



Infected Pseudotumor Induced by a Metal-on-Metal Total Hip Arthroplasty with a Misleading Presentation and Fatal Outcome: A Case Report and Review of the Literature and Guideline Management

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Abstract

Introduction: Adverse reaction to metal debris (ARMD) includes metallosis, aseptic lymphocytic vasculitis-associated lesion (ALVAL), and pseudotumors. ARMD is rare and has many clinical presentations that can be confusing. We report a case of an undiagnosed patient and discuss how this could be avoided.

Case presentation: A 75-year-old Caucasian male with a metal-on-metal (MoM) total hip arthroplasty (THA) of the right hip and a history of prostatic adenocarcinoma, right lower limb giant lymphedema, and homolateral deep venous thrombosis (DVT). Both lymphedema and DVT were attributed to his cancer.

In 2021, the patient presented with a misleading diagnosis of infected spondylodiscitis, which was later corrected to acute peri-prosthetic joint infection (PJI). Scans revealed a massive infected pelvic cyst. After reviewing the patient's old scans, we concluded that the cyst was a pseudotumor that had been present since 2019 but was neglected. The pseudotumor was compressing the iliac vein, which explains the DVT and the lymphedema, falsely attributed to his cancer. The patient underwent a two-stage revision. Pathology and cobalt levels confirmed the diagnosis of an infected metal-induced pseudotumor. At one month, the patient had a good outcome with significant shrinking of the lymphedema. Unfortunately, he died two days later, and no cause was found.

Conclusion: ARMD is the cause of 0.6% of THA failures and the most frequent cause of MoM THA failure. The main reasons for revisions related to ARMD are ALVAL and pseudotumor. Patients with MoM THA are at higher risk of developing PJI.

There are clear guidelines for monitoring these patients. We must pay closer attention to this specific and misleading complication.

Keywords: ARMD (Adverse Reaction to Metal Debris); Pseudotumor; ALVAL (Atypical Lymphocytic Vasculitis Associated Lesion); Arthroplasty; PJI (Periprosthetic Joint Infection); case report

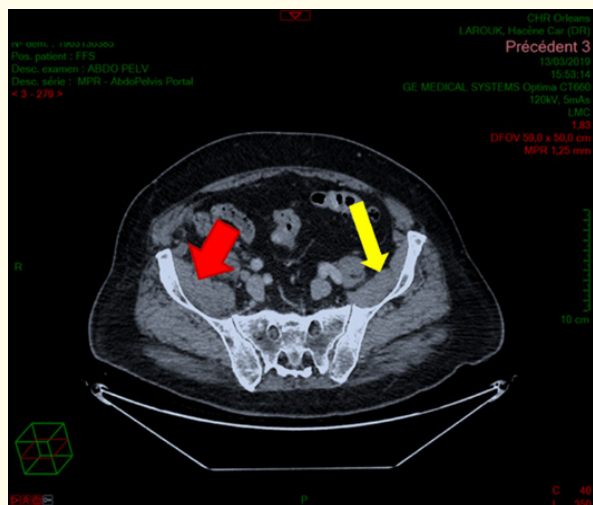


Figure 3: CT Scan from 2019 highlighting bursitis of the right ilio-psoas tract (red arrow) compared to the normal ilio-psoas tract in the left side (yellow arrow).

The patient had a medical history of hypertension, diabetes mellitus, dyslipidemia, and paroxysmal supraventricular tachycardia treated with rivaroxaban.

He was also diagnosed with prostatic adenocarcinoma in 2015, treated with radiotherapy, chemotherapy, and hormonal therapy, and was considered in remission.

In 2018, the patient presented with deep venous thrombosis (DVT) involving the iliac, femoral, and popliteal veins, associated with pulmonary embolism, treated with anti-Xa inhibitor (rivaroxaban).

Since the DVT, the patient progressively developed a massive lymphedema of the entire right lower limb.

Both the DVT and lymphedema were initially attributed to his prostate cancer and its treatment.

It is important to note that the radiologists and physician fortuitously detected psoas muscle bursitis on a CT scan performed in 2019 during cancer surveillance. However, neither the treating physician nor the radiologist raised concerns about this finding.

