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Case report

IL-17A–Mediated Immune-Inflammatory Periarticular Mass and Osteolysis From Impingement in Ceramic-On-Ceramic Total Hip Arthroplasty

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ABSTRACT

We present a rare case of symptomatic adverse local tissue reaction in a 54-year-old female patient who had undergone total hip arthroplasty with ceramic-on-ceramic bearing. Inflammatory periarticular mass and osteolysis developed in the absence of cobalt chrome alloy interfaces and a modular neck component. On the pathologic images, there was no clear evidence of gross metal staining of tissues, metal corrosion, and ceramic or metal wear particles. However, there were impingement scars on the titanium alloy femoral neck and acetabular cup associated with a high combined anteversion angle of 75° (stem: 40° and cup: 35°), suggesting titanium debris release in vivo. Immunohistochemical staining proved a predominant infiltration of CD4+ T cells and the corresponding IL-17A response to metal. We conclude that neck-rim impingement may lead to the development of adverse local tissue reaction (periarticular mass and osteolysis) due to a metal hypersensitivity with the production of proinflammatory cytokines (IL-17A) by CD4+ T cells even in ceramic-on-ceramic total hip arthroplasty.

Introduction

Ceramic-on-ceramic (CoC) total hip arthroplasty (THA) can provide excellent long-term outcomes with very low wear and osteolytic potential [1,2]. The reasons for revision THA differed between CoC and other bearings because of its inherent mechanical properties. CoC THA is especially sensitive to mechanical problems such as squeaking, bearing fracture, impingement, and incorrect ceramic insertion [3]. This results in the requirement of accurate component placement to prevent such mechanical complications.

There has been an increasing concern regarding the postoperative formation of periarticular mass as a result of adverse local tissue reactions (ALTRs) to ions or particles released from bearing surfaces or taper interface. Periarticular masses have been commonly reported to be associated with mechanically assisted crevice corrosion at the head-neck taper interface in large diameter metal-on-metal (MoM) THA [4–6]. Moreover, an ALTR with a similar mechanism has been reported in metal-on-polyethylene (MoP) bearings that this is related to mechanically assisted crevice corrosion [7–10]. In fact, metal hypersensitivity (eg, lymphocytic aggregates, granulomas [11,12]) may occur together with particle and ion reactions. A recent study showed that activation of danger signaling (the inflammasome/caspase-1) with subsequent production of proinflammatory cytokines (IL-17A) by CD4+ T cells can be a possible pathway to metal hypersensitivity [13]. Therefore, the histology of periarticular masses often includes features consistent with particle and ion reactions and hypersensitivity. However, histological features may vary from case to case and be related to particle bioreactivity, which may depend on particle size, material composition, and concentration [14]. We previously pointed out that polyethylene supramacroparticles >100 μm in size potentially trigger periarticular mass formation via a foreign-body reaction to the polyethylene particles in MoP THA, in which cases

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showed no signs of an adverse reaction to metal debris or severe corrosion at the interface [9].

On the other hand, very few studies have reported on ALTR associated with CoC bearings which have inherently no concern for bioincompatibility and corrosion or ion release from the articulation [3,15]. However, one recent study reported that, even in the absence of a source of metal debris and without elevation of either chromium or cobalt, ceramic wear debris may not be entirely bioinert and lead to the development of ALTR [15]. Such findings suggest a need for further investigation into a potential mechanism, such as immune responses, which accounts for the occurrence of ALTR in CoC THA.

In this report, we present a rare case of symptomatic immune-inflammatory periarticular mass and osteolysis in a patient after CoC THA. Written informed consent was obtained from the patient for publication of this case report.

