

Review Article

Clinical consequences of pseudotumors in hip arthroplasty

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The occurrence of pseudotumors currently constitutes an important topic of interest among orthopaedic surgeons who prefer metal on metal arthroplasty and especially hip resurfacing arthroplasty. Adverse reactions to metal ions are associated with the formation of such lesions and the orientation of implants has also been implicated in their pathogenesis. The diagnosis of pseudotumors is as difficult as complex. There is a variety of symptoms and patients with mild or tolerable pain may not seek medical attention. Revision surgeries may be the only solution in some cases. The goal of this article is to review the clinical presentation, prognosis of pseudotumors and associated complications, based on evidence published in the literature.

Keywords: Total hip arthroplasty, Metal-on-metal, Pseudotumor, Hip revision, Metal ions

Introduction

Joint arthroplasty has increased over the last decades as an effective treatment option for hip and knee osteoarthritis. Significant evolution in techniques and materials offer a better quality of life and long-lasting improvement in well-selected patients.

Metal on metal (MoM) hip arthroplasty and especially resurfacing arthroplasty has gained a wide interest and the main reason is the increased head-neck implant ratio which provides an increased range of motion and decreased femoral neck impingement and dislocation rate^{1,2}. Despite the fact that many surgeons tend to use implants like ceramic heads and High-density crosslinked polyethylene, the MoM articulation remains still appreciable.

Adverse effects can be seen to all types MoM arthroplasties, including Total Hip Arthroplasty (THA) with small (<36 mm) or large (≥36 mm) head diameter and Resurfacing Hip Arthroplasty (HRA). The incidence of local reactions is higher in articulations with large diameter heads³. Some of these reactions include metallosis, aseptic lymphocytic vasculitis associated lesion (ALVAL) and pseudotumors. The term pseudotumor has been used to describe non neoplastic cystic or solid mass around a MoM hip arthroplasty. These masses form as a result of a reaction to metal debris from the implants surfaces⁴.

Second and third generation MoM hip implants use new articulation surfaces made by improved materials and have been associated with only minimal problems concerning

durability like wear which can lead to aseptic loosening and revision surgery⁵. Nonetheless side effects still exist. Metal ions release from the articulation surfaces especially when larger heads (larger loads) used lead on to local reactions which can present clinically in many ways.

In 2012 Natu et al. made an effort to investigate the Adverse Reactions to Metal Debris (ARMD) after MoM hip arthroplasty. This umbrella term includes conditions like metallosis ALVAL (perivascular inflammatory infiltration of lymphocytes), granulomatous inflammation and pseudotumors⁶. In this review are included only articles referring in the term pseudotumor and not the other reactions mentioned above.

Method

A thorough search of the Medline database was performed. A number of 36 out of 158 articles which examined the occurrence of pseudotumors following hip

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arthroplasty in the last decade were identified. The terms of the search were “pseudotumors” combined with “metal on metal “ and “hip arthroplasty”. A second search in articles cited in the first results was performed excluding primary studies that have been updated. 7 (seven) case series, 3 (three) cohort studies, 2 (two) experts opinion articles and one meta-analysis are included in this review. The search consisted only of articles in the English language, and for studies performed in human subjects. Two studies were excluded because of manufacturer recall of the implants⁷. One of these studies was referring to ceramic-on-highly cross-linked polyethylene.

Definition

Most authors define Pseudotumor as a cystic or solid mass which is non neoplastic and is formed around a hip prosthesis^{4,8} with or without communication to the joint. These masses are usually discovered in patients with metal on metal hip arthroplasties. Their formation is the result of the inflammatory reaction to the release of metal debris from the articulating surface. Revising surgeons have described these lesions as aseptic soft tissue masses among many other definitions. Pseudotumors may range from small asymptomatic tissue reactions to severe destructive masses of bone and soft tissues. Based on experts' opinions their formation takes place at sites with decreased tissue resistance from surgical approach and dissection⁹. They can occur months after surgery even becoming evident after a relatively long period with an incidence of 1% at five years^{10,11}. The histological specimens of pseudotumors include macrophages with particles, lymphocytic aggregates, granulomas and extensive necrosis of connective tissue¹⁰. The differential diagnosis from low grade infection may be difficult.

