

ADVERSE REACTION TO METAL DEBRI Hip Arthroplasty

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OUTLINE

- History of Total Hip Arthroplasty
- MoM Prosthesis
- Production of Metal Particles
- Defining Terminology: Metallosis, ARMD, ALTR, ALVAL, pseudotumor, periprosthetic reactive masses
- Etiology of ARMD
- Risk Factors of ARMD
- Presentation
- Management of patients with MOM prosthesis
- Imaging findings
- Differential Diagnosis
- Treatment



PAST: Hip Arthroplasty

1891: Earliest recorded attempt in Germany

use of ivory to replace femoral heads to treat TB

Late 19th and early 20th century: Interpositional arthroplasty

- utilizing various tissues (fascia lata, skin, pig bladders submucosa) between articulating surfaces of the arthritic hip
- 1925: Marius Smith-Petersen and Philip Wiles
 - first stainless steel total hip prosthesis that was fitted to bone with bolts and screws



PAST: Hip Arthroplasty

1953: George McKee

- First to use a metal-on-metal prosthesis on a regular basis
- Modified Thompson stem + one-piece cobalt-chrome socket as the new acetabulum
- 28 year survival rate of 74%
- Fell out of favor in mid-1970's due to local effects of metal particles seen during revision surgery for prosthetic failure
- > 1960's: Sir John Charnley Father of modern THA
 - Low friction arthroplasty- small femoral head reduces wear due to its smaller surface area
 - Metal femoral stem + polyethylene acetabular component and acrylic bone cement





Metal on Polyethylene (MoP) Ceramic on Ceramic (CoC)

Metal on Metal (MoM)



• Advantages:

- Most commonly used
- Large volume of evidence to support use
- Predictable lifespan
- Cost effective
- Disadvantage

Metal on Polyethylene (MoP)

- Polyethylene debri leading to aseptic loosening
- Particle Disease
- High debri particles, high reactivity

Knight et al, Total hip arthroplasty– Over 100 years of operative history. Ortho Rev 3:72-74, 2011



Ceramic on Ceramic (CoC)

Ceramic on Metal (COM)-Not shown

Ceramic on Polyethylene (CoP)- Not shown

- 1970: French surgeon Pierre Boutin
- Developed to address problems of friction and wear
- Benefits:
 - Low friction
 - Low debri particles
 - Inert debri
 - Good choice for young and active patients due to reduced wearing

• Disadvantages

- \$\$\$\$
- High fracture rate of first generation ceramic bearings
- Produce noise on movement

MoM Prosthesis



Photo credit: http://www.qmed.com/news/why-metal-metal-hip-implants-are-troubling-biomet-jj-stryker-and-others



Metal on Metal (MoM)

- Advantages of THA:
 - Smooth and hard surface
 - Wear rate of MoM 60x less than MoP
 - Potentially longer lifespan than polyethylene due to reduced wear
 - Large femoral head → increase stability and lower dislocation rate
- Traditionally used to treat painful osteoarthrosis particularly in young active patients with good bone stock (men aged <65 yrs and women aged <60 yrs)
- HRA: conserves bone and lead to improved revision outcomes

Knight et al, Total hip arthroplasty– Over 100 years of operative history. Ortho Rev 3:72-74, 2011 Fehring et al. Modes of Failure in Metal-on-Metal Total Hip Arthroplasty. Orthop Clin N Am 46 (2015)185-192 Drummond et al. Metal-on-Metal Hip Arthroplasty: A Review of Adverse Reactions and Patient Management. JFB 2015, 6, 498-499.

Failing MOM prosthesis

- ~1 in 5 MoM hip replacements revised 10-13 years after insertion
 - Higher risk in larger head sizes (>36 mm)
- ~13% of hip resurfacing revised 10 yrs after insertion
- MoP revised <4% of cases 10 yrs after insertion

Australian Orthopaedic Association . Metal on Metal Bearing Surfce Total Conventional Hip Arhtroplasty. Supplement Report 2014. National Registry. National Joint Registry for England, Wales and Northern Ireland. 11th Annual Report 2014 Drummond et al. Metal-on-Metal Hip Arthroplasty: A Review of Adverse Reactions and Patient Management. JFB 2015, 6, 498-499.

