Adverse Local Tissue Reaction in Total Hip Replacement

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ABSTRACT

Total hip replacement (THR) utilizing metal-on-polyethylene articulations was successful for many years. Modifications in materials and implant designs were created to improve wear and allow greater ability to adjust the implant position, optimizing joint mechanics. Three recent cobalt-chromium designs that involve metal to metal contact (metal-on-metal or MoM, modular neck-stems, large metal femoral heads) have produced metal debris through corrosion, releasing cobalt ions around the implant. Unfortunately, these metal nanoparticles have led to a wide spectrum of soft tissue destruction called adverse local tissue reaction (ALTR). This review article assesses ALTR following THR using MoM cobalt-chromium designs, as well as the diagnostic testing used to identify at risk hips. Findings reveal that a possible explanation for ALTR is hypersensitivity to cobalt with lymphocytic perivascular infiltration, known as aseptic lymphocytic vasculitis associated lesion (ALVAL). Solid or cystic masses called "pseudotumors" may also form around the implant. Given the destructive nature of ALTR to the surrounding capsule, muscle, and bone, surgical revision of the MoM junction is generally required. In addition to physical examination and x-rays, diagnosis now depends on drawing serum cobalt and chromium levels, as well as the use of a metal artifact reduction suppression (MARS) MRI.

The authors believe that the optimal design and bearing surface for THR is a titanium femoral stem and acetabulum with a ceramic femoral head (32 or 36 mm) articulating on a polyethylene acetabular insert. Manufacturers have now produced a polyethylene with superior bearing characteristics, as evidenced by minimal wear after five to ten years of implantation.

1. INTRODUCTION

Total joint replacement (THR) is a highly successful treatment for degenerative hip disease. However, advances in technology continue to produce design changes with the goal of increasing the longevity of the prosthetic components, especially the bearing surfaces. Unfortunately, some recent modifications have led to a biologic reaction termed "adverse local tissue reaction," or ALTR. This reaction can cause early implant failure, requiring revision surgery due to pain and soft tissue destruction adjacent to the prosthetic implant. It is now commonly accepted that these adverse reactions are due to metal corrosion of cobalt-chromium (Co-Cr) at various interfaces [1].

For the last several decades, total hip designs have included a titanium femoral stem, titanium acetabular shell, metal or ceramic femoral head, and a polyethylene articulating surface (Figure 1A). Traditionally, the polyethylene liner has been the weak link in the system, eventually breaking down and forming wear products of microscopic particles that induce macrophage and giant cell production. These abnormal collections of cells generate bone resorption called osteolysis around the implants leading to loosening and failure. This has been the traditional failure mode for metal-on-polyethylene articulations.

Metal-on-metal (MoM) articulations were popularized in the mid 1990's due to demonstrated reduced wear in vitro, thus providing a potentially longer lasting bearing surface and eliminating polyethylene wear and subsequent osteolysis. In addition, MoM designs use larger head sizes that result in greater hip joint stability, reducing the chance of dislocation (Figure 1B). Another design that incorporated MoM articulations was surface replacement arthroplasty (SRA). In this replacement, the femoral head is resurfaced maintaining the femoral neck. This SRA design was thought to provide a higher level of function allowing for strenuous sporting activities in younger patients. Both the MoM and SRA designs utilize cobalt-chromium alloys. Unfortunately, clinical studies demonstrated early, catastrophic failure in some cases. This occurred because of the generation of metal ions of cobalt and chromium resulting in ALTR. One particular MoM hip system, the Articular Surface Replacement (ASR) hip system (DePuy, Warsaw, Indiana, USA), suffered a high rate of early failure resulting in a recall of the implant. Further studies have confirmed an unacceptable revision rate of the ASR hip [2]. While some designs have higher failure rates than others, the use of all MoM articulation devices has essentially disappeared because of concerns regarding the production of local and systemic reactions generated by harmful metal ions.

Another new design, called modular neck or dual taper, was created to provide the surgeon with greater ability to adjust the implant position and optimize joint mechanics. The interchangeable modular neck-stem provided the flexibility to adjust femoral anteversion, neck length, and head-neck offset (Figure 1C). Unfortunately, this additional taper junction can undergo corrosion and implant failure (Figure 2A).

