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Case Report

Adverse Local Tissue Reaction and Osteolysis After Ceramic-on-Ceramic Total Hip Arthroplasty

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ABSTRACT

Adverse local tissue reaction (ALTR) and osteolysis formation are more frequently described complications after total hip arthroplasty (THA) with metal-on-metal bearings. In this report, we present a unique case of ALTR and osteolysis formation with ceramic-on-ceramic bearing THA, which has been less commonly described in the existing literature. This rare case occurred in a 54-year-old patient who had a primary THA done 17 years prior to representing to our institution. As part of the workup for our patient to find out the underlying cause of his complications, we have carried out extensive investigations that have not been previously reported. We conclude that ceramic bearings in THA may not be entirely inert and may cause complications such as osteolysis and ALTR.

Introduction

Metal-on-metal (MoM) bearings in total hip arthroplasty (THA) were introduced in the first decade of 21st century as an alternative to the conventional metal-on-polyethylene (MoP) bearing due to the presumably better wear rates, improved stability, and greater longevity. However, its use also came with complications such as osteolysis or adverse local tissue reaction (ALTR) [1-3]. Recent interests in targeting complications from these bearing materials have involved the increased use of ceramic-on-ceramic (CoC) bearings for THA, which theoretically are more inert than cobalt-chromium metal bearing and have better wear properties.

ALTR refers to an aseptic granulomatous lesion that develops in the peri-implant region containing inflammatory exudates or necrotic tissue [3,4]. These lesions commonly cause patients abductor damage, discomfort, and pain and contribute to additional osteolysis, implant instability, or loosening subsequently. Despite ALTR being a more common finding in MoM THA [5-9], recently there have been a few reports that described similar findings in THA with CoC bearings [10-12].

To our knowledge, there are only three reports describing similar findings of osteolysis and ALTR within a CoC THA, and no reported cases of such complications resulting in elevated serum aluminum levels [10-12]. Herein this study, we report such a case of CoC THA and present unique findings in our patient's workup to discern the exact origin of these complications.

Case history

The patient is a 54-year-old Chinese gentleman with no known drug allergies or hypersensitivities and a past medical history of hypertension, hyperlipidemia, and central diabetes insipidus who was premorbidly ambulant without walking aids. He had previously undergone unilateral uncemented THA in 2005 for osteoarthritis secondary to seronegative arthritis. The THA was performed through a Hardinge approach and involved a Stryker (Kalamazoo, MI) trident titanium (Ti-6AL-4V) 52 mm acetabular cup, secured with three titanium cancellous bone screws, Stryker (Kalamazoo, MI) trident titanium-backed Al_2O_3 (alumina) insert, 32 mm

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alumina femoral head, and a Stryker (Kalamazoo, MI) accolade Ti-12Mo-6Zr-2Fe (TMZF) stem. His immediate postoperative course was uneventful, and he progressed in his rehabilitation without any complications. Postoperative radiographs revealed that both his acetabular and femoral components were secured in an acceptable position. There were no further clinical events after his index surgery thereafter.

In August 2022 (17 years later), he represented to our tertiary institution with complaints of significant acute mechanical pain coming from his right gluteal region, associated with a sensation of fullness in his right buttock and difficulty ambulating. His left hip was asymptomatic. He denied any preceding infective or constitutional symptoms, trauma or falls, and use of alcohol or steroids. Physical examination showed limitations in right hip range of motion due to pain, while his left hip was able to range pain-free. Blood investigations including a full blood count, electrolyte panel, and inflammatory markers such as erythrocyte sedimentation rate, C-reactive protein test, and serum white blood cell counts were unremarkable. Routine metal ion testing included checking his serum cobalt, chromium, and titanium levels, which were normal at 0.2μg/L, 0.1μg/L, and <1ng/ml, respectively. In view of this, his serum aluminum levels were added on as part of a comprehensive metal ions check, which were found to be elevated at 67μg/L (normal <10μg/L). His pelvic and right hip radiographs done on admission showed multiple areas of radiolucency around his implants in the acetabular region within all three DeLee and Charnley zones [13]. A computed tomography scan of his right hip revealed migration of his acetabular cup with increased periprosthetic lucencies concerning osteolysis. Furthermore, there was a 9.6 × 6.3 × 7.6 cm ALTR extending from his right hip joint into the gluteus medius muscle. A magnetic resonance imaging scan of his right hip with metal reduction protocol confirmed the presence of the ALTR. Figure 1 illustrates our patient's preoperative radiological images.

