Adverse Reactions in Metal-on-Metal Total Hip Arthroplasty: Two Cases Presenting as Pseudoseptic Acetabular Component Loosening

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The need to improve the longevity of total hip arthroplasties (THAs) has led to a global increase in use of alternative bearing surfaces, particularly first-generation cobalt–chromium and second-generation cobalt–chromium–molybdenum alloys.[1] Advantages of metal-on-metal (MOM) bearing surfaces include low volumetric wear rates, high fracture toughness, and the ability to use large femoral heads to increase hip stability.[2,3] However, the number of degradation particles released from MOM articulations is higher than that found for conventional metal-on-polyethylene bearing surfaces. In addition, there is concern regarding the potential for significant crevice corrosion at the large-diameter femoral head–neck junction. Once considered an important, but uncommon, novel cause of failure,[4,5] metal hypersensitivity reactions are now more prevalent than originally thought, and there is a diverse array of associated clinical and operative findings.[6-10]

Metal hypersensitivity failure mechanisms are thought to center on an immunologic type IV delayed hypersensitivity reaction to metal particles.[5,11,12] Histologic features include diffuse perivascular infiltrates of T and B lymphocytes and plasma cells, increased endothelial venules, fibrin exudates, and accumulation of macrophages and eosinophilic granulocytes with associated necrosis.[5] Thus far, metal hypersensitivity as a reason for revision surgery has been largely a diagnosis of exclusion, with patients typically presenting with increased or recurrent pain, joint effusion, decreased ambulatory capacity, and early osteolysis in the setting of normal perioperative infection parameters.[5,13] Mikhael and colleagues[8] found that metal hypersensitivity failure can mimic hip infection in that patients present with systemic symptoms and elevated inflammatory biomarkers. However, more recent reports have described metal hypersensitivity failure in patients with normal laboratory markers and insidious onset of pain with vague clinical findings.[6,7,9] Watters and colleagues[10] recently reported metal hypersensitivity failure presenting with a pseudotumor and lower extremity edema secondary to extrinsic femoral vein compression. Their report underscores the importance of early recognition and treatment of metal hypersensitivity reactions and adverse local soft-tissue responses in efforts to prevent devastating complications.

In the present report, we describe 2 cases of failure of MOM-THAs with negative presurgical infectious workups and radiographs indicating probable aseptic acetabular cup loosening. The patients were found, during acetabular component revision, to have murky, purulent-appearing synovial fluid with intraoperative cell counts and cultures consistent with an aseptic etiology for failure. To our knowledge, this is the first report to describe this combined clinical and intraoperative scenario, which represents an important consideration in the spectrum of presentation and management of metal hypersensitivity failure. The patients provided written informed consent for print and electronic publication of these case reports.

Case Reports

Case 1

A 57-year-old woman who underwent primary left MOM-THA at an outside institution 9 months before evaluation at our clinic presented with recurrent hip pain, difficulty ambulating, and generalized weakness. The patient reported having had a brief postoperative period of pain relief followed by increasing pain localized to the groin, buttock, and thigh. Nonsteroidal anti-inflammatory drugs (NSAIDs) and physical therapy had provided minimal relief, and a corticosteroid injection into the left trochanteric bursa had been ineffective in alleviating the pain. A thorough workup for spinal pathology or a lumbosacral etiology of pain included routine radiography and magnetic resonance imaging (MRI), both of which