Recent medical issue

In February 2023, the patient developed erysipelas of the right lower limb superimposed on his preexisting lymphedema, accompanied by acute pain in the right gluteal region radiating to the posterior thigh and leg, resulting in complete functional impairment. The patient also presented with fever, prompting admission to the rheumatology department for further evaluation.

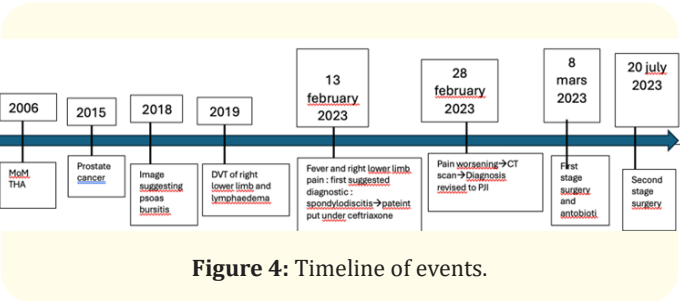
Two sets of blood cultures were obtained and revealed *Streptococcus agalactiae* bacteremia. Serum laboratory tests demonstrated significantly elevated inflammatory markers, with a C-reactive protein (CRP) level of 301.2 mg/L and an erythrocyte sedimentation rate (ESR) of 59 mm/h. A spine MRI was subsequently performed, revealing lesions suggestive of spondylodiscitis.

The patient was then initially placed on ceftriaxone for one week, however, due to progressively worsening right hip pain, a contrast-enhanced pelvic CT scan in the portal venous phase (using iodinated contrast medium, 90 mL of IOMERON 350 mg/mL) was performed days later. This demonstrated a massive iliopsoas muscle collection measuring 17.5×12 cm in the transverse plane and extending 22 cm in length. The collection featured thick walls, multiloculated morphology, and contained gas locules - findings highly suggestive of an infectious process.

Cobalt serum levels were measured and revealed elevated blood cobalt levels ($6.23 \mu\text{g/L}$) (normal value $< 0.45 \mu\text{g/L}$).

After multidisciplinary review and based on the modified Musculoskeletal Infection Society (MSIS) criteria and International Consensus Meeting (ICM) on Musculoskeletal Infection guidelines [6], the diagnosis was revised to periprosthetic joint infection (PJI) with an infected, metal debris-induced pseudotumor of the iliopsoas muscle.

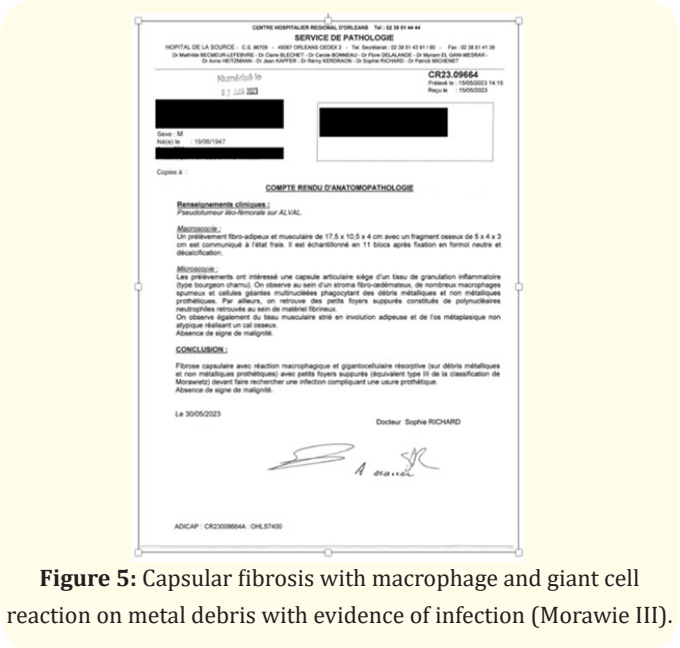
The diagnosis of spondylodiscitis was ultimately excluded based on MRI reassessment by a musculoskeletal radiologist and the convergence of clinical and paraclinical findings. The initially seen lesions on spine MRI were ultimately consistent with arthritic spinal changes.



Surgical management and progression

The patient underwent a two-stage revision of his THA. During the first stage, we performed prosthesis removal with multiple bacteriological samples, followed by placement of a Palacos cement spacer one week after symptom onset. Intraoperative cultures grew *Streptococcus agalactiae*, and the patient received a 3-month course of antibiotic therapy (amoxicillin).