He subsequently underwent right total hip revision arthroplasty, including a debridement of the ALTR. Intraoperative findings correlated with his preoperative scan findings of an ALTR containing straw-colored fluid extending from the hip joint into the gluteus medius. This, together with the surrounding bone, were sampled for histology, and intraoperative cultures were also taken,

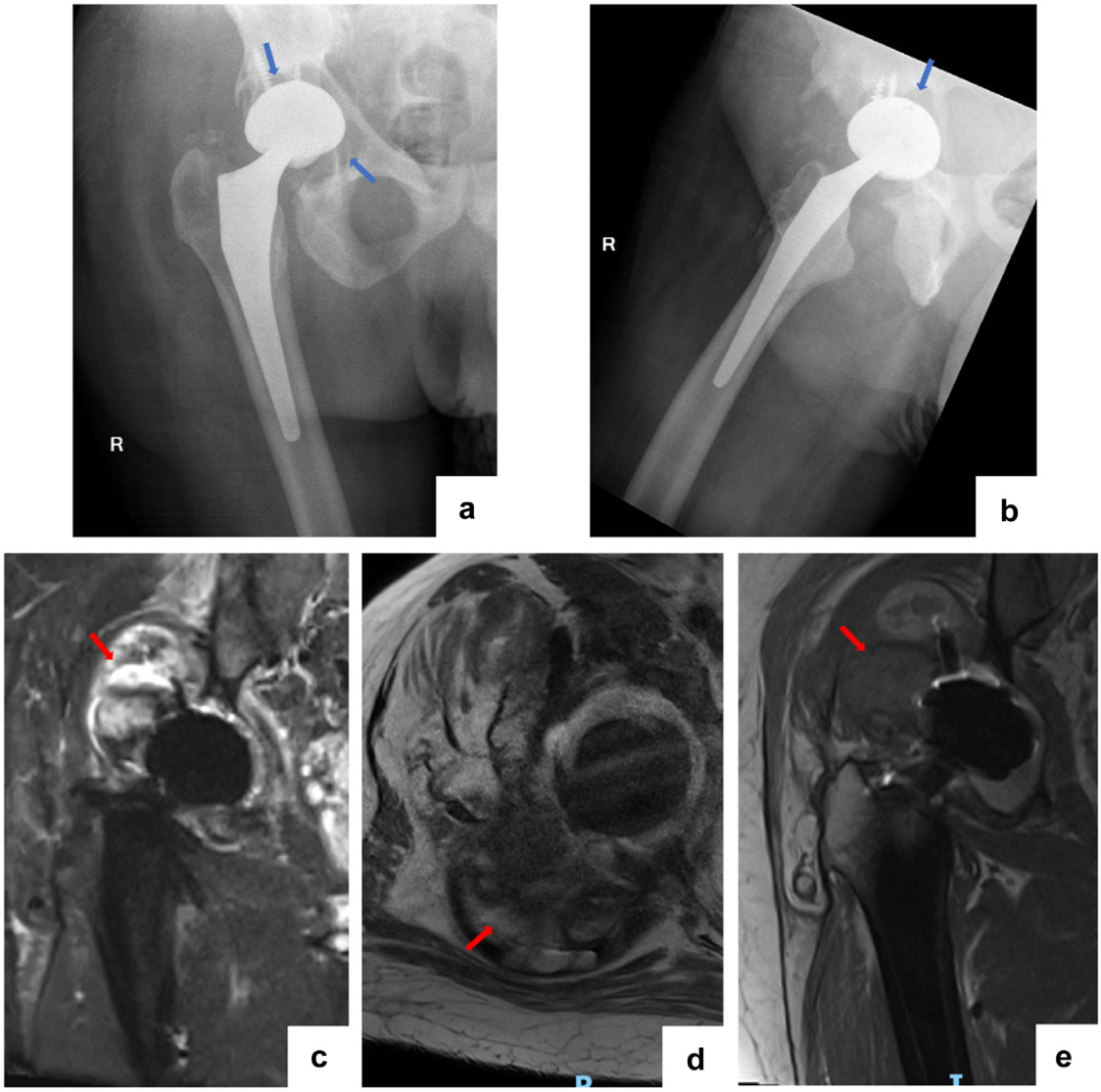

Figure 1. (a-b) Preoperative hip X-ray in orthogonal views showing areas of osteolysis; (c-e) magnetic resonance imaging delineating the soft tissue anatomy of the adverse local tissue reaction (ALTR) in coronal short tau inversion recovery, axial proton density weighted turbo spin echo, and coronal T1-weighted sequences, respectively. Blue arrows represent areas of osteolysis. Red arrows represent areas where the ALTR is visible.

all of which returned negative for infection and malignancy. In terms of his implants, the femoral stem appeared to be stable without evidence of impingement, and the trunnion was intact with no signs of fretting or corrosion. However, the ceramic femoral head demonstrated grossly discernible wear and a roughened surface. The acetabular cup was loose and one of the acetabular cancellous screws that broke was found embedded within the acetabulum. There was no evidence of backside wear on the titanium cup. Joint fluid appeared to be straw colored with no gross metallosis or metal staining as well. After the acetabular cup was removed, there were multiple small cavitary osteolytic lesions found within the acetabular region with Paprosky type 3B acetabular bone defect [14,15]. Figure 2 shows our patient's explanted implants, while Figure 3 illustrates our patient's intraoperative clinical pictures.

After thorough irrigation postremoval of his initial implants, augmented revision THA was performed with a 64 mm trabecular metal acetabular shell (Zimmer Continuum system, Zimmer Biomet, Warsaw, IN), trabecular augment, three posterosuperior acetabular bone screws, 36 mm highly cross-linked polyethylene elevated rim liner, and Stryker (Kalamazoo, MI) V40 36mm metal femoral head with a +10mm offset, which