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Case Report

Immunoglobulin A Nephropathy in a Patient With Bilateral Metal-on-Metal Hip Arthroplasty

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ABSTRACT

Immunoglobulin A (IgA) nephropathy in the presence of a metal-on-metal (MoM) hip arthroplasty is a rare condition that requires close monitoring. A 61-year-old male with bilateral hip osteoarthritis underwent resurfacing hip arthroplasty with MoM articulating surfaces. Prior to his four-year postoperative visit, the patient was diagnosed with IgA nephropathy. During this visit, the patient reported clicking in the left resurfacing hip arthroplasty, and serum metal ions were significantly elevated. Consequently, the patient underwent conversion to bilateral ceramic-on-cross-linked polyethylene total hip arthroplasty, which resulted in the restoration of metal ion levels to normal. This case highlights that IgA nephropathy played a critical role in impeding the clearance of metal ions. Routine metal ion counts are warranted in patients with MoM articulating interfaces and a newly diagnosed nephropathy.

Introduction

Metal-on-metal (MoM) implants were reintroduced in total hip arthroplasty (THA) by Weber in 1988 [1]. Several advantages have been proposed, including reduced volumetric wear and reduced risk of dislocation [2–4]. These bearing surfaces consist of a cobalt-chromium metal alloy, which is a source of metal ions, primarily cobalt and chromium ions [5,6].

Serious concerns have been raised regarding the high failure rates associated with MoM bearings, with the most common reason for failure being aseptic loosening of the acetabular component [7]. In addition, elevated levels of cobalt and chromium ions lead to adverse local tissue reactions (ALTR) requiring revision [8–10]. These ions can enter the systemic and lymphatic circulation, subsequently disseminate throughout the body, and accumulate in distant tissue [11–13]. Various adverse events can result locally (osteolysis and ALTR) and/or systemically (neurologic, cardiac, thyroid, and renal) [13–15].

We herein describe a rare case of an active patient diagnosed with immunoglobulin A (IgA) nephropathy and chronic renal disease who developed an increasing level of metal ions. Following removal of the MoM hip implants, metal ions declined and renal function improved. This case highlights the importance of careful monitoring of metal ions in MoM hip implant patients with renal disease. To the best of our knowledge, this is a rare presentation with diagnostic and therapeutic challenges.

Case history

A 61-year-old male with severe osteoarthritis underwent a right, followed by a left, resurfacing hip arthroplasty (RHA) in 2004 and 2011, respectively. He had a known history of deep venous thrombosis and was managed with chronic warfarin anticoagulation therapy for over 15 years, as well as antiphospholipid syndrome (positive for both lupus anticoagulant and anticardiolipin antibodies). At the time of his last RHA in 2011, his serum creatinine was 90 μmol/L (range: 55-120 μmol/L). Six weeks later, during his postoperative visit, cobalt and chromium metal ion

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levels measured 2.54 μg/L (range: 0.15-0.40 μg/L) and 1.77 μg/L (range: 0.36-0.99 μg/L), respectively.

His routine annual follow-up visits were normal with no complaints. However, in 2015, 4 years after the left RHA, he complained of left hip clicking. Upon physical examination, hip function was normal with a pain-free range of motion. An anteroposterior radiograph of the patient's pelvis and hips at the follow-up showed well-positioned components and within normal limits: right and left hip abduction angles were 40 and 41 degrees, respectively, while right and left hip anteversion angles were 15 and 20 degrees, respectively. (Fig. 1). The implant materials are described in Table 1. The patient's C-reactive protein and erythrocyte sedimentation rate concentrations were elevated (39.4 mg/L, range: 0-10.0 mg/L; 90 mm/hr, range: 2-39 mm/hr, respectively), and metal ions were elevated (Co: 247.8 μg/L, range: 0.15-0.40 μg/L; Cr: 63.9 μg/L, range: 0.36-0.99 μg/L). Elevated inflammatory markers warranted an aspiration of both hip joints, which were negative for periprosthetic infection.

Concurrently, the nephrologist was investigating the recent onset of hematuria and proteinuria. His serum creatinine was 108 μmol/L (range: 55-120 μmol/L) and no bacterial growth was found on urine culture. Consequently, a renal biopsy was performed. Immunofluorescence and electron microscopy studies revealed large mesangial dense deposits and IgA deposits, confirming the diagnosis of IgA nephropathy (Berger's disease). Moreover, with the nonproliferative biopsy revealing 50% sclerotic glomeruli and the patient's estimated glomerular filtration rate of 59 (range: >60 mL/min/1.73 m^2), a diagnosis of stage IIIa chronic kidney disease was made.

Increased metal ion levels warranted an evaluation of cardiac function. Transthoracic echocardiography revealed a normal left ventricular ejection fraction of 60%. Due to rising metal ion levels and declining renal function, a decision was made to revise both hip implants and convert to THAs with ceramic-on-cross-linked polyethylene (XLPE) bearing surfaces (Table 1).