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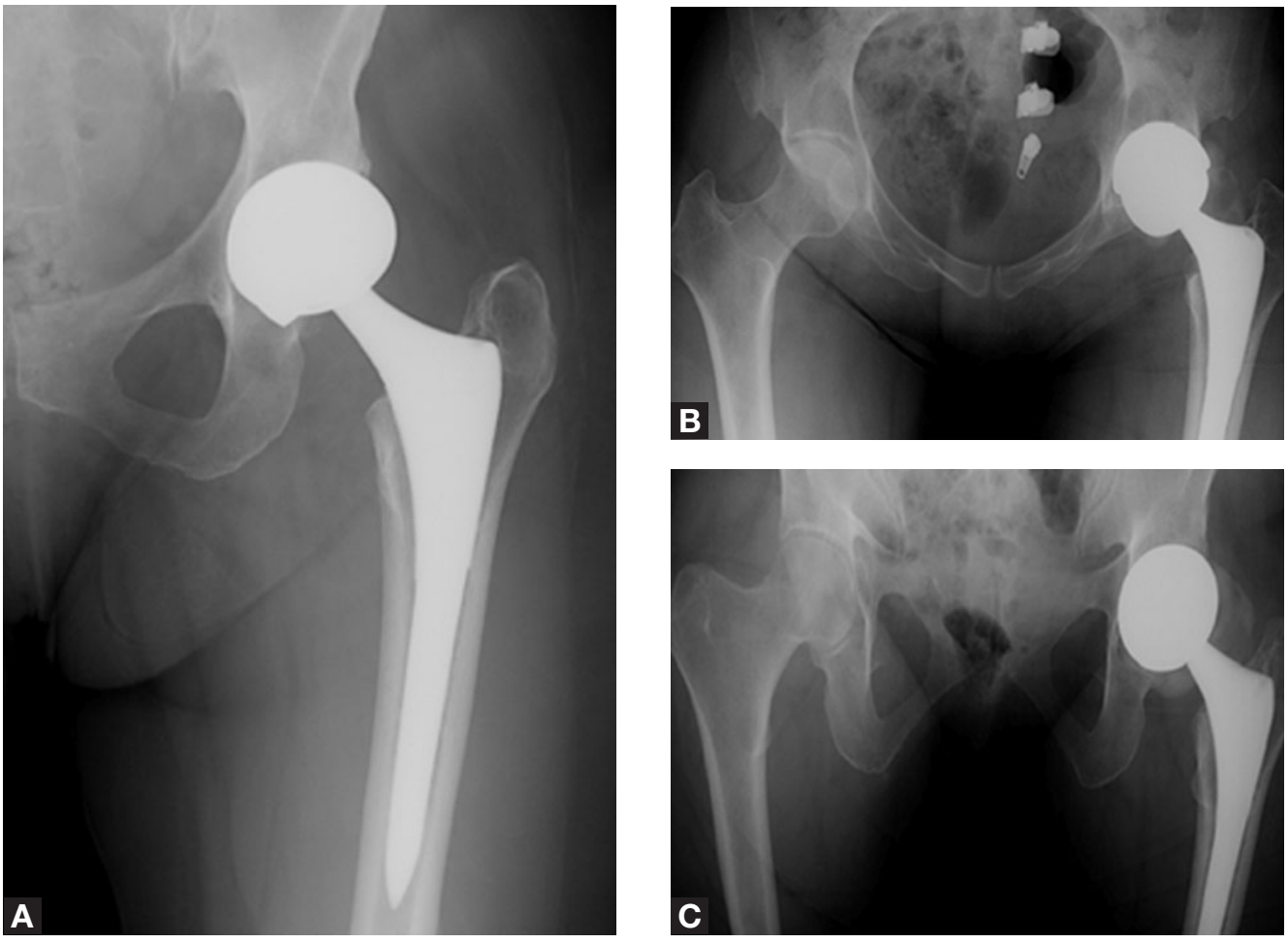

Figure 1. Case 1. (A) Preoperative anteroposterior radiograph of left hip shows metal-on-metal total hip arthroplasty with relatively large acetabular component and significant amount of cup not covered by acetabular bony cavity. (B) Preoperative pelvic inlet view. (C) Outlet view.

had been reported as normal and negative for a source consistent with the patient's pain pattern. Past medical history was significant only for mitral valve prolapse. The initial postoperative course was unremarkable for infection, wound healing problems, and other complications.

On initial examination, the patient exhibited a Trendelenburg gait on the operative limb. The incision was well healed, and there was no evidence of infection, local soft-tissue swelling, or effusion. Hip range of motion was not significantly limited, and it was painful only with flexion, adduction, and internal rotation. Neurologic examination was normal and lacked specific localized findings. Localized tenderness to the trochanteric region was present on examination, and there was notable weakness (4/5) of the abductor musculature, secondary to pain, on the affected side. A preoperative Harris Hip Scale (HHS) score of 39 indicated significant hip dysfunction. Radiographs showed a large-head MOM-THA consisting of an ASR cup and a Summit stem (DePuy, Warsaw, Indiana). The femoral stem appeared in anatomical alignment, and the acetabular component had 30° inclination and 40° anteversion (Figures 1A–1C). Preoperative evaluation consisted of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) tests, a pain clinic referral, and a complete psychosocial evaluation.