would provide the patient better stability. The decision was made to keep the well-fixed femoral stem to prevent complications such as prolonged operation time, additional blood loss, risk of periprosthetic fracture, and further damage to existing bone stock from the added procedure of revising the femoral stem [Fig. 4]. Limb length and range of motion were tested thereafter, and his revised hip was found to be stable. Our patient's postoperative course was uneventful, where he started progressive weight bearing from postoperative day one.

Histologic examination of the ALTR and surrounding bone revealed fibroadipose tissue with extensive necrosis, inflamed granulation tissue, aggregates of foamy macrophages, and multinucleated giant cells, in keeping with a foreign body giant cell reaction. Foci of refractile nonpolarizable foreign material were observed in association with the multinucleated giant cells [Fig. 5].

Inductively coupled plasma mass spectrometry (ICP-MS) analysis was performed on the intraoperative ALTR and bone samples to detect the levels of metal ions within these tissues. To ensure accuracy, the tissue samples were divided into three and analyzed multiple times by mass spectrometry, eventually giving a mean value. As we did not have available bone samples that were guaranteed to be completely devout of exposure from these metal implants, normal aluminum and titanium levels in our patient could not be ascertained. Since the hip prosthesis system contained minimal amounts of chromium, chromium levels were used as a benchmark comparison instead. Aluminum and titanium levels were found to be substantially elevated at 2.83 ± 1.07 mg/kg and 83.64 ± 8.92 mg/kg—more than 2 and 68 times the tissue level of chromium, respectively. In view of the high relative standard deviation of aluminum, a further ICP paired with optical emission spectrometer analysis was carried out to cross-validate the results of the ICP-MS analysis, which is more sensitive in picking up minute metal ion levels. Aluminum and titanium levels were still found to be high at 20.97 ± 18.07 mg/kg and 75.55 ± 7.60 mg/kg, respectively. Table 1 summarizes our data.