Pathological examination confirmed the diagnosis of metal-induced pseudotumor, demonstrating fibrinous exudate, macrophage infiltration with metal debris deposition, and multiple suppurative foci confirming infection also (Figure 5).



The surgical wound completely healed with no signs of inflammation in two weeks.

After 3 months of antibiotic therapy leukocyte count was 4,700 G/L and CRP level was 5.8 mg/L.

Pelvic imaging revealed significant reduction in pseudotumor size (Figure 6).



The patient subsequently underwent the second-stage revision, receiving a THA with a 59-mm Smith and Nephew acetabular reinforcement device and a cemented 53-mm dual mobility Capitole-Evolutis acetabular component with a 28-mm metal head on polyethylene cup and non-cemented femoral stem Evolutis Stemsys size 12 (Figure 7).

Perioperative biological lab cultures grew *Staphylococcus capitis* and *Staphylococcus epidermidis*, prompting treatment with rifampicin and doxycycline.

At 29 days postoperatively, the patient showed excellent outcomes with no inflammatory signs at surgical sites, Leukocyte count was 3,900 G/L and CRP level at 27.7 mg/L Unfortunately, the patient died two days later. The cause of death could not be determined as the family declined autopsy.

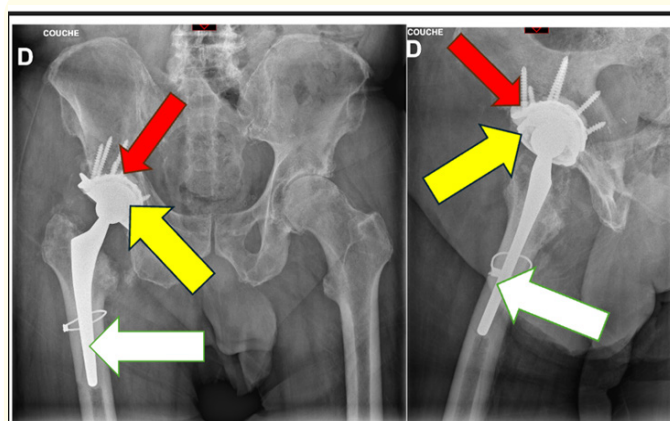


Figure 7: Radiographsshowing post op aspect after second stage revision with a 59-mm smith and nephew acetabular reinforcement device (red arrow) with a cemented 53-mm dual mobility Capitole Evolutis acetabular component with a 28-mm metal head on polyethylene cup (Yellow arrow) and non-cemented femoral stem Evolutis stemsys size 12 (White arrow).

Discussion

Our patient presented with a rare but well-described complication of MoM arthroplasty and his dramatic evolution prompted us to review and critically evaluate his entire medical monitoring.

Metal-on-metal (MoM) total hip arthroplasty had been introduced by Wiles in 1958, then by McKee, Chen and Farrar in the 1960s. Initially, it was abandoned due to high failure rates but was reintroduced in the 1980s with second-generation MoM thanks to considerable advances in metallurgy, tribology and biomechanics to address complications and loosening seen in metal-on-polyethylene THA [7].

We can distinguish MoM Protheses with small heads and standard heads (28 and 32 mm respectively) from prostheses with large heads (36 mm and larger).

Small head prostheses can also be divided in two groups: High-carbon heads and low-carbon heads.

Low-carbon heads are made of an alloy composed of 0,05% of carbon while high carbon heads are made of an alloy of 0,2% of carbon [8]. It seems that heads with a high concentration of carbon present less loosening [9].

Multiple risk factors have been identified in ARMD. Female patients, age over 40 years, large femoral head prostheses (>36 mm), cup inclination over 50° and high acetabular cup anteversion appear to be risk factors of developing ARMD [9,10], but not metal hypersensitivity [11].

It is important to note that the presence of metal debris around the articular region in MoM THA, particularly with DUROM cups, results from corrosion causing metal wear at the head-neck junction of a total hip implant in addition to metal loss from bearing surfaces [12].