MRI of the pelvis and sacral region—obtained to rule out intrapelvic, lumbar, and sacroiliac pathology—showed mild spondyloarthropathy and minimal lumbar stenosis. The conclusion was that the patient's symptoms were more likely originating in the hip and pelvic region. At follow-up, ESR was 8 mm/h (normal range, 0-20 mm/h), and CRP level was 0.7 mg/L (normal range, 0-8 mg/L). Repeat physical examination revealed tenderness in the trochanteric region and a snapping iliotibial band, but whether this area was the epicenter of pain was not clear. The patient was given another corticosteroid injection to the trochanteric bursa, and images of a prior bone scan were reviewed. The scan showed increased uptake around the acetabular component. The results were interpreted with caution, as bone scans can be positive for up to 18 to 24 months after surgery.[14] At the patient's subsequent visit, repeat hip radiographs, compared with the original postoperative radiograph, showed a subtle change in acetabular inclination. These radiographic and bone scan findings indicated her symp-

Figure 2. Case 1. Postoperative anteroposterior radiograph of left hip after revision of acetabular component (cup revised to trabecular metal acetabular component with screw fixation and polyethylene insert and exchange of femoral head).

Figure 3. Case 2. Preoperative anteroposterior radiograph of left hip shows metal-on-metal total hip arthroplasty.

toms were likely caused by a loose acetabular component and possible soft-tissue impingement from the large MOM femoral head. Revision THA for probable aseptic loosening was recommended, and the patient agreed to undergo surgery.

A standard posterior approach was taken through the patient's previous incision. On aspiration of the hip joint, grossly purulent-appearing fluid was found. Intraoperative white blood cell count was 750 white blood cells/mL with 78% polymorphonuclear leukocytes and 18% lymphocytes, and intraoperative red blood cell count was 125,000 red blood cells/mL. The intraoperative frozen section of the hip capsule showed synovial necrosis and fibrin but was negative for acute inflammation. Results of intraoperative cultures and Gram staining were also negative. The ASR cup was found to be grossly loose and positioned in 20° inclination. The cup was easily extracted and revised to a trabecular metal modular acetabular component (Zimmer, Warsaw, Indiana) with supplemental screw fixation and a highly cross-linked polyethylene insert (Figure 2). The femoral head was also exchanged to a ceramic head (DePuy) to eliminate cobalt, chrome, and nickel from the construct, and the femoral component was noted to be well-fixed and was left intact.

Given the overt purulent-appearing material, and despite the negative laboratory results, the infectious disease consultant recommended a peripherally inserted central catheter and a 6-week course of intravenous antibiotics. Unfortunately, the antibiotics caused adverse effects, including leukopenia and thrombocytopenia, that required a change to ceftazidime and daptomycin. At postoperative follow-up, metal allergy testing demonstrated only a mild reactivity to aluminum. At 3-month follow-up, the patient was doing appropriately well, with decreased pain, increased range of motion and ambulation, improved HHS score (39 before surgery, 61 after surgery), and no complications. Fourteen months after revision surgery, she still had vague reports of trochanteric bursitis and thigh pain but had resumed her routine daily activities and was back to work.

Case 2

A 61-year-old man who underwent primary left MOM-THA at an outside institution 8 months earlier presented to our clinic reporting increasing hip pain. The patient reported having had a brief postoperative period of pain relief followed by worsening pain greater than that before the initial procedure. He reported difficulty ambulating plus associated weakness, stiffness, and numbness necessitating use of a cane. Minimal relief was gained with NSAIDs, opiate pain medications, multiple bursal corticosteroid injections, and courses of physical therapy. Past medical history included hypertension, hypercholesterolemia, and type 2 diabetes.

On initial examination, the patient walked with a notable antalgic gait on the operative extremity. The surgical scar was nicely healed, and there was no swelling or cutaneous signs of infection. The patient was significantly apprehensive during flexion and internal rotation; flexion was only 60° to 70°. Straight-leg raise on the operative side was painful. The patient was neurovascularly intact distally to motor and sensory function (HHS score, 32). Radiographs showed what appeared to be a well-fixed large-diameter femoral head THA. The monoblock cobalt–chromium acetabular component was identified as an ASR cup mated with a Trilock stem (Depuy) (Figure 3). Assessment for prosthetic infection consisted of ESR and CRP tests and fluoroscopy-guided hip arthrocentesis performed by a local radiologist. Hip aspiration yielded minimal synovial fluid for analysis, and cultures were negative.