Our patient was last reviewed in the outpatient setting and remained complication-free for more than a year postrevision THA. A repeat serum aluminum level was not reperformed in view of the resolution of his symptoms.

Discussion

Conventional MoP bearing has been the mainstay of THA in the past, popularized previously by success from the Charnley Prosthesis in the early 1970s [16]. Despite being cost-effective and providing a relatively predictable outcome postoperatively [17], polyethylene debris formed from long-term use incited strong inflammatory responses, causing periprosthetic osteolysis [18-20]. MoM THA prostheses were popularized as an alternative, where being an estimated 60 times stronger than conventional MoP bearings could be manufactured as a larger diameter due to their strength, increasing joint stability, and decreasing risk of implant dislocations [21,22]. However, although no formal studies have been done on it to our knowledge, these prostheses formed potentially carcinogenic particles due to increased serum cobalt and chromium levels [23]. This was of particular concern as younger patients tended to receive MoM THA due to its lower wear characteristics, leading to prolonged exposure to raised serum metal ions across their lifetime. In addition, metal ions commonly generated from MoM bearings THA resulted in ALTR, leading to further complications [24-27]. Highly cross-linked polyethylene

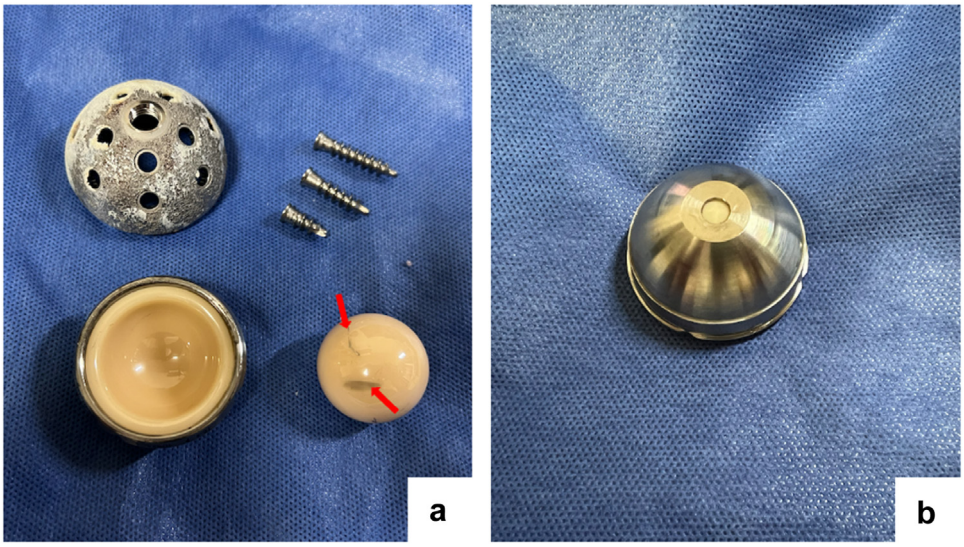

Figure 2. (a-b) Clinical photograph of implants removed from patient, illustrating wear over femoral head but intact acetabular components. Red arrows represent areas of wear along the ceramic head.