Epidemiology

The 2016 annual registry of joint replacement in USA (AJRR) show that year by year surgeons are moving away from MoM that predominated. Ceramic head usage continues to grow each year¹². In 2012 the composition of CoCr femoral heads was 63.1% (7.513) and ceramic 36.2% (4.317). In 2015 CoCr usage was 49.6% (30.368) and ceramic 48.8% (29.878). Hip resurfacing also decline, in 2015 were performed 1.560 procedures out of 169.060 (0.9%). A meta-analysis in 2013 by Wiley et al. reported the incidence of pseudotumors to be 0.3% in a total of 13898 MoM hip arthroplasties¹³. Pandit et al. in 2008 estimate the incidence of pseudotumor in patients with MoM HRA at 1% within 5 years¹⁰. They performed over 1300 resurfacing hip arthroplasties over a period of nine years and identified a group of 17 patients with pseudotumors.

Implants size and type

HRA is designed to minimize the changes in hip joint kinematics by replacing only the surfaces been affected,

thus maintaining a greater amount of bone stock than conventional hip arthroplasty, however, it is technically more demanding than THR and the positioning of acetabular implant is more critical¹⁴.

Many studies report the presence of pseudotumors after large diametral metal on metal total hip replacement. Bosker et al (2012) show an incidence of 39% in a total of 108 patients. Primary uncemented MoM THRs were performed with a mean follow up of 3.6 years but patients with body mass index (BMI) >30 kg/m² were excluded³.

The prevalence of these tumor-like lesions is reduced with the use of smaller implants. W. van der Weegen et al. performed a one year follow up with metal artifact reduction sequence-magnetic resonance imaging (MARS MRI) in 37 patients. The first MRI was performed at a mean post operative time of 4.3 (2.2-8.3) years and the second 8 months later. Little to no change has been shown in symptomatic pseudotumors with 28 mm MoM hip resurfacing arthroplasty¹⁵.

Risk factors

Implants malposition, bearing surfaces, diametral clearance and sector angle are associated with high ions level. Position of the implants is vital for the outcome of MoM HRA. Mal-positioning of the implants and especially the acetabular component, increase the risk of impingement and edge loading¹⁶. Daily living activities affect the forces applied to the implants in a different way. While walking, the edge loading area is in the outer superior zone of acetabular implant at 12.00 o'clock. During stair climbing and rising from a chair, the edge loading predominates at the same zone at 10.00 o'clock position. Edge loading etiology is multifactorial but in a small group of MoM HRA (33 cases) the patients presenting with pseudotumors had an increased angle of anteversion and inclination of acetabular components with 67% outside the safe zone of Lewinnek¹⁷. Hartmann et al in a 10 year follow up of HRA identified that high cup inclination was associated with high cobalt levels¹⁸.

An other risk factor is the corrosion on the taper and trunnion contributing to the formation of metal debris also in well-positioned implants³. On the other hand, the free motion between bearing surfaces is also a reason for producing wear debris. Diametral clearance is the gap between the two mating metal surfaces forming a gland's internal cavity. The low clearance of the implant is associated with increased wear due to reduced fluid film formation¹⁹.

There is no significant association of metal allergy to pseudotumors, but the result of that study was based on a small group of cases²⁰. Patients age seems to be another factor. The younger the patient, the greater the risk for revision surgery²¹. A study of 1419 MoM HRA with a follow up of 8 years shows a greater risk for patients under the age of 40. Maybe this can be explained by the higher activity level. Finally, as for the gender but not as an independent risk factor, most of the patients affected are women^{10,21}.

Without having sufficient evidence women tend to edge-load more than men because at the standing gait phase the hip remains in a more adducted position. In 2009 S. Glyn-Jones et al found that the coexistence of young age (<40), woman gender and small size implants increase the risk of failure and the need for revision (13.1% in six years).

Metal Ions

The bearing surfaces of MoM implants are mostly made of chromium (Cr) cobalt (Co) and molybdenum (Mo). Additionally, in smaller amounts, they contain nickel (Ni), iron (Fe), manganese (Mn), silicon (Si) and vanadium (V). Metal on metal wear releases metal particles and metal ions enter the systemic circulation but as long as renal clearance mechanism is effective the levels of ions remain low. Some of the metal particles are phagocytosed by macrophages and giant cells. Through the lymphatic system, these particles are deposited in the lymph nodes, liver, and spleen. The metal particles or ions originate either from the bearing articulation surface or the taper junction between prosthesis head and stem as a result of corrosive process or mechanical wear. They consist mostly of chromium (Cr) and cobalt (Co). Their blood levels can use as markers for screening patients with MoM implants. Inductively coupled plasma mass spectrometry (ICPMS) and electrothermal atomization atomic absorption spectrometry (ETAAS) are used for the measurement of metal ions in biological samples. ICPMS is preferable having lower detection limits.