Case history

A 54-year-old female patient underwent a primary THA at an outside institution for the diagnosis of secondary osteoarthritis in the left hip. The third-generation alumina CoC bearing with a diameter of 28 mm was implanted with a self-locking TriAD HA acetabular cup and Super Secur-Fit HA femoral stem. All these implants were from Stryker (Mahwah, NJ). A right primary CoC THA using the same implant devices was performed for secondary osteoarthritis at 5 years after the left primary THA. Osteolytic lesions were found in the proximal regions of the stem (Gruen zones 1 and 7 [16]) and around the cup (DeLee and Charnley zone 3 [17]) in an anteroposterior radiograph taken at 6-year follow-up after the left primary THA (Fig. 1a). The previous study suggested a desirable combined anteversion within a range of 25°–50° [18]. A high combined anteversion angle of 75° (stem: 40° and cup: 35°) was noted in the left hip by computed tomography imaging (Fig. 2). In contrast, the combined anteversion on the right hip was within the ideal range (45°; stem: 25° and cup: 20°). A radiological sign of cup loosening was found with a progressive osteolytic lesion (Fig. 1b). Metal artifact reduction sequence magnetic resonance imaging identified a 42 × 40 × 64-mm soft-tissue mass around the femoral neck (Fig. 3) that had been asymptomatic for several years. The patient experienced mild pain in her left hip at 10 years postoperatively and was referred to our institution because of aggravated pain and the need for revision THA using allogeneic bone grafting for treating the large bone defect associated with periprosthetic massive osteolysis formation (Fig. 4).

The patient had a body mass index of 36.1 kg/m^2 and hypertension, and a history of contact allergy to metal jewelry was noted. The levels of C-reactive protein and white blood cell count at the time of admission were 0.7 mg/dL (reference range: <0.3) and 4500 μ/L (reference range: 2700–8800 μ/L), respectively. The level of serum chromium ion was below detectable levels (<0.2 μg/L), and the level of cobalt ion was 0.4 μg/L. Note that serum cobalt and chromium ion levels of <2.0 μg/L are of no clinical concern [19]. Bacterial isolates in blood culture and alpha-defensin test were conducted for rapid and specific diagnosis of prosthetic joint infection with the aspiration of the hip revision surgery, both of which returned negative results. Skin patch testing to cobalt, chromium, and titanium returned negative results. No gross metal staining of the tissues and taper junction corrosion were found at the revision (Fig. 5a). Impingement scars were clearly observed at the distal part of the neck taper and the posterior peripheral rim of the acetabular cup (Fig. 5a and b),

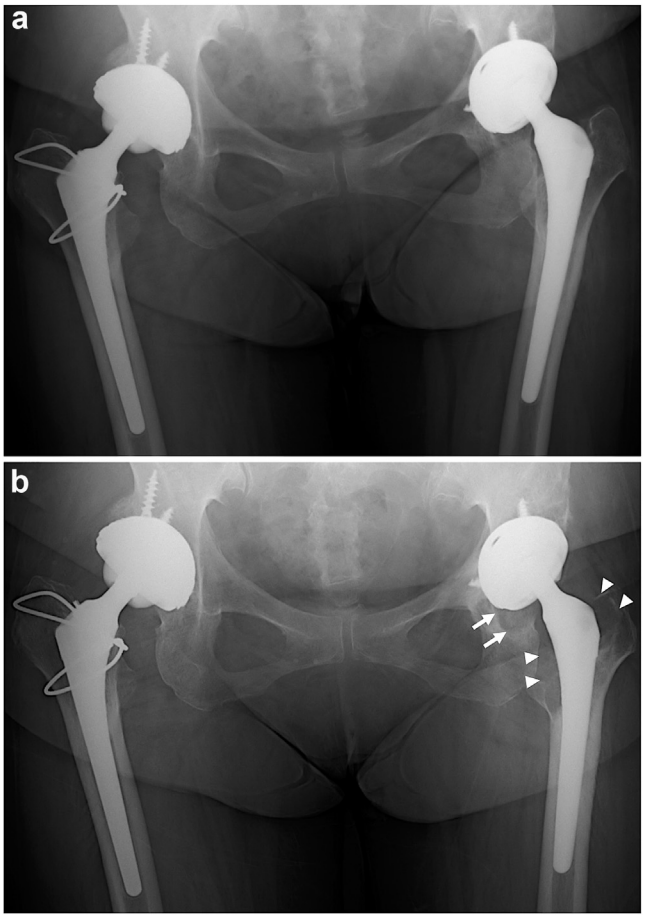

Figure 1. (a) Six-year postoperative anteroposterior (AP) pelvic radiograph showing an early stage of femoral osteolysis in Gruen zones 1 and 7 and acetabular osteolysis in DeLee and Charnley zone 3 in the left hip. (b) Ten-year postoperative AP pelvic radiograph showing progressive femoral (arrowheads) and acetabular (arrows) osteolysis in the left hip.