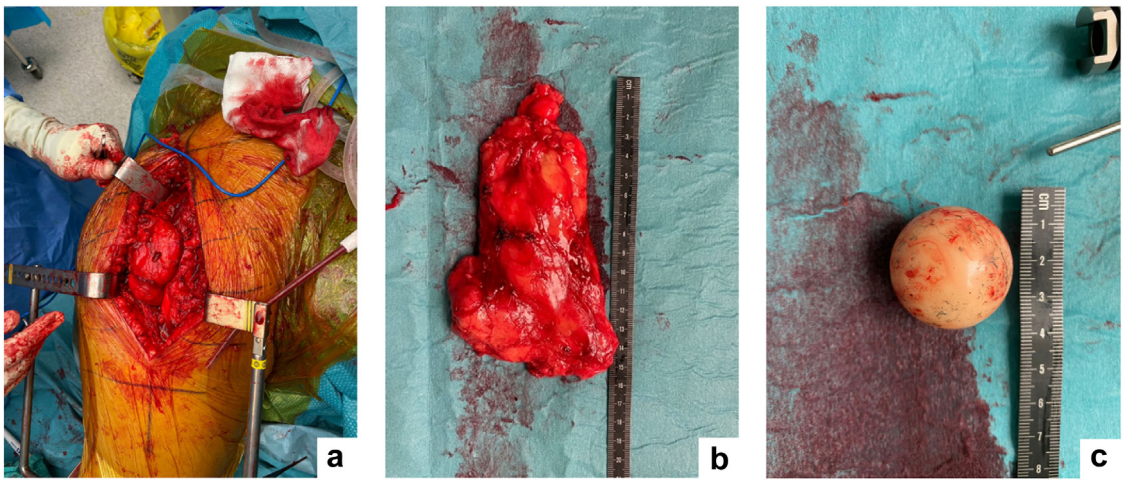

Figure 3. (a) Intraoperative clinical picture of the adverse local tissue reaction (ALTR) grossly visible; (b) clinical picture of the ALTR excised; (c) clinical picture of the femoral head removed, illustrating wear pattern across its surface.

served as a viable alternative to the issues arising from using conventional polyethylene, where cross-linking of the material was supposedly able to reduce abrasive wear and increase its strength, leading to a reduction in particles being formed that caused osteolysis [28,29]. However, despite a dramatic reduction in the incidence of osteolysis and wear-related revision surgery, multiple cases of such complications are still reported in the literature [30].

Another alternative bearing used in THA is ceramic, which consists of mainly alumina and was first developed by Pierre Boutin in 1970. It was theorized to be more chemically inert to circumvent and prevent the issue of periprosthetic osteolysis as it does not incite as great an inflammatory reaction compared to polyethylene or metal particles [31]. In addition, it has been shown to have an even higher level of hardness, scratch resistance, and greater lubrication, which reduces friction and wear between the bearing surfaces, making it an excellent choice in younger and more active patients [31,32]. Despite these theoretical advantages, rare cases of ALTR from CoC THA have been reported [10-12], raising the notion that ceramic debris may not be as chemically inert as what was initially theorized. To our knowledge, there have only been three cases reporting this phenomenon thus far [10-12]. However, none of the previous reports have thoroughly investigated the serum metal ions and performed mass spectrometry on the intraoperative tissue samples. By methods of exclusion, ALTR was attributed to ceramic debris in these reports.

In our workup to analyze the cause of ALTR and osteolysis, we found a discrepancy between intraoperative tissue and serum metal ion levels. In our study, serum aluminum levels were found to be six times above normal limits, while serum titanium was normal despite both titanium and aluminum ions being high on mass spectrometry in the intraoperative tissue sample. Despite a study carried out by Swiatkowska et al. revealing that a mean plasma titanium level of 2.5 mcg/L was indicative of a well-functioning hip at 8.5-year follow-up, our results question the

Figure 4. (a-b) Postoperative hip X-ray in orthogonal views.

