, 2% ethylene glycol dimethacrylate, 2% N,N-dimethyl-paratoluolidine, 5% hydroxy-ethyl-methacrylate, 2% benzoyl-peroxide, and 1% hydroquinone monobenzyl ether. Vaseline, which was the carrier in the patch testing, was assayed as a negative control. A drop of each hapten was smeared on an adhesive bandage, which was applied to the dorsum of the patient. After 48 hours, skin reactions were evaluated and graded as 0 (no reaction), 1 (erythema), 2 (edema), 3 (vesicle), or 4 (bulla). The results were expressed as frequency distribution of positivity to different haptons. Statistical significance was evaluated by the Fisher’s exact test.

RESULTS

Patch testing was successful in 34/35 patients. 56% of patients resulted positive to at least one hapten, while 44% were negative. Forty-five percent of hip implants were positive (10% to one hapten, 21% to 2 haptons, and 3% to 4 or more haptons, respectively). Cobalt chloride (21%) and nickel sulfate (17%) were the most frequently positive haptons, followed by methyl-methacrylate (10%), potassium dichromate, chromium trichloride, ethylene glycol dimethacrylate, and hydroxyethylmethacrylate (7%), ferric chloride, manganese chloride, butyl-methacrylate, triethylene glycol dimethacrylate, hydroquinone monobenzyl ether, and N,N-dimethyl-paratoluolidine (3%). All 5 patients with a knee prothetic loosening were positive for at least one hapten. The difference among the frequency of positivity in hip and knee prostheses was statistically significant (P=0.027). No patient with a knee prosthesis reported a history of hypersensitivity. Sixty percent of patients with a knee prosthesis was positive to one hapten, 20% to 2 haptons, and 20% to 3 haptons. Cobalt chloride (40%) and methyl-methacrylate (40%) were the most frequently positive haptons, followed by nickel sulfate, chromium trichloride, vanadium trichloride, and manganese chloride (20%). Hypersensitivity was confirmed in all patients with a previous history.

DISCUSSION

Cutaneous hypersensitivity to metals is common, affecting 10% to 15% of the whole population (2). Although nickel is the most common metal sensitizer in humans, followed by cobalt and chromium, sporadic reactions to titanium and vanadium have also been reported. The prevalence of cutaneous sensitivity in patients with a failed total joint implant has been shown to be higher than in the general population (1), ranging from 13% to 71% of cases. In our series, 56% of patients had a positive patch testing, with a higher prevalence among patients with a loosened knee arthroplasty. Hypersensitivity reactions to stainless-steel or cobalt-alloy implants have been reported to be more frequent than to titanium-alloy components. In our series, a positivity for cobalt chloride was found to occur in over 20% of cases, with no positivity to titanium or aluminium. Data on the sensitivity to polymeric materials among patients with a failed implant have been previously reported. In one study, patch testing and monocellular cell subset analysis have demonstrated polymethyl-methacrylate hypersensitivity in 50% of patients with a loosened total hip prosthesis (3). A remarkable finding of our study is the high proportion (41%) of sensitized individuals with no history of metal allergy. Our data also show the reliability of the panel utilized for skin testing, which was always found to be positive in individuals with a history of metal hypersensitivity. At this time, we are not able to establish the diagnostic utility of skin testing in patients with orthopedic implants. This assay can identify the hypersensitivity status, but cannot establish if the sensitization is the cause or a consequence of implant failure. It is conceivable, however, that hypersensitivity may actually play some role in the network of events that are responsible for prosthetic loosening. In some individuals corrosion products behave like haptons: if the subject has been previously sensitized, the hapten-protein complex may stimulate memory-lymphocytes. On the contrary, when the patient has been sensitized for the first time, the localized immune response can influence both the initiation and the progression of the inflammatory process up to the final failure of the prostatic implant.

REFERENCES