There are many possible clinical presentations due to the presence of metal wear in the periarticular region in metal-on-metal (MoM) prostheses. These presentations can range from simple metallosis or Aseptic Lymphocyte-dominated Vasculitis-Associated Lesion (ALVAL) to the final stage of this disease, which is pseudotumor [2].

All these presentations were subsumed under the designation adverse reaction to metal debris (ARMD) introduced by Jameson, which covers all failures due to metal wear, associating pain, sterile effusion, and the presence of macroscopic metallosis or necrosis [2]. ARMD is the source of 0.6% of failures in THA [2].

It represents a local immune reaction caused by chromium and cobalt debris release in the articulation but it's also caused by the direct toxicity of metal ions[13].

These metal ions are small enough to be disseminated throughout the body [Effort] or Involve a type IV lymphocyte-mediated hypersensitivity reaction [2] and more specifically CD4+ T cells, while a non-specific immune reaction to other debris is mediated by macrophages and giant cells [14-16].

It's also important to know that patients with metal ions in the periarticular region and blood will not necessarily develop ARMD as there are many other factors such as genetics and age that play a significant role in metal hypersensitivity [14].

Pathological findings characteristic of ALVAL and pseudotumor include vasculitis, perivascular and intramural capillary lymphocyte infiltration with endothelial swelling, localized hemorrhage, and necrosis [14]. These findings were observed in our case, confirming the diagnosis of metal debris-induced pseudotumor.

In a retrospective study, Gröbl, *et al.* reported a 98.6% survivorship rate for MoM THA at 10 years [17]. A prospective study of 99 MoM THAs by Neumann found 10-year survivorship rates of 98% for the stem and 96% for the acetabular cup [7].

Another study by Yoshitoshi nuances all these findings, reporting that radiographic osteolysis rates are significantly higher in MoM bearing surfaces compared to ceramic on ceramic at 10-years follow-up but without more revisions [18]. However, this study should lead us to consider the consequences of this osteolysis on long-term prosthesis survivorship beyond 10 years.

A more recent study by Holappa reports a survivorship of 89,6% at 10 years and 82,9% at 14 years with a revision rate of 13,4% and 55,9% these revisions were for ARMD while ARMD prevalence was 12,4% [19].

Varnum, referring to the Nordic Arthroplasty Register Association, reports a higher revision rate for MoM prostheses compared to polyethylene on metal prostheses [20]. Moreover, studies based on the Australian Arthroplasty register and the British Arthroplasty register have made the same observation [21,22].

In a systematic review, Drummond reports that about one in five MoM prostheses will need a revision surgery at 10 or 13 years,

especially for large-head prostheses (>36mm) [23]. Palazzulo finds that the most frequent cause of failure in MoM THA is ARMD with a frequency of 59% at 13-year follow up [24].

In a meta-analysis, Wiley reports that ARMD incidence is about 6.5% for all types of MoM prostheses [4]. The main reasons for hip prosthesis revision related to ARMD are ALVAL and pseudotumor. These two complications are often misdiagnosed. The primary differential diagnosis is prosthetic joint infection (PJI) [4].

In another study, Lainiala reports that the survivorship of revisions for MoM THA was 69% [25].

Finally, it's important to remember that French National Agency of Drugs and Medical Products Safety (ANSM), although it has not formally forbidden the use of MoM THA, insists on the fact that the benefits/risk balance remains negative [8] and a close monitoring of these prostheses is mandatory.

Biological monitoring in MoM prostheses is done by serum dosage of chromium and cobalt. We consider that cobalt blood level is high when it's superior to 7µg/L but a cobalt serum level between 2µg/L and 7µg/L in symptomatic patients is an indication to push investigations and have regular monitoring [26].

Regarding imaging, X-rays are the first test to do in symptomatic patients but they are not an effective method for the detection of ARMD.

Ultrasound is a useful test with a sensitivity of approximately 100% and a specificity of 96% [11]. MRI with artefacts treatment (MARS) is an excellent exam with a sensibility of 92% and a specificity of 100% [11].

Clear guidelines were published in 2014 for the monitoring of a patient with MoM THA [26]: (Figure 8,9).