What is causing the increased revision rates of MoM prosthesis?

Metallosis

& Adverse Reaction to Metal Debri (ARMD)



- Mechanical wear of bearing surfaces
- Corrosion
- Trunnionosis (modular junctions)



- Mechanical wear of bearing surfaces
 - Abrasion from normally positioned metallic WB surfaces



- Mechanical wear of bearing surfaces
 - Edge loading from abnormally positioned acetabular component



- Mechanical wear of bearing surfaces
 - Edge loading from abnormally positioned acetabular component



 Mechanical wear of bearing surfaces

 Neck on cup impingement



PINCER TYPE IMPINGEMENT:

Excessive anteversion of acetabular component resulting in impingement of metal liner and notching on the posterior aspect of the femoral stem.

- Mechanical wear of bearing surfaces

 Neck on cup impingement
 - Pincer type: inadequate removal of acetabular osteophytes and malposition of acetabular components
 - CAM type: small head-toneck ratio
 - Mix type
 - Occur early or late following loosening and substantial rotation of acetabular cup



Corrosion

- Deterioration of metal through an electrochemical process of oxidation and reduction reactions producing metal ions
- Most common form is rust
- Requirement for metal components to have high corrosion resistance by formation of a passive surface film to prevent oxidation
 - Disrupted in vivo by fretting and micromotion
- Tribocorrosion: complex interaction where corrosion hastens wear and vice versa
- Metal release from corrosion can cause particle deposition within local tissues & elevated serum metal levels causing metallosis & adverse reaction to metal debri
- Prevalence of corrosion among retrieved specimens ranged from 0%-57% at 0.5-5.5 years

Where does wear & corrosion occur in non-MoM THA?



- Adverse reaction to metal debri have been typically defined in the context of the bearing surfaces of MoM hip arthroplasty
- But similar findings have been more recently described in non-MoM prosthesis....
- TRUNNIONOSIS: Wear and/or corrosion at a tapered modular interface with resultant metal ion release most commonly at the head-neck junction.

Where does wear & corrosion occur in non-MoM THA?



- Trunnion originates from the French word trognon meaning stump; a pin or pivot on which something can be rotated or tilted
- Trunnion- cylindrical protrusion forming one half of a modular interface
- Modular interfaces
 - + Head-Neck junction
 - Neck-Body junctions
 - Mid-Stem junctions
- Thought to account for the adverse reaction to metal debri regardless of bearing surface

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CASE: 81 yo F with Wright medical Mom with a large femoral head and Profemur Z modular femoral neck THA in 2011 with worsening right hip pain. NI WBC. NI Serum Chromium. Elevated Serum Cobalt at 13.1 μg/L (nl </= 1).



Courtesy of Dr. Evelyne Fliszar

ALTR to MoM with a large femoral head & modular femoral component THA.



Courtesy of Dr. Evelyne Fliszar

ALTR to MoM with a large femoral head & modular femoral neck THA.



CASE: 69-year-old with MoP present with a left hip mass nearly tripled in size over the last 2 years.

Serum Cobalt = 11.9 microgram/L (<=1). Serum Chromium serum= 3 microg/L (<=5)



Particle disease with polyethylene wear-induced synovitis VS Particle disease with ARMD through metal corrosion???

Courtesy of Dr. Ed Smitaman

CONFUSING TERMINOLOGY

- ALTR- Adverse Local Tissue Reaction
- ARMD- Adverse Reaction to Metal Debri
- Metallosis
- ALVAL- Aseptic Lymphocytic Vasculitis-Associated Lesions
- Periprosthetic reactive mass
- Inflammatory pseudotumor



ALTR = ARMD = ALVAL = Pseudotumors

Metallosis

ALTR/ARMD/ALVAL/Pseud otumor

Maloney et al. Imaging of Adverse Reactions to Metal Debris. Semin Musculoskeletal Radiol 2015;19:21-30

Metallosis

- Chronic inflammatory process caused by the infiltration of periprosthetic soft tissues and bone by metallic debris from mechanical wear--> aseptic fibrosis, local necrosis or loosening of a device.
- Described in total hip, total shoulder, total knee and unicompartmental knee arthroplasties.
- Increased frequency in titanium prostheses compared to chromiumcobalt prosthesis suggesting increased propensity for wear
- Grossly appears as oily black fluid in the joint and grey/black discoloration of the periprosthetic soft tissue