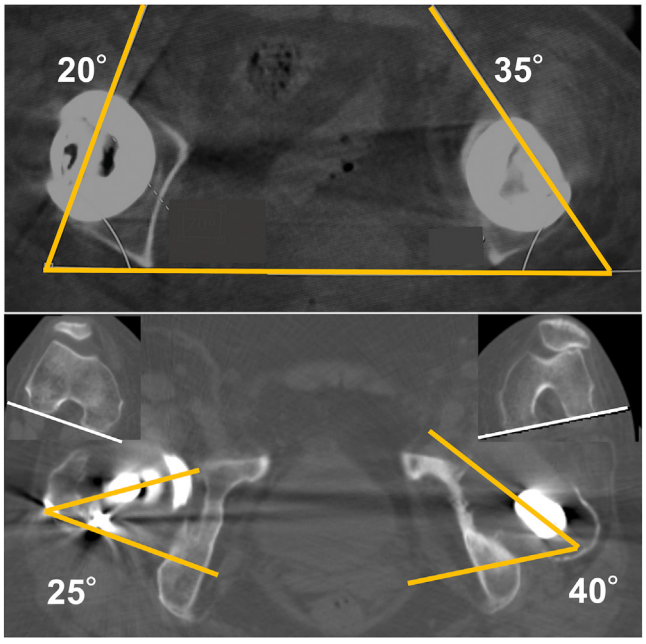

Figure 2. Computed tomography (CT) images showing the combined anteversion angles of 75° (stem: 40° and cup: 35°) and 45° (stem: 25° and cup: 20°) in the left and right hips, respectively.

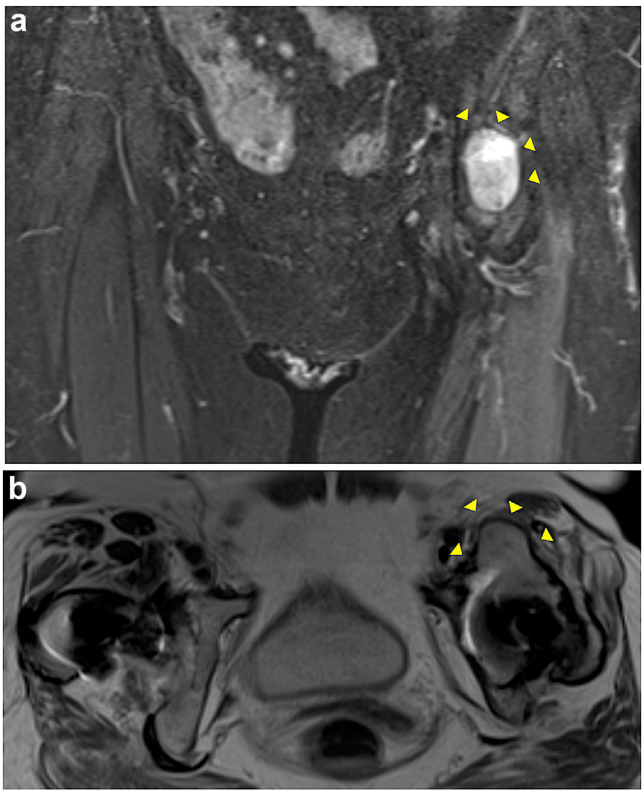

Figure 3. Coronal T2-weighted short tau inversion recovery (STIR) (a) and axial T2 MRI (b) showing periarticular mass (arrowheads) located anterior to the femoral stem in the left hip.