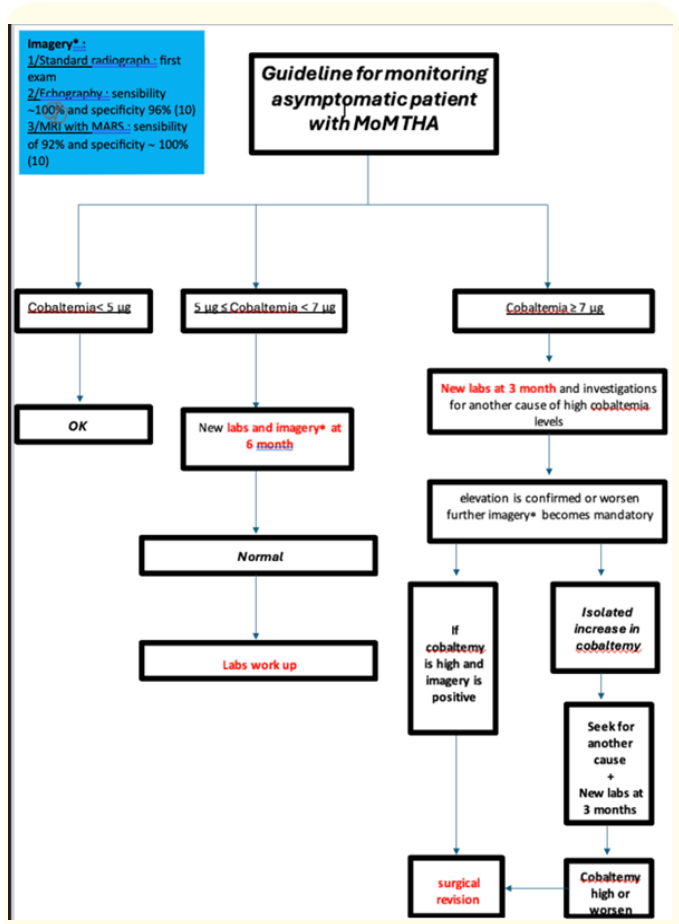


Figure 8: Guideline of monitoring asymptomatic patient with MoM THA.

For MoM THA with small femoral heads, a conventional clinical and radiologic follow-up is recommended with no serum dosage of cobalt levels regardless of whether it is done with high or low carbon content devices.

For MoM THA with large heads, an annual clinical and radiographic follow-up is mandatory along with the theoretical survivorship of the implant with the obligation to convene the patients. A unique dosage of cobalt blood level can be done at the third year after surgery and must be renewed every three years.

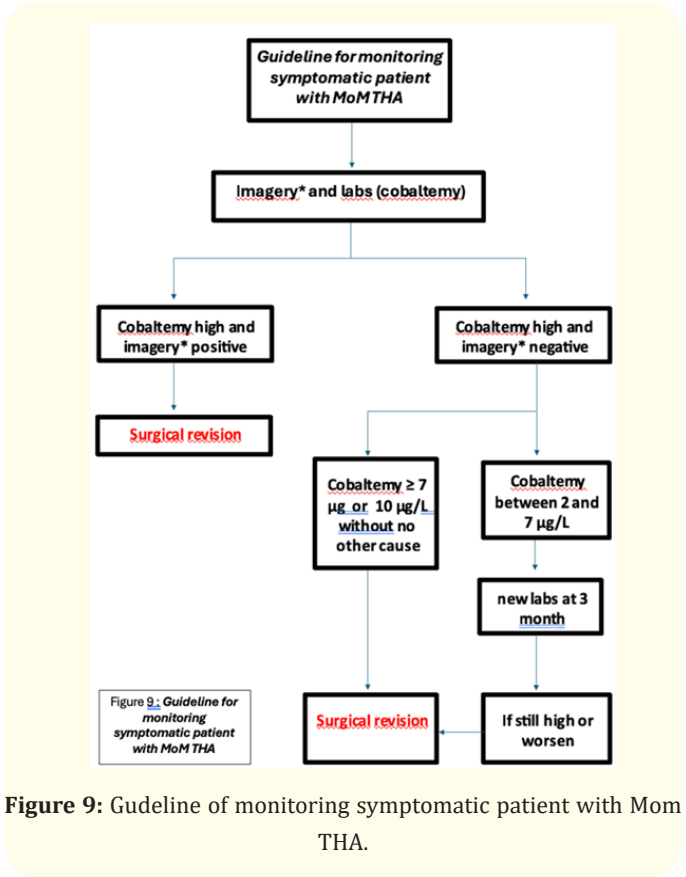


Figure 9: Guideline of monitoring symptomatic patient with MoM THA.