FOREIGN BODY RESPONSE

MACROPHAGES MULTINUCLEATED GIANT CELLS

RELEASE OF CYTOKINES





FOREIGN BODY RESPONSE

MACROPHAGES MULTINUCLEATED GIANT CELLS



RELEASE OF CYTOKINES





RELEASE OF CYTOKINES





FOREIGN BODY RESPONSE

HISTIOCYTES MULTINUCLEATED GIANT CELLS



RELEASE OF CYTOKINES





RELEASE OF CYTOKINES


Metallosis Pathophysiology

METAL PARTICLES

TUT



HISTIOCYTES MULTINUCLEATED GIANT CELLS



RELEASE OF CYTOKINES



Heffernan et al. The imaging appearance of metallosis. Skeletal Radiol (2008) 37:59-62 Gracia et al. Imaging appearances of Metallosis: A pictorial review. ESSR 2014.

Imaging Findings: Metallosis





Chew & Manner. Severe Periprosthetic Metallosis and Polyethylene Liner Failure Complication Total Hip Replacement: The Cloud Sign. Radiology Case Reports October 2007. Romesburg et al. Metallosis and Metal-induced Synovitis Following Total Knee Arthroplasty: Review of Radiographic and CT findings.

Imaging Findings: Metallosis

METAL FADE SIGN



POST-OP

7 YEARS AFTER SURGERY

Slon et al. The Meta-fade sign: A new sign of Metallosis. RSNA 2013+

Adverse local tissue reaction (ALTR)

- Umbrella term describing all periprosthetic adverse reaction
- Spectrum of abnormality include osteolysis, periprosthetic soft tissue masses/pseudotumors, to extensive necrosis.

Shulman et al. Trunnionosis: the latest culprit in adverse reactions to metal debris following hip arthroplasty. Skeletal Rad (2015) 44:433-440 Harper GD, Bull T, Cobb AG, Bentley G. Failure of the Ring polyethylene un- cemented acetabular cup. J Bone Joint Surg Br. 1995;77:557-61. Drummond et al. Metal-on-Metal Hip Arthroplasty: A Review of Adverse Reactions and Patient Management. JFB 2015, 6, 498-499.

Adverse Reaction to Metal Debri (ARMD)

- Often used synonymously with ALTR, inflammatory pseudotumor, ALVAL.
- Umbrella term describing all periprosthetic reactions attributable to metal alloy
- Spectrum of abnormality include asymptomatic small cysts to large soft tissue masses/pseudotumors.

Shulman et al. Trunnionosis: the latest culprit in adverse reactions to metal debris following hip arthroplasty. Skeletal Rad (2015) 44:433-440 Harper GD, Bull T, Cobb AG, Bentley G. Failure of the Ring polyethylene un- cemented acetabular cup. J Bone Joint Surg Br. 1995;77:557-61. Drummond et al. Metal-on-Metal Hip Arthroplasty: A Review of Adverse Reactions and Patient Management. JFB 2015, 6, 498-499. Inflammatory Pseudotumor/ Periprosthetic Reactive Mass:

- Imprecise definition and correspond to a wide variety of imaging appearances
- Describes the clinical and radiologic presentation of an aseptic periprosthetic solid or cystic mass.
- Can be seen in foreign body reactions such as in particle disease or metallosis as well as in ARMD/ALTR.



Aseptic Lymphocyte mediated Vasculitis Associated Lesions Aseptic lymphocytic vasculitisassociated lesions (ALVAL)

- Histologic diagnosis describing the unique cellular change that occur in aseptic periprosthetic masses in response to metal ions namely cobalt and chromium ions.
- Believed to be a T-lymphocyte mediated type IV hypersensitivity reaction with tissue damage occurring as a result of cytotoxic T cells and activated monocytes/macrophages.