Cause of corrosion is likely multifactorial (incomplete junction fitting, higher offset, excessive patient weight and activity, or metallurgy mismatch), since this failure is not seen in all modular neck designs [3]. One specific design, the Rejuvenate hip system (Stryker Orthopedics, Mahwah, New Jersey, USA), was recalled by the company because of an alarming failure rate at less than five years after implantation due to corrosion at the taper neck junction [4].

Finally, corrosion of the femoral stem at the neck-head junction (the trunnion) can occasionally be a site of corrosion (Figure 1D and Figures 2 B,C). The corrosion seen at the junction of the femoral neck and metal head has been termed "trunnionosis." The source of this mechanically assisted crevice corrosion and resultant metallic debris may be due to metal mismatch, low rigidity of the neck, mechanical forces of a large head on a narrow neck taper, and greater torque acting along the taper interface. Recent studies indicate corrosion and fretting at the taper junction may be a greater problem when larger head sizes (>36mm) are used [5]. Large head sizes articulating with polyethylene were adapted by surgeons to minimize the risk of postoperative dislocation which can occur in 1-2% of primary THR cases and even higher rates after revision THR.

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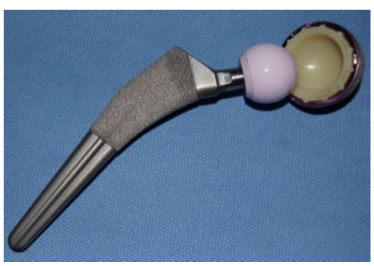

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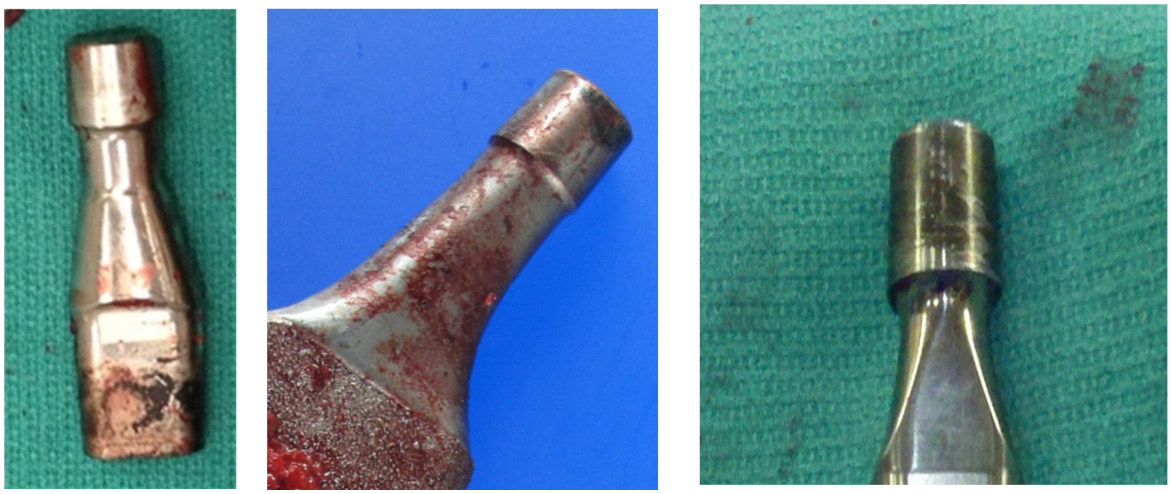
Figures 1A,B,C,D.