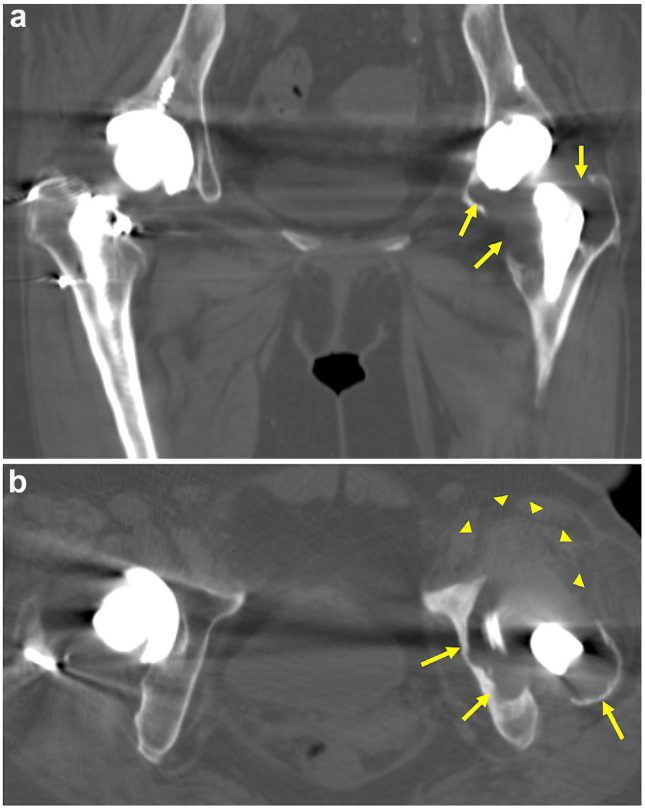

Figure 4. Coronal (a) and axial (b) CT images showing massive osteolysis (arrows) and soft-tissue mass (arrowheads) around the cup and the proximal stem.

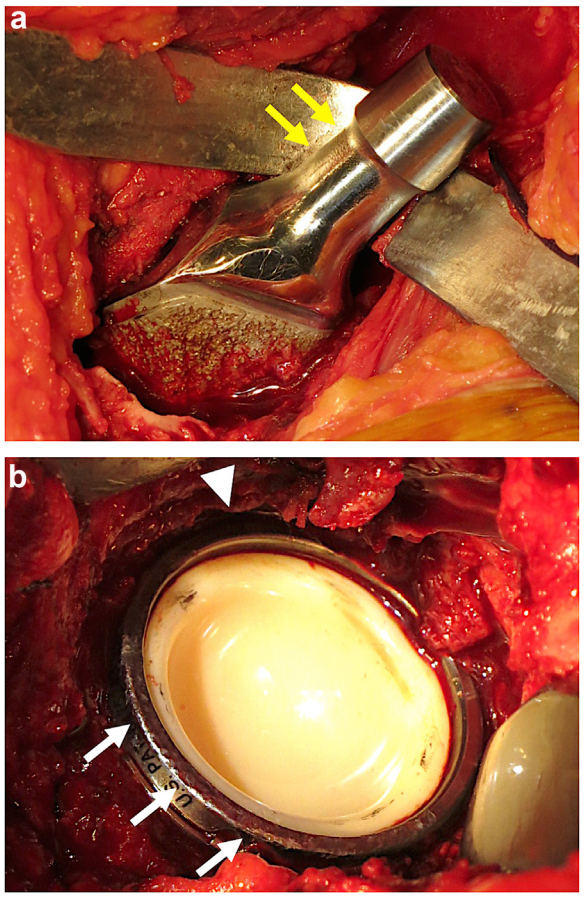

Figure 5. Intraoperative photographs showing impingement scars on the femoral neck (a, yellow arrows) and acetabular rim (b, white arrows). The white arrowhead indicates the superior region of the cup.