One month later, the patient returned for follow-up and in our office underwent repeat hip arthrocentesis under fluoroscopy. We retrieved 6 mL of cloudy brownish-orange fluid with a white blood cell count of 2300 white blood cells/mL (75% neutrophils) and negative cultures. ESR was 40 mm/h (normal range, 0-20 mm/h), and CRP level was 19.4 mg/L (normal range, 0-8 mg/L). At this point, the diagnosis remained unknown, as clear criteria for infection, aseptic loosening, or metal hypersensitivity had not been established. Given our experience with large-diameter MOM-THAs, revision of the acetabular component was recommended for a presumed variant of a hypersensitivity reaction. Infection was deemed less likely given 2 negative synovial fluid cultures, despite the elevated ESR and CRP results.

A standard posterior approach to the hip was taken through the patient's previous incision. During the

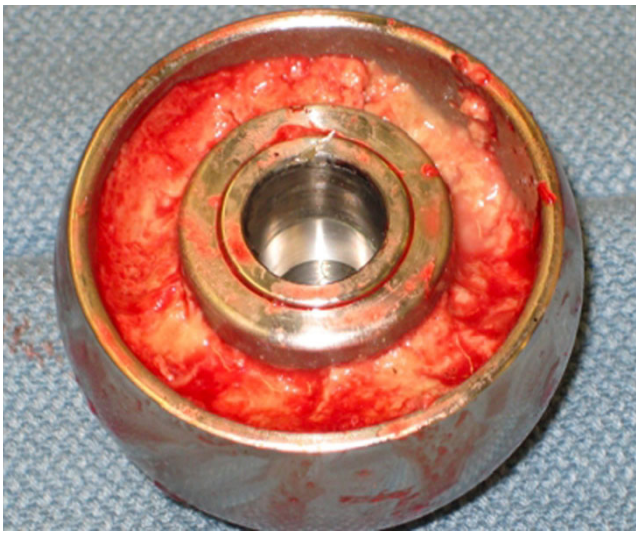

Figure 4. Case 2. Corrosion material within acetabular vault with metallosis on femoral neck, as seen during surgery.

approach, brown, purulent-appearing synovial fluid was found in the joint space. A tremendous amount of corrosion material was also found within the acetabular vault, with metallosis surrounding the femoral neck (Figure 4). Intraoperative synovial fluid cell count was 100 white blood cells/mL with 50% polymorphonuclear leukocytes and 50% lymphocytes, and intraoperative red blood cell count was 115,000 red blood cells/mL. Intraoperative frozen section of the left hip capsule showed necrosis and granulation tissue without evidence of any acute inflammation. Results of intraoperative Gram staining and cultures were also negative. The acetabular component was removed easily. The backside of the implant had minimal to no bone ingrowth, and most of the implant was covered with fibrinous tissue. This component was revised to a porous tantalum modular acetabular component (Zimmer) with a highly cross-linked polyethylene liner (Figure 5). The femoral head was exchanged for a Biolox zirconia-toughened ceramic head (Depuy), and the femoral component was found to be well-fixed and was left intact. At 6-month follow-up, the patient was doing well, with decreased pain and increased ability to ambulate. He had had no postoperative complications, and overall he was very pleased with his outcome. Nine months after revision surgery, he was ambulating without an assistive device and had resumed all his normal activities of daily living. In addition, his HHS score was now 80, improved from 32 before surgery.

