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Posted Date: 9 September 2025

doi: 10.20944/preprints202509.0759.v1

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Case Report

Massive Pseudotumor Despite Normal Serum Metal Ions in Metal-on-Metal Total Hip Arthroplasty

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Abstract

The development of periprosthetic soft tissue reactions is a well-documented complication in patients who have previously undergone metal-on-metal (MoM) total hip arthroplasty (THA). Adverse reactions resulting from the shedding of intraarticular metal ions have been broadly classified into several modes of failure, including pseudotumor development and aseptic lymphocyte-dominated vasculitis-associated lesion (ALVAL). We present a case report of a 76-year-old female with a history of MoM THA who presented with left thigh pain and swelling. Radiographic and histologic analysis were consistent with ALVAL and pseudotumor, despite normal serum metal ion levels. The patient underwent revision total hip arthroplasty with pseudotumor debridement of 3300 mL cystic fluid, and at nearly five years postoperatively, is functioning well with no recurrence of pain or swelling. Review of the literature demonstrates an average pseudotumor area of 73 cm2. Further literature review reveals that serum metal ion levels may not reliably exclude clinically significant pseudotumor formation. As such, this case report challenges the assumption of elevated serum metal ions as an indicator for MoM failure by demonstrating a massive pseudotumor in the context of normal serum levels. Clinicians should maintain a high index of suspicion for adverse local tissue reactions in patients with MoM THA, regardless of serum metal ion levels. Advanced imaging and clinical correlation remain essential for diagnosis and management.

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Introduction

Total hip arthroplasty (THA) is one of the most common orthopedic procedures performed in the USA. The conventional THA was introduced in the early 1960s and consisted of a metal acetabular cup, cup liner, and metal femoral stem component. Early models made use of a plastic polyethylene liner, although these designs were eventually associated with problems such as asymmetric wear, osteolysis, and particle debris. As a result, new bearing surfaces were developed, including 'soft' materials such as crosslinked polyethylene, and 'hard' materials like ceramic and metal.

Initially, metal-on-metal (MoM) bearings were believed advantageous over metal-on-polyethylene (MoP) designs. Lack of a thick polyethylene liner allowed for a larger head:neck ratio, maximizing range of motion and stability while minimizing femoral neck impingement and dislocation [1]. As a result, MoM surfaces demonstrated less volumetric wear and smaller particle generation compared to MoP constructs, which was believed to decrease rates of osteolysis [1]. However, large-scale registry data eventually revealed significantly increased revision rates for MOM THAs and led to DePuy (Warsaw, IN) recalling their Articular Surface Replacement (ASR) MoM hip arthroplasty components in 2010 [2]. Still, complications from MoM implants continue to be seen more than a decade later.

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Current evidence suggests that metal-on-metal (MoM) implant failure is driven by the intra-articular shedding of cobalt and chromium particles through volumetric wear, a consequence of increased metal bearing surface area [3]. Metal ion release is now recognized as a key factor in MoM failure and is encompassed within Adverse Reactions to Metal Debris (ARMD), a broad term describing various failure mechanisms.

Aseptic lymphocyte-dominated vasculitis-associated lesion (ALVAL) and pseudotumor formation are two predominant manifestations of ARMD. ALVAL is a lymphocyte-mediated hypersensitivity reaction to locally shed metal debris, characterized histologically by widespread necrosis and periarticular infiltration of T cells and macrophages [3]. Pseudotumors frequently occur alongside ALVAL and have been reported in up to 35% of patients with MoM implants [3]. For clarity, we define a pseudotumor as a non-neoplastic, non-infectious mass that typically manifests as a fluid collection or granulomatous reaction associated with hip arthroplasty.

Here, we present a case report detailing the presentation, diagnostic work-up, and treatment for a 76-year-old female presenting with massive pseudotumor following MoM THA. We also review the existing literature and case reports on this rare presentation. This article was previously presented as a meeting poster at the American Physician Scientist Association (APSA) Meeting on February 17, 2023.

Case Presentation

A 76-year-old female presented with progressive left hip and thigh swelling 15 years after her primary MoM THA in 2005. Her swelling had markedly increased over the past six weeks after a minor motor vehicle collision where she was unharmed. Symptoms included progressive thigh swelling, constant and diffuse thigh pain rated seven out of 10 and characterized as “tightness”, stiffness, weakness, night pain, and instability. There was no recent episode of trauma, injury, or change in activity level. She had a BMI of 25 and her medical history was significant for hypertension, type two diabetes, and transient ischemic attack. The remainder of her history was unremarkable.