A B C

Figures 2A,B,C

2. ADVERSE LOCAL TISSUE REACTION (ALTR)

The entity termed ALTR involves a wide spectrum of local tissue destruction surrounding a prosthetic implant, usually associated with nanoparticles of metal debris. This process takes on many forms but the end result may lead to capsule, muscle, tendon, and bone degradation. One type of soft tissue periprosthetic abnormality is thought to result from a hypersensitivity to the metal ions similar to a delayed type IV hypersensitivity reaction. Willert et al. described this distinct histologic pattern of diffuse perivascular lymphocytic infiltrate with associated plasma cells, leading to the term aseptic lymphocytic vasculitis associated lesion (ALVAL) [6]. This ALVAL reaction is now recognized in a large number of failed MoM arthroplasties and corrosion neck-stem cases [7]. Later, Pandit et al. defined the term "pseudotumor," where soft tissue growth may occur in either solid or cystic form. These destructive masses may be small or large and can result in pain and limited mobility. Extensive necrosis of connective tissue with heavily scattered macrophages and lymphocytes was reported in this tissue reaction [8]. Metal suppression MRI scans prove particularly helpful in identifying joint effusion, fluid collections, cysts, and pseudotumors seen in these cases.

3. HISTOLOGY

A variety of microscopic findings can be seen in adverse tissue reactions following total hip replacement. The term ALVAL refers to a specific perivascular inflammatory pattern (Figure 3). However, other histologic findings may be less specific such as capsular thickening and fibrosis, synovial proliferation, and tissue necrosis. A fluid-filled mass in the adjacent soft tissue (pseudotumor) results from varying degrees of inflammation, necrosis, and fibrin deposition.

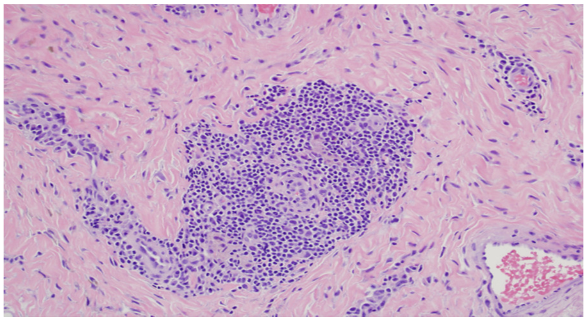


Figure 3

4. SYSTEMIC CONSEQUENCES OF METAL ION RELEASE

Adverse local tissue reaction is the local reaction around the implant; however, the metal ions when generated in larger amounts can be disseminated widely in the body through the bloodstream and the lymphatic system with the possibility of systemic adverse effects. Cobalt has been the metal ion most closely associated with toxicity. Cobalt-induced myocardial toxicity was found as a result of occupational exposure [9]. Chen et al. in 2013 examined serum cobalt levels and their impact on liver, kidney, and immune markers. They found only changes to the immunologic system, but could not show that these abnormalities were able to compromise true host defense mechanisms [10]. Prentice et al. conducted a cross-sectional health screen in patients with well-functioning MoM implants to identify if any organ systems may be susceptible to chronic metal exposure. Their data showed positive effects on increased body mass, but deleterious effects on the left ventricular function of the heart [11]. Recently Cheung et al. reviewed systemic cobalt toxicity in total hip replacements. They examined possible damage to the cardiac, thyroid, hematologic, neurologic, and hepatic systems in addition to the carcinogenic potential. Only 18 cases have been reported with true toxicity, of which ten involved MoM. They summarized that although patients with cobalt-chromium bearing surfaces have a theoretical risk of systemic cobalt toxicity, this is a rare phenomenon [12].

5. DIAGNOSIS OF ADVERSE LOCAL TISSUE REACTION (ALTR)

5.1 Physical Exam

MoM hip replacement patients now require routine surveillance given the discovery and complications of ALTR. Patients can be asymptomatic and symptomatic. Careful physical examination can determine if symptomatic patients have an intrinsic or extrinsic source to their hip discomfort. Pain with joint motion should be assessed. Masses associated with pseudotumor are rarely palpable.

5.2 Infection Work-up

All symptomatic patients require at minimum a sedimentation rate, C-reactive protein, and complete WBC with differential. ATLR often has a similar appearance to infection, and highly suspect patients may also need a hip aspiration for cultures. Repeat laboratory evaluation of these key tests is indicated when the symptoms persist despite a negative work-up for ATLR. In a small percentage of patients the sedimentation rate and C-reactive protein can be elevated in non-infected cases of ATLR, however these should not increase over time.