Discussion

We have described 2 cases of failed MOM-THA in patients who presented with signs and symptoms of aseptic acetabular component loosening and local soft-tissue inflammation with intraoperative findings mimicking deep hip infection. Metal hypersensitivity was deemed the likely cause of failure given the clinical and radiographic findings and negative preoperative and intraoperative infectious workups. To our knowledge, this constellation

Figure 5. Case 2. Postoperative anteroposterior radiograph of left hip after revision of acetabular component (cup revised to trabecular metal acetabular component with screw fixation and polyethylene insert and exchange of femoral head).

of findings was not previously reported. Specifically, until now, presence of murky, purulent-appearing synovial fluid with negative cell count and cultures during revision surgery was not reported in the spectrum of MOM hypersensitivity presentations. Mikhael and colleagues[8] described presence of a "milk-stained" fluid within the joint during revision surgery in a patient with elevated preoperative inflammatory markers, fevers, and systemic signs of hip infection. Other reports have described extensive hip effusion, fibrinous and necrotic exudation of tissues, and metallosis reaction associated with metal hypersensitivity, but never any purulent-appearing fluid.[6-8,10] Watters and colleagues[10] recently reported a case of pseudotumor leading to superimposed periprosthetic infection after MOM-THA in which, during surgery, there was thickening of the joint capsule and soft-tissue necrosis without metallosis. Our case 1 patient did not have any systemic signs of infection (aside from subjective pain), and ESR, CRP level, cell count, and cultures were all within normal ranges, despite subsequent gross appearance of intraoperative synovial fluid. Our case 2 patient had elevated ESR and CRP level, but infectious workup after 2 hip aspirations was negative, and the increased inflammatory markers were likely caused by tissue hyperreactivity secondary to the large amount of metal debris confirmed during surgery.

MOM hypersensitivity reactions are increasingly being recognized as a cause of osteolysis, loosening, and subsequent failure in the short- to intermediate-term follow-up of MOM-THAs. Although metal hypersensitivity reactions are considered cell-mediated type IV

reactions, it is unknown if the perivascular infiltrates found on histology are a true vasculitis or a novel form of immune response.[5] Authors have reported that the incidence of metal sensitivity was roughly 6 times higher in patients with poorly functioning MOM hip replacements than in the general population and 2 to 3 times higher than in all patients with metal implants.[15] When a patient with a MOM-THA presents with persistent pain with or without signs of early component loosening, and infectious workup is negative, a diagnosis of some form of metal hypersensitivity should be considered early on. Preoperative metal allergy testing should be considered in the workup, but we caution that allergy patch testing and clinical history are not always clear or indicative of underlying pathology.[9,15,16] If metal hypersensitivity is suspected, and symptoms warrant surgery, then during hip revision the component should be exchanged with one having a different bearing surface to remove any cobalt, chrome, or nickel from the articulating surface.

The risk for infection after THA remains approximately 1%,[17,18] and arthroplasty surgeons must be vigilant regarding any signs or symptoms of deep hip infection. Our case 1 demonstrated the potential risks in deciding to initiate antibiotic treatment given intraoperative findings worrisome for infection. The patient in that case received a 6-week course of antibiotics solely on the basis of the purulent-appearing fluid found during revision surgery and despite a negative infectious workup. In addition, the patient experienced antibiotic-associated complications that prolonged recovery. This scenario can be challenging for surgeons, as using an antibiotic to treat an intraoperative finding of "infection" is not always benign. In our case 2, the intraoperative synovial fluid was also brown and murky but was more notable for extensive corrosion material and metallosis than for signs of infection. The findings in these 2 cases emphasize the idea that we do not completely understand the in vivo behavior of and reactions between the body and MOM articulations.

Despite the theoretical advantages of MOM-THA and its promising short- to intermediate-term results, there is still much to be learned about these bearing surfaces and their long-term results. Metal hypersensitivity is a unique cause of failure not seen in other coupled bearings, such as conventional metal-on-polyethylene, and these hard-on-hard bearings can lead to pseudotumors and significantly higher levels of serum cobalt and chromium ions.[10,19-21] However, the enduring effects of these phenomena are still unknown because of lack of long-term follow-up data. The problem of metal hypersensitivity failure of MOM implants has been reported to be rare, with incidence of 1% to 2% and up to 5% depending on alloys used.[22] However, increasing evidence suggests that metal hypersensitivity failure mechanisms are more common than previously thought.[6-10] Therefore, it is vital that surgeons be aware of the variable clinical presentations and operative findings associated with metal hypersensitivity failure so that they can expedite diagnosis and definitive treatment. In both patients described here, symptoms resolved after revision of the acetabular component and conversion to a bearing of ceramic on highly cross-linked polyethylene, thus eliminating cobalt, chrome, and nickel from the construct.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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This paper will be judged for the Resident Writer's Award.