Shulman et al. Trunnionosis: the latest culprit in adverse reactions to metal debris following hip arthroplasty. Skeletal Rad (2015) 44:433-440 Harper GD, Bull T, Cobb AG, Bentley G. Failure of the Ring polyethylene un- cemented acetabular cup. J Bone Joint Surg Br. 1995;77:557-61. Drummond et al. Metal-on-Metal Hip Arthroplasty: A Review of Adverse Reactions and Patient Management. JFB 2015, 6, 498-499.

METALLOSIS vs ARMD

- Wear related
- Foreign body reaction to metal debri
- Predominantly macrophage and MNGC-mediated response
- Osteolysis
- >Titanium

- Metal sensitivity
- Type-IV delayed hypersensitivity reaction to metal ions
- Predominantly lymphocyte-mediated response
- Soft tissue damage, necrosis and pseudotumor formation
- >Chromium and Cobalt

Same spectrum of disease vs separate process? Usually an overlap between the two: metallosis is frequently seen in joints with ARMD. CASE: 71 yo M with MoM THA 8 yrs ago presents with vague right hip and buttock pain as well as decreased ROM of the hip.



Chromium= 17.2 elevated (<5) ug/L Cobalt= 67.1 elevated (<1 ug/L)

Courtesy of Dr. Evelyne Fliszar

CASE: 71 yo M with MoM THA 8 yrs ago presents with vague right hip and buttock pain as well as decreased ROM of the hip.



Metallosis with ARMD

Unfortunately, it is not that simple...

Pseudotumors in ARMD found to be also wear related!

SYMPOSIUM: COMPLICATIONS OF HIP ARTHROPLASTY

Histological Features of Pseudotumor-like Tissues From Metal-on-Metal Hips

Pat Campbell PhD, Edward Ebramzadeh PhD, Scott Nelson MD, Karren Takamura BA, Koen De Smet MD, Harlan C. Amstutz MD

- 32 samples from 32 revised MoM hip replacements with pseudotumorlike reactions
- Used a 10 point grading scale to rank the degree of ALVAL by examining synovial lining integrity, inflammatory cell infiltrates, and tissue organization.
- Quantified implant wear
- Cases divided into pts suspected of having HIGH WEAR vs METAL HYPERSENSITIVITY based on clinical, radiographic, and retrieval findings

Table 1. Histologic scoring criteria for ALVAL score					
Points	S Synovial lining				
0	Intact synovial lining				
1	Focal loss of synovial surface, fibrin attachment ma occur				
2	Moderate to marked loss of synovial surface, fibrin attachment				
3	Complete loss of synovium, abundant attached fibrin and /or necrosis of lining tissue				
Points	Inflammatory infiltrate				
0	Minimal inflammatory cell infiltrates				
1	Predominantly macrophages, occasional lymphocytes may occur				
2	Mix of macrophages and lymphocytes, either diffuse and/or small (< 50% of hpf) perivascular aggregates				
3	Mix of macrophages and lymphocytes, large (> 50% hpf) perivascular aggregates may occur				
4	Predominantly lymphocytes, mostly in multiple, large (> 50% hpf) perivascular aggregates, follicles may be present				
Points	Tissue organization				
0	Normal tissue arrangement				
1	Mostly normal tissue arrangement, small areas of synovial hyperplasia, focal necrosis may occur				
2	Marked loss of normal arrangement, appearance of distinct cellular and acellular zones, thick fibrous layers may occur				
3	Perivascular lymphocytic aggregates mostly located distally, thick acellular areas may occur				
	Sum				
	Low = 0-4				
	Moderate = $5-8$				
	High = 9-10				

Results of the semiquantitative evaluation of histologic features for cases revised for suspected high wear and for unexplaiend pain/suspected metal sensitivity.

Variable (p value)	Suspected wear related		Suspected metal sensitivity	
	Average	SD	Average	SD
ALVAL score ($p < 0.001$)	3.6	2.5	8.5	1.4
Macrophages (p < 0.001)	2.7	0.5	1.7	0.5
Lymphocytes ($p = 0.001$)	1.4	0.6	2.5	0.7
Metal particles $(p = 0.008)$	1.5	0.7	0.7	0.5
Necrosis $(p = 0.29)$	1.0	0.7	1.4	0.7
Tidemark ($p = 0.03$)	0.2	0.4	0.7	0.5

Campbell et al. Histological Features of Pseudotumor-like Tissues From Metal-on-Metal Hips. Clin OrthopRelat Res (2010) 468:2321-2327.