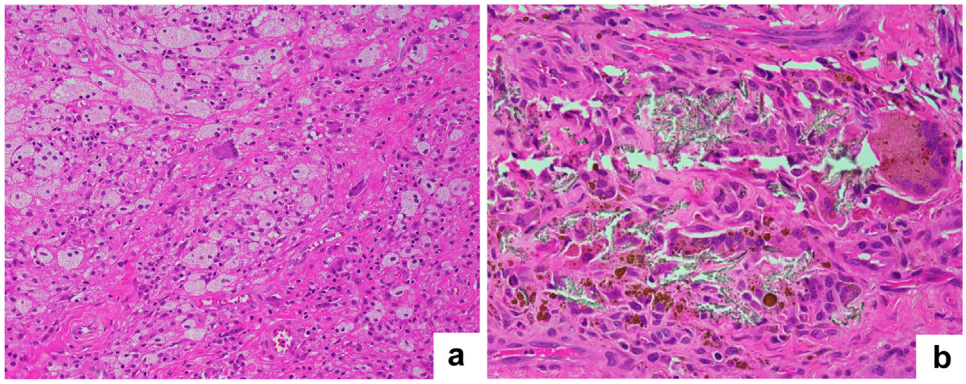

Figure 5. (a) Histologic sections from the peri-implant tissue show aggregates of foamy macrophages and multinucleated giant cells; (b) focally associated with deposits of refractile, nonpolarizable foreign material.

validity of serum metal ion levels in the workup of these patients given that serum metal ion levels may not accurately reflect metal ion levels within the hip joint [33]. There is a lack of literature about the role of serum aluminum level and its implications in a patient with a THA. Further studies with longer follow-up are needed to assess the impact of elevated aluminum ion in patients with CoC THA.

As both aluminum and titanium were elevated in the peri-implant tissue, it is difficult to pinpoint which metal ion (or both) was the cause of our patient's complications post-THA. In our patient, histology revealed a predominantly histiocytic reaction, characteristic of foreign body giant cell reaction, and deposits of refractile, nonpolarizable foreign material, which could represent extruded metal elements from the worn implants (metallosis). In terms of the responses incited by titanium, the current literature presents a mixed view on the histology. Previous studies have reported a predominantly lymphocytic infiltration as a result of titanium debris from the neck and trunnion in CoC THA from impingement, which was not seen in this study [11,34-38]. However, other studies have described a similar foreign body giant cell reaction as our case, which may be histiocyte or lymphocyte-rich, in response to alumina, titanium in both CoC and MoP THAs [39]. In our case, we cannot rule out the possibility of local synergistic adverse effects of both aluminum and titanium metal debris on local tissue resulting in ALTR.

Table 1
Inductively coupled plasma mass spectrometry (ICP-MS) and optical emission spectrometer (OES) results.

Elements	ICP-MS concentration (mg/kg)	ICP-OES concentration (mg/kg)
^{23} Na	10604.70 ± 279.14	-
^{24} Mg	293.56 ± 58.96	-
^{27} Al	2.83 ± 1.07	20.97 ± 18.07
^{39} K	117.68 ± 7.17	-
^{43} Ca	2334.47 ± 957.59	-
^{47} Ti	83.64 ± 8.92	75.55 ± 7.69
^{52} Cr	1.22 ± 0.07	-
^{55} Mn	0.56 ± 0.06	-
^{56} Fe	4123.56 ± 518.96	-
^{59} Co	0.02 ± 0.00	-
^{60} Ni	0.94 ± 0.07	-
^{65} Cu	3.38 ± 0.15	-
^{66} Zn	37.66 ± 1.24	-
^{75} As	0.01 ± 0.00	-
^{78} Se	0.88 ± 0.04	-
^{111} Cd	0.12 ± 0.02	-
^{201} Hg	0.16 ± 0.02	-
^{208} Pb	0.36 ± 0.03	-