On initial examination, she denied any focal tenderness and displayed an antalgic gait with use of cane. There was extensive edema about her left thigh that measured circumferentially twice as large as the right. Range of motion was painful (10° passive internal and 20° external) accompanied by hip abduction weakness but no change in quadricep strength. There were no signs of infection. Initial radiographs demonstrated a MoM THA with well aligned components, but aseptic loosening of the acetabular cup, osteolysis about the acetabulum and proximal femur, and degradation of the calcar (Figure *1*). Further workup consisted of metal artifact reduction sequence (MARS) magnetic resonance imaging (MRI) of the hip and thigh, non-contrast commuted tomography (CT) scan of the pelvis, and laboratories, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and complete blood count (CBC).

MARS MRI showed a massive, encapsulated fluid collection extending superiorly from the hip joint into the greater sciatic foramen, distending the iliopsoas and greater trochanteric bursae, and compressing the gluteus medius and minimus (Figure *2*). Below the hip, this mass emanated down the anterior femur to ~ four cm above the patella. In its entirety, the collection measured 43 cm craniocaudal x 18 cm transverse x 14 cm AP. Non-contrast CT confirmed the fluid collection and revealed additional acetabular osteolysis with a small area of complete medial wall erosion. There was also osteolysis of the femoral component involving the greater and lesser trochanters as well as the anterior and posterior intertrochanteric regions (Figure *3*). Laboratory workup was negative for infection, with normal CRP (0.9 (<1.0 mg/dL)), ESR (14 (0-30 mm/ h)), and WBC (7.3 (4.1-11.1 K/μL)). Serum metal ion concentrations were also normal with serum cobalt < 1 (0-9 ug/L) and serum chromium 0.5 (0.1-2.1 ug/L).

Revision of her acetabular cup with pseudotumor decompression was performed through a posterior approach nine days after initial presentation. Intraoperatively, 3300 mL of brown fluid with particulate debris was found inside of a pseudocapsule, which was evacuated with suction while the

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remaining solid portion was dissected. Multiple specimens were taken for culture, which remained negative for infection, but revealed "predominantly anuclear fibrinous material and focal soft tissue with chronic inflammation" of her pseudocapsule, along with chronic lymphohistiocytic inflammation of her femur, acetabulum, and posterior capsule. This was all consistent ALVAL.

Next, revision of the acetabular component to a standard metal-on-polyethylene construct was carried out. After extensive irrigation and debridement, the original femoral stem appeared well fixed, but with some proximal femur necrosis, trunnionosis, and eccentric polyethylene liner wear. The trunnion was thoroughly cleaned, and the rest of the femoral stem was retained. Conversely, the acetabular cup showed little signs of osseointegration and appeared aseptically loose; this was revised to a metal femoral head with a dual mobility polyethylene liner given her abduction weakness. Postoperatively, the patient's course was uneventful.

At nearly five years postoperatively, she ambulates without pain or assistance and denies any recurrence of her swelling. She is able to put on shoes and socks, use stairs one foot at a time, and rise from a seated position without difficulty. Range of motion is 10° internal and 20° external rotation. She continues to be followed annually due to previous elevations in ESR and CRP, although infectious work up has remained negative. XR continue to demonstrate revision THA components in good position without evidence of complication (Figure 4).

Discussion

The natural history of MoM THA pseudotumors is not well understood given they are a relatively new phenomenon with variable and inconsistent clinical presentations. Similar cases of massive pseudotumor with normal metal ions appear rare, although it can be difficult to qualify given most case reports omit quantification of pseudotumor size, volume, or serum metal ion concentrations. As such, a review of the literature identified only 14 case reports that explicitly detail both pseudotumor size (measurements vs fluid volume) and serum metal ion concentration. Nine of 14 cases report MoM THA while five report MoM hip resurfacing. Further details of each case are reported in Table *1*. Of these cases: (1) 71% of patients were female, (2) the average age was 58 years old, (3) the average pseudotumor size was 73 cm^2 (defined as product of two largest dimensions), (4) 29% of patients had normal serum metal ion levels, and (5) 100% of all patients underwent revision surgery. Here we will review the associated case reports alongside our patient's more relevant findings.

On initial presentation, our patient reported hip pain with abductor weakness, instability, and circumferential swelling. Comparatively, our review of pseudotumors found that hip pain was the most commonly reported (71%) followed by swelling (52%). Other described symptoms included instability [4], weakness [5–8], and hip "clicking/squeaking/popping" [4,9,10]. Only our patient exhibited abductor weakness, perhaps because our mass was comparatively so large that it disrupted the abductors.

On imaging, our patient's mass measured 43 cm x 18 cm x 14 cm (774 cm^2), while intraoperative evacuation revealed 3300 mL of fluid. Of our fourteen identified case reports, pseudotumor size ranged from 20 cm^2 to 137 cm^2 with an average size of 73 +/- 44 cm^2. The largest area was 137 cm^2 and volume 1350 mL [5,6]. The majority of pseudotumors were reported as dimensions while only three cases reported a volume [5,9,10].