Pseudotumors are associated with elevated metal ions in blood sample. Kwon et al. Measure the levels of metal ions in a study performed in 158 patients who underwent a MoM HRA at least 3 years before. In 7 patients, most of them females, pseudotumors were found. This group compared with a control group of MoP THA and a non pseudotumors group was associated with significantly higher median metal ion levels: cobalt 9.2 µg/L, chromium 12.0 µg/L. Additionally, hip aspirate metal ion levels were elevated (cobalt 1182 µg/L chromium 883 µg/L). This group was found having mild pain and a mean Oxford hip score at 41. None of them reported mass lesion symptoms⁸. Bosker et al. also identify an increased risk developing a pseudotumour in patients with serum cobalt levels >5 µg/l.

In 2014 the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) determined critical threshold ranges for Co at 2 to 7 µg/L in whole blood. As some metals, particular chromium, tend to concentrate within erythrocytes serum analysis may have underestimated the metal levels. The appropriate blood fraction for the measurement of metal ions remains controversial²². The use of metal needles for collecting blood sample may show higher metal ion than reality.

Local symptoms

Pain is the essential predictor of the presence of a pseudotumor with a variety of locations, in the thigh, groin

or buttock. Bosker et al performed a follow up in 706 MoM concluding that pain dominates to cobalt levels and swelling⁹. Patients with mild or tolerable pain may not seek medical attention but follow up is essential for everyone⁸. Osteolysis and aseptic loosening give rise to pain and loss of function of the hip and the need for a revision arthroplasty to prevent it from progressing on to extensive bone loss and catastrophic structural failure. Signs of swelling, discomfort or pain in the groin may indicate a sizeable pseudotumor with local tissue distraction, pressure effects on vital structures and the need for revision. Symptoms may develop slowly and the patient will report good to excellent scores. Pandit et al. report a common symptom of discomfort and pain in the groin, buttock or at the lateral side of the hip. A smaller group describe symptoms from Irritation of the femoral and lateral cutaneous nerve of the thigh¹⁰. If the lesion is superficially and enlarged it may be palpable or visible as a lump.

A deeper forming lesion can potentially cause local pressure effects causing necrosis and compression of nearby structures such as the iliac vessels, femoral vessels, and the femoral or sciatic nerve²³. A case report of Werner Maurer-Ertl et al. presented with swelling of the leg and hip discomfort with no evidence of deep venous thrombosis (DVT). They underwent a u/s, and CT found a solid mass compressing the external iliac vein. In an other case of Daniel J. Parfitt et al. with the same CT findings, the patient presented with DVT. This patient was older and presented with symptoms 16 months after arthroplasty also he had a medical history with ischemic heart disease.

Muscles atrophy and their irreversible destruction is another conserve which may lead to revision. Soft-tissue abnormalities can identify with the use of MRI. These findings are the results of local distraction causing by pseudotumors and by an inflammatory response to metal wear debris. A study of Berber et al. based on MARS MRI findings, report an increase in atrophy of the gluteus minimus or medius in 17 out of 74 cases .progressive atrophy was more obvious in female patients with metal ion levels above 7 ppb¹⁵. This study has some limitations considering the small number of cases, the different surgeons and hip approaches and the absence of preoperative MRI evaluation for muscle atrophy. Despite that, it is the only study evaluating the changes of muscle atrophy in large diameter MoM implants with MRI scanning. In 2015 Aleksy Reito et al. reported a low prevalence of gluteal muscle atrophy in 263 patient with no association with elevated metal ions in blood sample.

Toxicity

Metal ions like chromium cobalt, nickel and molybdenum are essential microelements found in our body in traces being a part of a normal cell function.