The analysis of metal ions in tissues involves a highly complex process, ranging from the collection of tissue or serum samples to the analysis and reporting of these results. In our study, the high standard deviation of the aluminum ions compared to titanium ions is postulated to be due to the inconsistent distribution of aluminum in different parts of the peri-implant tissue, most probably higher in the immediate vicinity of the rough ceramic surface of the femoral head, which was likely scratched from the dislodged acetabular cup and broken cancellous screw. In our study, serum aluminum levels were found to be high, while serum titanium was normal despite elevations of both metal ions in the intraoperative tissue sample. A study carried out by Savarino et al. in 2008 investigating if serum levels of metal ions differ between alternative-bearing THAs postulated that using serum metal ion levels to correlate with local peri-implant metal ion levels are difficult due to the lack of free exchange between synovial fluid and blood [40]. This likely accounts for the discrepancy in our serum and peri-implant samples. The high levels of titanium in the peri-implant tissue could be due to wear between the titanium acetabular cup and its titanium back insert and from the broken cancellous screw.

In terms of implants, our patient received an early generation Stryker (Kalamazoo, MI) Tritanium primary acetabular component. A recent study published by Bingham et al. revealed that 30% of radiographic loosening was found surrounding the acetabular implant, while screw augmentation prevented loosening [41]. In that study, the follow-up period was a minimum of 1 year with a maximum follow-up period of up to 4 years. While the poor track record of ingrowth in the acetabular component that our patient received could account for his clinical presentation, we feel that the aforementioned study is not applicable to our patient as he had screw augmentation done during his index surgery, which was shown to be protective in the study carried out by Bingham et al [41]. In addition, radiographs done post-index hip replacement surgery showed no radiolucency, migration and demonstrated good ingrowth, and clinically, our patient was well and returned to his premorbid function, where he only represented with symptoms 17 years later, where wear of the bearing surface is more likely. Hence, bearing surface wear is more likely to account for his symptoms than the poor ingrowth. In a similar vein, there are multiple reports of the Stryker (Kalamazoo, MI) Accolade (TMZF) stem causing issues such as trunnionosis and secondary failure thereafter [42,43]. We recognize that the presence of a combination of elements picked up on serum and metal ion testing could also mean that the source of failure could be from the trunnion or stem

initially leading to secondary ceramic wear. However, given that the patient's stem and trunnion were grossly intact, coupled with the obviously worn-out ceramic bearing surfaces, it is likely that these complications arose from the ceramic bearing surfaces instead.

This is the first case report detailing peri-implant osteolysis and ALTR in a CoC-bearing THA coupled with more extensive investigation into peri-implant tissue and serum metal ion levels using mass spectrometry. The significantly elevated levels of both aluminum and titanium, in addition to the histologic findings of foreign body giant cell reaction and deposition of refractile, nonpolarizable material in the peri-implant tissue, strongly suggest their contributory role in osteolysis and ALTR. On hindsight, we recognize a preoperative aspiration would have been helpful in determining synovial metal ion levels and given a more accurate assessment of local tissue metal ion levels. However, despite undergoing attempted hip aspiration with radiological guidance, there was insufficient fluid that could be aspirated for investigations in our case.

Summary

Peri-implant osteolysis and ALTR are more commonly found in MoP or MoM THA. A rare case of ALTR is reported here in a CoC THA with wear observed in the ceramic femoral head, where high local levels of aluminum and titanium were found contributing to it. The CoC bearing used in THA may not be as chemically inert as previously thought. This case also illustrates how serum metal ion levels may not correlate with local peri-implant ion levels. The value of serum metal ion analysis and correlation with peri-implant tissue and synovial fluid levels may benefit from larger cohort studies.

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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

Yogen Thever: Writing – original draft, Investigation, Formal analysis, Conceptualization. **Lynne Goh:** Writing – review & editing, Investigation. **Sam Fong Yau Li:** Writing – review & editing, Investigation. **Dahlia Ho Siu Ling:** Writing – review & editing, Investigation. **Sean Yi Rong Chia:** Writing – review & editing, Investigation. **Moo Ing How:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Conceptualization.

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.2024.101584.

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