The underlying causes of such a large fluid collection in this context are not well understood. We hypothesize that pseudotumor size is the result of interplay between component wear and individual immunosensitivity. Studies have shown that elevated plasma metal ions are associated with larger pseudotumor sizes [18]. Thus, factors influencing MoM component wear, such as shorter taper lengths or implant malpositioning, may play a role in modulation of pseudotumor size via production of metal ions. Other modulators of component wear may also play a role, such as patient activity level and time since MoM implantation. Larger femoral head sizes may also influence pseudotumor size. Here, our patient's femoral head measured 39mm compared to an average size of 44mm among six of our identified THA cases [6,8,9,12–14]. Lastly, individual immunosensitivity may

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also play a role in development of large pseudotumors as some patients can have a heightened immune response to metal particles, analogous to metal hypersensitivity reactions.

Upon suspicion for pseudotumor, radiographic examination is naturally the first diagnostic step. In our case, x-ray and CT scan revealed osteolysis about the proximal femur and acetabular cup with subsequent loosening of the cup. However, radiographic evidence of THA compromise is not consistently present in patients with ALVAL; six of our review's 14 cases explicitly denied any evidence of osteolysis or loosening [4,6,10,12,15,16], with only three reporting signs of osteolysis [5,7,8]. Given a lack of consistency in x-ray findings, we advocate for the use of CT and/or MARS MRI for patients with high suspicion for pseudotumor or ALVAL.

In our patient, laboratory results were negative for elevated serum metal ion concentration. In comparison, ten of 14 (71%) reviewed cases reported an elevation in serum metal ions. Both the Food and Drug Administration in the USA and the United Kingdom's Medicines and Healthcare Products Regulatory Agency both officially recognize elevated serum chromium and cobalt as markers for ARMD [19]. It is unclear why our patient had no elevations in serum metal ions with such a large pseudotumor. We hypothesize that local metal ions were sequestered by activated macrophages as part of the ALVAL response, while others became trapped within surrounding tissues and the pseudotumor rather than entering systemic circulation. Serum metal ion levels may also fluctuate over time. Given our patient's increasing pain and swelling, her reduced activity-level may have resulted in decreased component wear, subsequently limiting metal ion release into the bloodstream. Nonetheless, our patient challenges the conventional notion that metal ions are a reliable biomarker for the presence of pseudotumor and ALVAL in a MoM THA.

Our decision to proceed with revision surgery was predicated on several factors, including the patient's leg swelling with pain, osteolysis, and loosening of the acetabular cup. According to AAOS's risk stratification algorithm for MoM THA, revision should only be considered for high-risk patients who are severely symptomatic, show implant osteolysis/loosening, or at high risk of developing ARMD [20]. 100% of reviewed cases underwent revision, with 86% (12/14) undergoing mass excision/evacuation. Excision was contraindicated in Memon et. al. due to tumor involvement with iliac vessels [17]. Sassoon et. al. elected for revision without pseudotumor resection, instead opting for in situ resolution [12].

While MoM revisions carry generally favorable clinical outcomes, we do not advocate for surgery as a baseline recommendation given the risks of complications such as infection, recurrence of ARMD, or failed ingrowth. Pseudotumors (especially when intrapelvic) can also involve the iliac vessels which may complicate revision surgery; five cases reported vessel involvement, several of which required consult with vascular surgery [10,15–17,19]. Surprisingly, our patient's femoral vessels were reported to be only 'mildly effaced'. Other complications include risk of peritonitis from spreading pseudotumor during evacuation in the lateral decubitus position, a concern for Cottino et. al [5]. In patients with high grade pseudotumor, such as ours, risks of revision are inconclusive in the literature. Nonetheless, revision of MoM THA with pseudotumor is an increasingly risky procedure, requiring thoughtful and nuanced consideration from both physician and patient.

Conclusions

ALVAL and pseudotumor development are known complications of MoM THA. The archetypical pseudotumor patient presents with pain, swelling, and elevated serum metal ion levels necessitating revision total hip arthroplasty. Our case demonstrates an atypical presentation of a large, symptomatic pseudotumor in the absence of elevated serum metal ion levels. This presentation challenges the conventional understanding of serum metal ions as a biomarker for pseudotumor. As patients continue to present with MoM complications, orthopedic surgeons should not solely rely on metal ions as an indicator for adverse reactions to metal debris. Continued investigation into the pathogenesis and presentation of ARMD will be key in identifying more specific markers for this phenomenon.

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