5.3 Serum Cobalt and Chromium Levels

Elevated serum cobalt and chromium levels have been observed in patients with ALTR. Numerous studies have attempted to define which levels of either cobalt or chromium indicate a hip at risk for ALTR [13-15]. Cobalt appears to be a more accurate indicator of local tissue reactions, but chromium levels can still be useful. Although there is no universally accepted normal cobalt level in MoM hip surgeries, the consensus for a well-functioning, not at risk hip, is 1.5-3.5µg/L [16, 17]. Langton et al. recommended surgery for any patient with cobalt levels > 10µg/L even those who are asymptomatic [13]. The question remains as to those patients with values between 3 and 10µg/L. specifically, at what value is it important to start further investigations? The British Medicines and Healthcare Products Regulatory Agency (MHRA) stated that cobalt and chromium metal ion levels above 7µg/L indicate potential ALTR. While this has been accepted as a good guideline for the clinician, Hart et al. suggested lowering the value to > 5µg/L to increase sensitivity in identifying potential failures [15]. Malek et al. compared cobalt levels with MARS MRI findings and determined that their sensitivity increased to 86% if the value was lowered to > 3.5µgL [18]. Current recommendations by several orthopedic associations use > 5µg/L as a threshold for further investigation [14]. Serum metal values alone should not determine a clinical decision for revision of the implant but must be utilized with all other diagnostic modalities. However, cobalt and chromium levels should be used as a clinical screening tool for routine MoM implant surveillance. It should be noted that it is difficult to know what comprises a normal cobalt or chromium level for the patient with an implant at risk.

5.4 Radiographs

Except in cases of osteolysis, the majority of plain radiographs are normal in cases with ALTR. However, these should be used for routine screening as soft tissue abnormalities can sometimes be evident or early radiolucent lines may appear. Radiographs may be useful in determining prosthetic alignment. Campbell et al. found a direct correlation between acetabular inclination > 50 degrees on an AP view of the pelvis and increased levels of serum cobalt [19]. Radiographs can identify at risk patients for closer surveillance.

5.5 Metal Artifact Reduction Suppression MRI (MARS MRI)

A major advancement in evaluating soft tissues around a hip implant has been the development of a metal artifact reduction suppression (MARS MRI). The metal does not scatter the image and pericapsular tissues can be visualized with this technique. The main use for this technique is when clinical and serum ion levels suspect ALTR. The MARS MRI can be useful in detecting synovitis around the implant in addition to pseudotumors. In a study of 68 consecutive patients, Nawabi et al. confirmed that a MARS MRI could detect and reproducibly quantify ALTR in hip resurfacing. MARS MRI has become a diagnostic standard and is generally recommended for two populations, those with hip symptoms and those who are asymptomatic but with elevated serum cobalt and chromium levels. Some centers prefer diagnostic ultrasound, however this can be operator dependent [20].

5.6 Ultrasound and CT Scanning

CT scanning has been useful in patients unable to tolerate an MRI due to pacemakers or other contraindications to this study. CT scanning can be used to examine acetabular cysts and determine acetabular inclination. Popularized early to detect ALTR, it has now been replaced with the MARS MRI. Recently ultrasound has proven beneficial in detecting joint fluid and pseudotumors.

6. TREATMENT OF ALTR

Ultimately, revision hip surgery should be performed for those with a confirmed diagnosis of ATLR. The main goals of surgery are to remove the destructive soft tissues and to eliminate the MoM articulation that is generating metal ions. In the case of MoM total hips, acetabular revision is usually required unless a polyethylene head can replace the metal head in situations where the metal cup has no appreciable wear or damage. However, in the case of modular neck implants, the femoral component may require removal even if well fixed [21]. In trunnionosis cases, conversion to a standard total hip with ceramic heads on polyethylene is most commonly performed. If the femoral neck is severely damaged, the femoral component may also need to be revised. Given the aggressive soft tissue debridement and prosthetic exchange, post revision complications may occur including dislocations and abductor weakness. In general, revision surgery in ALTR is not as successful as standard metal-on-polyethylene prosthetic revision surgery because of extensive soft tissue damage.