suggesting the occurrence of impingement between the femoral neck and acetabular rim. Although severe bone loss associated with osteolysis at the proximal zone of the stem was found, no femoral loosening was noted; thus, the femoral stem was retained. The acetabular cup was exchanged with a cemented cup because of acetabular loosening associated with extensive osteolysis and modification of the anteversion angle. We modified the combined anteversion angle from 75° to 50° by decreasing the cup anteversion from 35° to 10° (ie, stem: 40° and cup: 10°). The alumina head was exchanged with a 36-mm CoCr head. There was no evidence of stripe wear and impingement scars in the retrieved alumina head and liner. All visible periarticular masses were resected and histologically proven as an aseptic lymphocytic vasculitis-associated lesion (ALVAL). The histological finding of the resected periarticular mass included thick collagenous fibers around scattered perivascular lymphocyte-predominant aggregates (Fig. 6a). The severity of ALVAL was histologically classified as low if the score was 0–4, moderate if it was 5–8, and high if it was 9–10 [20]. In this patient, the ALVAL score was 8 and classified as moderate. Although histologically no obvious metal staining of the tissues and metal/ceramic wear particles were observed, diffuse infiltration of CD4+ T cells predominantly in perivascular regions was confirmed by immunohistochemical staining of anti-CD4 antibody (Fig. 6b). In contrast, CD68+ macrophages and CD8+ and CD20+ lymphocytes were less abundant, and their infiltrations were limited to only the perivascular regions. Most CD4+ T cells were also immunohistochemically stained by proinflammatory cytokine (IL-17A)

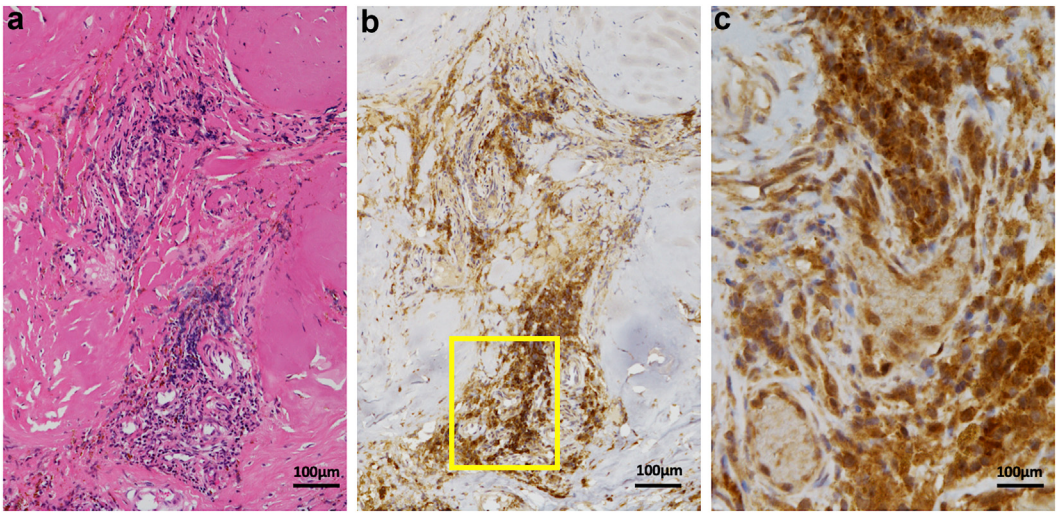

Figure 6. (a) Hematoxylin and eosin staining (x100 magnification) of the periarticular mass showing an intense perivascular lymphocytic infiltration; (b) immunohistochemical staining (x100) showing a diffused distribution of CD4+ T cells, which were predominantly infiltrated in the perivascular sites; (c) IL-17A antibody staining (x400) showing CD4+ T cells and vascular endothelial cells, corresponding to the yellow rectangle in (b).

antibody (Fig. 6c). This patient was followed up for 2 years after the revision surgery, and no pain and implant loosening were noted.

Discussion

According to a recent multicenter survey in France [3], implant fracture, prosthetic impingement, squeaking, and incorrect insert position accounted for 16% of all the recorded reasons for CoC revision in THA, while these accounted for 3.0% and 0.7% in MoM and MoP THAs, respectively. The findings suggest that CoC THA is more sensitive to mechanical problems than other bearings. It was also shown that revision THAs were performed less by up to nearly 6-fold because of osteolysis in CoC than MoP [21]. The use of ceramic bearings in the form of CoC or ceramic-on-polyethylene THA was associated with a significantly lower risk of revision due to ALTR than MoP and MoM [22]. In the aforementioned contexts, periarticular mass and osteolysis are pretty rare events in CoC THA, and the relevant histological images and descriptions in the literature remain limited.