In case of an asymptomatic patient, we can find one of the following scenarios:

- If the cobalt blood level is high, we must see the patient at three months and do a new blood dosage and search for other causes of this elevation (renal failure, existence of other metallic medical implants). If the high level is confirmed or higher, other exams must be done (ultrasound, CT scan or MARS MRI).
- If the cobalt serum level is high and further exams (imaging) are positive, revision surgery is indicated.
- If the cobalt high level is isolated: we must search for another etiology and do the dosage again at three months.

- If the cobalt concentration remains high or elevated between two measurements, revision surgery must be discussed especially when cobalt blood level is greater than 10 µg/L with no evidence of other cause and after considering benefits/risk balance.
- If cobalt concentration is between 5 and 7 µg/L it's recommended to renew the blood dosage and imagery at six months. If imagery is normal and blood concentration is still the same, an annual biological monitoring is recommended.
- If the patient is symptomatic:
- It's mandatory to push investigations and do imagery exams (X-rays, ultrasound, CT scan or MARS MRI) and cobalt blood level dosage.
- If the cobalt blood level is high and the complementary exams are positive, the patient should formally have a revision surgery after evaluation of the benefits/risk balance.
- If the cobalt serum level is high but the complementary exams are negative:
 - If the level is higher than 7 or 10 µg/L with no explanation of this elevation, revision surgery indication must be retained after evaluation of the benefits/risk balance.
 - If the cobalt blood level is between 2 and 7 µg/L, a new dosage must be done at three months, and if it remains the same or higher, a revision surgery must be planned.

Concerning systemic effects of metal debris, multiple secondary effects have been reported as renal failure [27], cardiac dysfunction and central neurologic disturbances such as tremor and cognitive disorders, and peripheral neurologic disorders such as deafness and optic neuropathy with visual disturbance [28].

There is no evidence currently of any established *in vivo* clear link between the presence of metal debris and the emergence

of cancer or fetal malformation, even if there is no doubt about cytotoxic, genotoxic and mutagenic effects of metal ions *in vitro*. However, even though those studies are comforting, we must be careful because of the very known latency of some cancers, especially because of the fact that these implants are generally put in young patients because of their high activity level [29].

We have found in literature some cases of patients presenting pelvic localization of metal-induced pseudotumor. Abdul reports a case of pelvic localization and abdominal symptomatology that have needed a revision surgery [30]. Filho reports another case of pelvic localization with urinary symptomatology that also needed revision surgery [31]. Mak also reports a case of metal-induced pseudotumor with pelvic localization [32]. DeFang reports a case of a persistent lymphedema of the lower limb secondary to cystic mass compressing the femoral vein; this cystic mass was due to polyethylene debris [33].

It's important to remember that our patient himself had a chronic lymphedema of the whole lower limb that had been initially put down to his radiotherapy for prostatic adenocarcinoma, and this lymphedema regressed after surgery. After reviewing old CT scans of our patient with radiologists specialized in osteoarticular imagery, we can confirm that the pseudotumor was compressing the iliac vein and the lymphatic vessels, explaining the history of thrombosis and chronic lymphedema. (Figure 10).

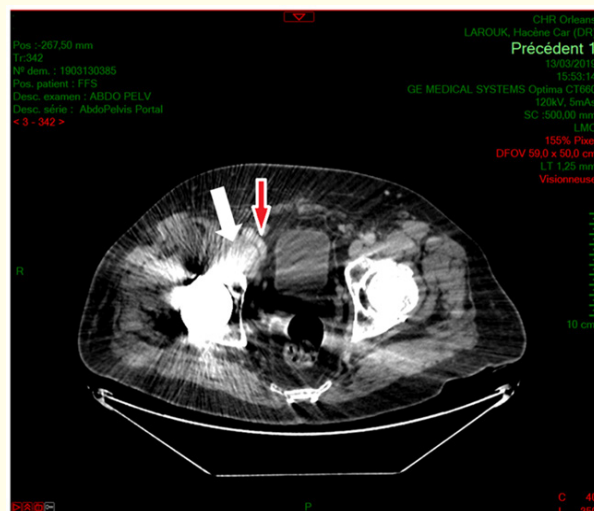


Figure 10: Axial CT scan done 2019 showing the compression of the iliac vein (Red arrow) by the Pseudotumor (White arrow) abutting the Prothesis.