7. CONCLUSIONS

Adverse local tissue reaction (ATLR) results from release of metal ions found in metal-on-metal articulations. The local soft tissue destruction seems to be either a hypersensitive reaction to the metal ions (ALVAL) or a granulomatous reaction with formation of a solid or cystic “pseudotumor.” Systemic side effects from serum ions are rare, and currently the local periarticular destruction is the primary problem leading to revision surgery. Accurate diagnosis relies on physical exam, plain x-ray, serum cobalt and chromium levels, and MARS MRI. The decision to revise the implant is multifactorial and the goal is to prevent further soft tissue destruction and implant failure if the process is in the active phase.

The important question is: Are all MoM and modular neck designs doomed to failure? It is our belief that some designs are more likely to fail, but all of these designs are at risk and require closer clinical follow-up than traditional designs. This view may be shared by most orthopedic surgeons evidenced by the substantial decline in the selection of these devises (MoM, SRA, modular neck-stems, large metal femoral heads). The good news in the field is that polyethylene manufacturing techniques have produced superior bearing characteristics producing very little wear after 5-10 years of implantation. Currently, it is our belief that the optimal design and bearing surface for total hip replacements is a titanium femoral stem and acetabulum with a ceramic femoral head (32 or 36 mm) articulating on a polyethylene acetabular insert.

Disclosures

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FIGURE LEGENDS

Figures 1A,B,C,D:.

(A) Conventional titanium cementless femoral stem and modular (removable) ceramic head, which articulates with a titanium acetabular shell and polyethylene liner; (B) Large metal head articulating with a cobalt-chrome acetabular shell with no intervening polyethylene. This is termed a metal-on-metal (MoM) total hip replacement (THR); (C) Modular neck femoral stem design; (D) Large diameter metal head on a trunnion.

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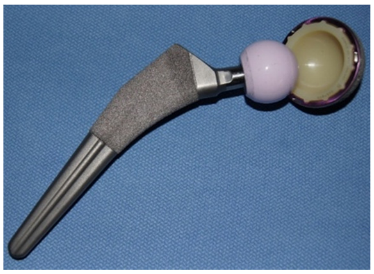

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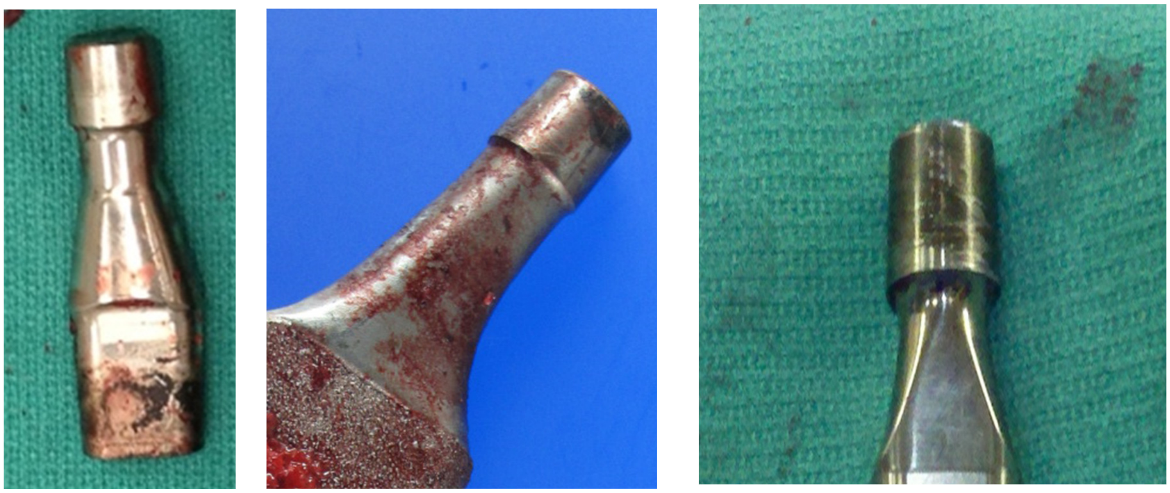
Figures 2 A,B,C:

(A) Modular neck corrosion at the neck-stem junction.

Examples of corrosion of the femoral stem trunnion: (B) Moderate and (C) Severe.



A B C

Figure 3:

Dense perivascular inflammation, characteristic of ALVAL.