The revision surgeries were performed simultaneously via a posterior approach. Frozen sections were prepared from aspirates of joint fluid and tissue obtained intraoperatively from both hips; no infection was detected on frozen sections and cultures. However, an intraoperative examination of the right hip revealed marked metallosis with tissue staining, while the left hip tissue did not reveal signs of ALTR. The patient had an uneventful postoperative course and was discharged 4 days postoperatively. Postoperative

Figure 1. AP radiograph of the patient's right and left RHA at the 4-year follow-up visit (2015). All components were well positioned and within normal limits: right and left hip abduction angles were 40 and 41 degrees, respectively, while right and left hip anteversion angles were 15 and 20 degrees, respectively. AP, anteroposterior.

Table 1
Implant materials and specifications for primary RHA and revision THA.

Primary implants	
Right (April 2004)	ASR Hip Resurfacing System (DePuy Orthopaedics, Inc., Warsaw, Indiana). Head diameter: 49 mm Cup size: 56 mm Interface: metal-on-metal
Left (October 2011)	Adept Hip Resurfacing System (MatOrtho Limited, Surrey, UK) Head diameter: 48 mm Cup size: 54 mm Interface: metal-on-metal
Revision implants	
Right (October 2016)	Cementless Head diameter: 36 mm Cup size: 56 mm Interface: ceramic-on-XLPE
Left (October 2016)	Cementless Head diameter: 36 mm Cup size: 56 mm Interface: ceramic-on-XLPE

radiographs are shown in Figure 2. He continued outpatient physical therapy. At his 6-week postoperative THA revision visit, serum metal ion levels had declined (Co: 73.5 μg/L, range: 0.15-0.40 μg/L; Cr: 20.8 μg/L, range: 0.36-0.99 μg/L). At the 1-year follow-up examination, the patient's blood metal ion concentrations were near normal (Co: 2.06 μg/L, range: 0.15-0.40 μg/L; Cr: 7.80 μg/L, range: 0.36-0.99 μg/L). Two years postoperatively, his metal ion levels normalized (Co: 0.83 μg/L, range: 0.15-0.40 μg/L; Cr: 4.89 μg/L, range: 0.36-0.99 μg/L) and his kidney function stabilized (estimated glomerular filtration rate >60 mL/min/1.73 m^2, range: >60 mL/min/1.73 m^2).

Discussion

In 2017, the UK Medicines and Healthcare products Regulatory Agency published a safety alert that recommended orthopaedic follow-up and monitoring of blood cobalt and chromium ion levels along with metal artifact reduction sequences-magnetic resonance imaging for patients receiving a MoM hip prosthesis [16]. Similarly, the United States Food and Drug Administration has recommended clinical monitoring for signs and symptoms of multisystem effects of metal ion release, including neurological, cardiovascular, thyroid, and renal system effects, in patients with a MoM hip implant, regardless of the symptoms [17]. The Medicines and Healthcare products Regulatory Agency and Food and Drug Administration recommendations assisted in detecting elevated metal ions, even though our patient was initially asymptomatic and both MoM hip implants were well-functioning. At our institution, serum metal ion levels are followed routinely for all patients with MoM RHA or THA. Despite the cobalt and chromium ion elevation, our patient had no cardiac or thyroid abnormalities, as confirmed by cardiac blood markers, thyroid function tests, and echocardiography.

Several reported studies have demonstrated that both cobalt and chromium ions are excreted almost exclusively by the kidneys [13,18,19]. Therefore, continuous monitoring of blood metal ion levels is important for patients with a MoM bearing and renal dysfunction. MoM bearings are contraindicated in patients with chronic renal failure [20–22] or in patients that can develop chronic renal failure (eg, diabetes, systemic lupus erythematosus). However, investigators have found that well-functioning MoM implants in patients with normal kidney function will not increase the risk of renal disease [23–25].

Berger et al. [26] first described IgA nephropathy by marked IgA deposition in glomerular mesangial cells. Secondary IgA nephropathy can be associated with an already recognized pathology

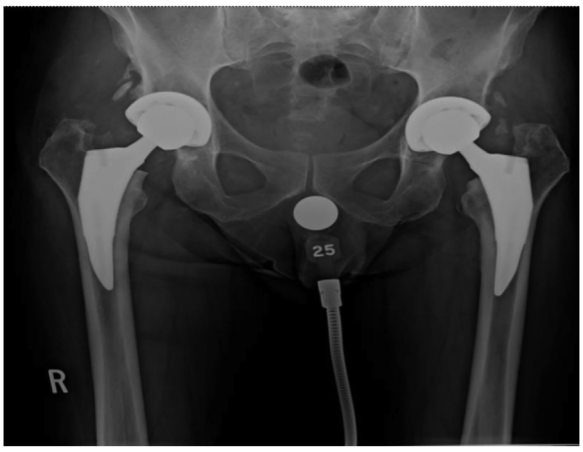

Figure 2. AP radiograph of the patient's pelvis obtained postoperatively displaying the revision ceramic-on-XLPE THA (October 2016). AP, anteroposterior.