It has been reported that patients with MoM prostheses are at a greater risk of periprosthetic joint infection (PJI) than patients with other bearing surfaces prostheses [5,34].

Huang, in his study on the Australian register, found a higher rate of revision due to PJI in patients with MoM THA (36.9%) at seven years compared to those with other bearing surfaces prosthesis (2%). He also reported that this risk is higher in the first two years following the surgery [5].

Leal him reports a higher rate of PJI in patients with pseudotumors compared to patients with MoM hip arthroplasty but without pseudotumors [35]. Judd and Noiseux found that, besides a higher risk of PJI, there is a significant prevalence of atypical germs in this population [36]. Anwar showed that chromium and cobalt particles are not toxic for bacteria and rather accelerate their development *in vitro* [37].

This susceptibility to infections is probably due to the fact that the released debris lead to an excessive macrophage activation and production of oxygen derivatives causing local defense depletion and damage in adjacent tissues. In addition, cytokine cascade will perpetuate the inflammatory phenomena which will have as a result a local inflammatory zone with compromised immune defense and so a higher risk of infection [38].

In our case we followed the modified MSIS and ICM criteria for the diagnosis of PJI [6].

Concerning the patient death, it's well known that patients undergoing THA revision for infection experience a significant excess risk of death during the first year of surgery that persists several years after [39].

This death is due to the elevated rate of medical complication following revisions surgery for PJI that can reach 15,3% generally and even 22,4% in elderly patients during the six months after the surgery [40].

Zmistowski identified advanced age, higher Charlson Comorbidity Index, history of stroke, polymicrobial infections, and cardiac disease, as risk factors of death after revision for PJI [41], and it's important to remember that our patient was 75 years old, had history of paroxysmal supraventricular tachycardia and hypertension.

In his study, Lainiala reports a complication rate of 11% in revision surgery for ARMD among hip arthroplasty, and if we look for non mechanical complications, we find that the three first complications are DVT, pulmonary embolism and bowel occlusion [42].

Main causes of death after arthroplasty are pulmonary embolism, cerebrovascular event, pulmonary compromise, acute myocardial infarction, cardiac complications and finally pneumonia and sepsis [43].

Our patient already had a history of pulmonary embolism and could have a recurrence which can explain the death.

He also had a history of paroxysmal supraventricular tachycardia, diabetes mellitus and dyslipidemia, which can be the cause of a cerebrovascular event or a cardiac complication.

Metal debris is known to have cardiac toxicity, and this could be an aggravating factor specially concerning his well-known cardiac disease. Moreover, it's well known that cobalt induced cardiomyopathy can persist and even worsen after revision surgery [28]. However preoperative cardiac evaluation didn't reveal any cardiomyopathy and the transthoracic echocardiogram was normal, so we think that accepting a possible acute cardiac event related to his paroxysmal supraventricular tachycardia or a myocardial infarction especially in our patient medical background of diabetes and dyslipidemia aggravated by surgical stress, the possibility of death related to cardiac cobalt toxicity seems unlikely.

Sepsis and pneumonia also don't seem to be a cause of death for us as well as the patient was medically stable 2 days before death, there was no signs of wound inflammation and labs showed no alarming values (3,900 G/L and CRP at 27.7 mg/L)

Finally, patients with MoM prostheses seem to have higher risk of haematopoietic cancers, and this could also be a possible cause of death for our patient, but regarding the fact we have only one complete blood count at the last follow up we cannot neither confirm or deny this hypothesis [44].

Conclusion

MoM THA are currently less used, but we still see them especially in cases of revision for simple loosening or in more serious and specific complications related to metal debris or infections. These complications can have multiple and intertwined manifestations and are sometimes difficult to differentiate.

It is crucial to maintain a high index of awareness in front of patients with MoM THA and follow the existing guidelines of learned societies.

Clinical Message

- ARMD can have misleading presentations.
- Metal-on-metal total hip arthroplasty follow-up is well codified.
- Hip arthroplasty surgeons must know these guidelines well.

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