Campbell et al. [15] first reported a unique case of an inflammatory periarticular mass formation after third-generation alumina-on-alumina THA without a CoCr alloy interface and modular neck component as a common source of metal ion or particle release, suggesting that the occurrence of ALTR may be associated with ceramic wear debris. Mochida et al. [23] demonstrated a macrophage response to alumina debris within the tissues adjacent to failed CoC bearings. Furthermore, some studies on alumina-on-alumina THA reported a prominent predominantly perivascular lymphocytic infiltration, the occurrence of which was interpreted as a consequence of titanium debris generated by neck-rim impingement rather than ceramic debris [24,25].

Recent studies have proposed that a hypersensitivity reaction to particulate debris generated from implant alloys including titanium may result in a periarticular mass formation [26,27]. Soluble and particulate metal implant debris can induce human monocyte/macrophage proinflammatory cytokine secretion and upregulation of surface T-cell costimulatory molecules essential for the activation and proliferation of metal-reactive lymphocytes [28]. The exposure to metal particles requires processing by active NLRP3 inflammasome complexes in innate immune cells and induces CD4+ T cells and the corresponding IL-17A responses to implant metal [13]. IL-17A–producing CD4+ (Th17) cells stimulate the production of proinflammatory cytokines such as TNF-α and IL-1 and IL-6 and the activation of synovial fibroblasts and macrophages [29]. Furthermore, Th17 cells also act on osteoblasts and promote osteoclast differentiation via RANKL [30]. Therefore, IL-17A may lead to the promotion of immune-inflammatory periarticular mass and osteolysis due to metal hypersensitivity. To our knowledge, this is the first report of describing the mechanism by which the release of metal debris associated with a neck-rim impingement in CoC THA can activate CD4+ Th17 cellular immune responses to induce a hypersensitivity response. However, further studies in patients with ALTR are needed to deepen our understanding of the role of IL-17 and Th17 cells.

In our patient, the cause of the periarticular mass was not apparent. There was no clear evidence of gross metal staining of the tissues, metal corrosion, and ceramic/metal wear particles on the pathological images. Also, skin patch testing gave negative results. However, the patient had a documented history of contact allergy to metal jewelry, and histopathological findings of the periarticular mass showed an ALVAL score of 8 points, with T-lymphocyte–dominant infiltration. Further immunohistochemical staining clearly indicates a predominant infiltration of Th17 cells suggestive of a hypersensitivity reaction to metal particles (Fig. 6). The impingement scars on the femoral neck and acetabular rim (Fig. 5) provide direct evidence of metal particle release from titanium alloy (Ti-6Al-4V) components, potentially promoting Th17 cell infiltration. The occurrence of hypersensitivity reactions was previously suggested to be independent of the amount of particulate wear debris due to the possibility of an idiosyncratic response to metal [31]. In line with this, it is reasonable to assume that the development of periarticular mass and osteolysis in our patient may be responsible at least in part for the hypersensitivity reaction to metal (probably, titanium) released by neck-rim impingement. This is further supported by the absence of ALTR in the contralateral CoC THA with the ideal implant position (Fig. 2). Therefore, it is necessary to keep in mind the risk of ALTR as well as ceramic wear and fracture in CoC THA, and patient background such as metal allergic conditions should be carefully considered. Furthermore, accurate component placement is an important factor in avoiding impingement and edge loading, which can be a source of metal particles.

Summary

We presented a rare case wherein an immune-inflammatory periarticular mass and osteolysis developed after CoC THA. These occurred in the absence of metal corrosion and excessive metal or ceramic wear. Note that the patient had a high score on the ALVAL grading, but the serum cobalt and chromium ion levels were normal. Immunohistochemical staining proved a predominant infiltration of $CD4^+$ T cells and the corresponding IL-17A responses to metal. The evidence of metal particle release was confirmed by the observation of impingement scars on the titanium alloy femoral neck and acetabular rim. The case illustrates that high combined anteversion for the cup and stem followed by neck-rim impingement may lead to the development of ALTR and osteolysis via a hypersensitivity reaction to particulate metal debris even in CoC THA.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

Informed patient consent

The author(s) confirm that informed consent has been obtained from the involved patient(s) or if appropriate from the parent, guardian, power of attorney of the involved patient(s); and, they have given approval for this information to be published in this case report (series).

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