(cirrhosis, hepatitis B infection, irritable bowel disease, spondyloarthritis, Hashimoto's thyroiditis, psoriasis) [27] or can occur coincidentally. IgA nephropathy is the most common primary glomerulonephritis that can progress to renal failure and typically follows a waxing and waning course [28]. There is no evidence in the literature suggesting that elevated serum metal ion levels can cause IgA nephropathy. Thus, it is most probable that the patient had primary IgA nephropathy, which consequently hindered renal clearance of metal ions. No significant difference in outcomes has been found between primary and secondary IgA nephropathy [27]. In this case, the presence of IgA nephropathy prevented renal clearance of the metal ions. After the removal of the MoM hip prostheses, metal ion levels decreased significantly (Co: 0.83 μg/L, range: 0.15-0.40 μg/L; Cr: 4.89 μg/L, range: 0.36-0.99 μg/L).

Some investigators have looked at the use of metal ion chelators for the treatment of elevated serum metal ion levels originating from MoM hip prostheses [6,29–32]. Giampreti et al. [29] reported a successful decline in both cobalt and chromium ion levels in 2 patients with MoM hip implants after administrating high-dose oral N-acetyl-cysteine without revising the prostheses. However, Choi et al. [31] used edetate calcium disodium as chelation therapy for 2 patients with elevated serum metal ion levels due to hip implants, and in both cases, the metal ion levels decreased only modestly and the ALTR did not resolve. Whether metal ion chelators can be used to resolve elevated serum metal ion levels resulting from MoM hip implants remains controversial—no consensus has been reached. Both clinical and experimental evidence remains insufficient to support their use as definitive therapy [6,30].

The Articular Surface Replacement (ASR, DePuy Orthopaedics, Inc., Warsaw, IN) Hip Resurfacing System was recalled in 2010. The acetabular cup was less than hemispheric and had a tendency to be implanted with an increased abduction angle, leading to increased edge loading [33]. On intraoperative examination, marked metallosis with tissue staining was observed only in the right hip, which had been implanted with the ASR cup.

Hemodialysis is not considered an option in the management of renal failure in the presence of elevated serum metal ion levels. Cobalt and chromium metal ions are mainly protein-bound, and hemodialysis will not remove them from the circulation [30,34,35]. Therefore, revision of MoM hip implants to nonmetal-bearing material should be a consideration in cases of elevated serum metal ion levels. Neither metal chelating agents nor hemodialysis are definitive treatment options in such cases. The cobalt and chromium levels will continue to elevate as long as renal clearance is impaired.

It is pertinent to closely monitor patients with MoM-bearing surfaces and renal dysfunction, as metal ion concentrations can steadily increase over time, which can lead to systemic complications. At our institution, patients with MoM RHA or THA have their serum metal ion levels measured annually. Additionally, patients undergoing revision surgery due to elevated metal ion levels have them routinely measured to monitor the decline in metal ion levels. Elevated metal ion levels are not always associated with ALTR [36]. In the patient presented in this report, the clicking in the left hip was likely independent of the elevated metal ions. The etiology of hip clicking following THA or RHA is multifactorial, including implant malposition, impingement, and iliopsoas tendon subluxation [37,38]. The conversion of the MoM RHA to ceramic-on-XLPE THA halted the generation of metal ions, thus reducing the ion load requiring renal clearance. While IgA nephropathy can have a waxing and waning course, it may be that the reduction in ion generation and/or a gradual spontaneous improvement in this patient's autoimmune disease led to decreased serum ion levels and improved renal function. Physicians should maintain a high index of suspicion when a patient with a MoM implant presents with renal disease or deterioration in renal function. Once a decline in renal function is noticed, revision surgery becomes a priority over other medical options upon mutual agreement with the consulting nephrologist.

Summary

This case report highlights the elevation of serum metal ions in the presence of IgA nephropathy. It reinforces the importance of monitoring serum metal ion levels in patients with MoM hip arthroplasty and renal dysfunction of any etiology, as ion accumulation can lead to local or systemic complications. Revision surgery was indicated to eliminate the possibility of increased metal ions attributable to the MoM hip implants. Following the conversion to ceramic-on-XLPE THA, the patient's serum metal ion levels returned to normal and renal function stabilized.

Conflicts of interest

The authors declare there are no conflicts of interest.

For full disclosure statements refer to https://doi.org/10.1016/j.artd.2024.101407.

Informed patient consent

The author(s) confirm that written 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).

CRediT authorship contribution statement

Jordan J. Levett: Writing – original draft, Investigation, Formal analysis. **Raheef Alatassi:** Writing – original draft, Formal analysis,

Data curation. **Olga L. Huk:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. **John Antoniou:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Data curation, Conceptualization.

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