Chromium aids in glucose metabolism and glucose tolerance^{25,26}. Molybdenum works as an enzyme catalyst for certain amino acids breakdown and its deficiency have linked with esophageal carcinoma²⁷. Cobalt contained in vitamin

B12 essential in red blood cell formation. The chemical form of these elements seems to be responsible for the systemic effects. Hexavalent Cr[Cr(VI)] is a well-known carcinogen, and some studies relate it with MOM, but evidence is not supported by others²⁸. Cobalt has been associated with cardiomyopathy^{29,30}. Seven cases have been described having peripheral neuropathy do to co levels above 250 µg/L in blood sample³¹. Ikeda et al performed a biopsy in suran nerve with the finding of axonal degeneration, such findings in central nervous system can affect cranial nerves³². Hearing loses, also in co poisoning, may coexist with headache vertigo tinnitus^{31,33}. These symptoms are rarely presented³⁴ and in some cases seem to subside after revision surgery³⁵.

Diagnosis

The diagnosis of pseudotumor is as difficult as complex, when they occur the progression is slow and annually imaging is sufficient to identify any change. Every patient must perform a systematic infection workup because an infection may confound the clinical picture. Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) and standard infection lab test must be performed followed up by hip aspiration and imaging. Metal ion measurement is advisable for systemic exposure and wears rate. They reach a peak 6 to 12 months postoperatively. Based on Effort guidelines, all MoM large diameter arthroplasties with risk factors need an annual follow up. Risk factors include femoral head size <50 mm, female gender. HR asymptomatic arthroplasty needs an annual follow up for the first 5 years. Imaging rather than x-rays are needed if metal ions are >2 µg/l or abnormal findings in x rays

X rays include anteroposterior (AP) and lateral views of the hip and an AP view of the pelvis are needed for long-term surveillance, but radiographs have poor sensitivity for detection of Pseudotumors. Ultrasonography is a good initial examination in the suspicion of pseudotumor it can also identify abnormalities in tendons. CT scanning has the advantage over ultrasound that is less operative dependent and more readily available than MRI MARS³, it has a lower cost, and the surgeon can observe the position of the implant and identify osteolysis. MARS MRI has greater sensitivity and specificity for lesions detection at any depth.

Based on experts opinion large heads implants, as well as THR, need an annual follow up and if metal ions level is normal after two years postoperatively, the following investigation is based on local protocols for conventional THR³⁶. Consider revision in symptomatic patients with progressive osteolysis or other imaging abnormalities, large pseudotumors or metal ions concentration above 7 µg/L or progressive rising at follow-ups. Co levels above 20 µg/L associated with severe cardiac and neurological complications from metal poisoning and is an indication for revision by itself³⁷. Metal ion concentration can reduce to close to normal levels after one year of MOM removal³⁸.

Hartmann et al. in 2012 reviewed 100 HRA with a 10

year follow up. The survivorship for revision was 88%. Revision due to pseudotumor presence was performed in 3 female patients after 10.2 to 10.5 years. In these patients, the primary implant was small in size (46 mm head size)¹⁸. Complications of malpositioning will be reduced by placing the acetabular implant in 40° of abduction (30° to 50°) and 20° of anteversion (15° to 25°)³⁶.

Conclusion

In 2012 the European Federation of National Associations of Orthopaedics and Traumatology (EFORT) made a common statement with European Hip Society (EHS), German Arbeitsgemeinschaft Endoprothetik (AE) and Deutsche Arthrosehilfe (DAH) based on experts opinion and concerning the management of MoM bearings. These implants have the total commercial control on surface replacement preserving bone stock compared to conventional total hip replacement. Comparing with ceramic on ceramic (CoC) they have smaller risk of fracture, and the availability of large heads (≥36 mm) minimize the risk of dislocation. In contrast, the risk for adverse reaction to metal debris (ARMD) is bigger than conventional bearings when large heads are used. HRA has a risk of femoral neck fracture in nonwell-selected patients (lower femoral neck bone quality and coverage) and finally health effects when metal products entering blood circulation causing organ disfunction

Some implants have been recalled because of the large number of complaints of pain and the increased need for revision surgery⁷. Longitudinal study is required to determine whether asymptomatic pseudotumors will progress to destructive lesions causing severe symptoms.

The definition of pseudotumors remains controversial making it difficult to search medical databases. The need for the establishment of a term of pseudotumors is essential.

The number of patient with artificial joints is rapidly increasing. Therefore more attention and investigation is needed to find the proper material to minimize local and systemic side effects.

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