Conclusion

- Pseudotumors from ARMD can be seen in both high wear (metal reactivity) and low wear (metal sensivity).
- Histologic features including synovial integrity, inflammatory cell infiltrates, tissue organization, and metal particles may help differentiate these causes.
- Metal sensitivity should be considered in patients with painful hips with periprosthetic masses if high-wear is excluded.

RISK FACTORS FOR ADVERSE REACTION TO METAL DEBRI



Acetabular malpositioning

Female Preoperative sensitization to metal?

MoM Modular Design non-MoM Optimize fit of femoral head and acetabulum

Campbell et al. Histological Features of Pseudotumor-like Tissues From Metal-on-Metal Hips. Clin OrthopRelat Res (2010) 468:2321-2327.

Bestic et al. Current Concepts in Hip Arthroplasty Imaging: Metal-on-Metal Prostheses, Their Complications, and Imaging Strategies. Semin Roentgenol. 2013 Apr;48(2):178-86.

CLINICAL PRESENTATION

- Suspect in MoM, MoP, and THA with modular components
- Variable presentation including asymptomatic, mild discomfort, severe hip pain, palpable mass, dislocation, and neuropathy
- May present months or years after surgery

LABORATORY WORKUP

- Serum cobalt and chromium levels
- No correlation was found between serum cobalt and/or chromium ion levels and the extent of necrosis, degree of macrophage infiltration, or ALVAL score.
- Patients with markedly elevated metal ions tend to have high ALVAL score.
- Although high ion levels are elevated in most MoM failures, a normal metal ion level does not exclude the diagnosis.

RADIOLOGIC WORKUP

RADIOGRAPHS

- Standard imaging exam
- Baseline and follow-up XR most useful in evaluating component position and integrity
- Easy diagnosis of common complications
 - Mechanic loosening/subsidence, osteolysis, periprosthetic fracture, and heterotopic ossificaiton
- Pseudotumor typically no XR finding

CASE: 61 yo F s/p MoM THA 4.5 yrs ago with vague anterior hip discomfort and clunking with activity.



Negative XR

Serum Cobalt 21.4 Serum Chromium 16.7 μg/L (nl </= 1).

Courtesy of Dr. Evelyne Fliszar

CASE: 61 yo F s/p MoM THA 4.5 yrs ago with vague anterior hip discomfort and clunking with activity.



SURGICAL FINDINGS:

- 1. Severe adverse reaction to metal debri
- 2. Abnormal membranous bursa
- 3. Small osteolysis around the acetabulum.

PATHOLOGY: Fibrous tissue with chronic inflammation and numerous histiocytes containing metal particles.

CASE: 71 yo M with MoM THA 8 yrs ago presents with vague right hip and buttock pain as well as decreased ROM of the hip.



Negative XR???

Courtesy of Dr. Karen Chen

CASE: 71 yo M with MoM THA 8 yrs ago presents with vague right hip and buttock pain as well as decreased ROM of the hip.









Aspiration: 20 cc of very dark brown fluid, looks like dirty engine oil consistent with ARMD/Metallosis.

Teaching point: WINDOW for ST abnormality.

Oliveira et al. Metallosis: A diagnosis not only in patients with metal-on-metal prostheses. European Journal of Radiology Open 2 (2015) 3-6

ULTRASOUND

- Useful screening tool as it avoids metalrelated artifacts
- Smaller lesions closer to hardware may be better appreciated than in US
- Operator dependent
- MRI still more sensitive particularly when using metal susceptibility reduction techniques
- Aspiration/Biopsy guidance



- Evaluating extent of osteolysis, cement interfaces, heterotopic ossication and metallosis
- Limited by beam hardening artifact from hardware
- Not a good screening tool for ARMD given poor ST resolution

MRI

- Preferred over CT in evaluating periprosthetic abnormalities owing to superior soft tissue differentiation
- Metal susceptibility artifact reduction protocol
 - Lower magnetic field strength
 - Increasing bandwidth
 - Susbtituting STIR for FS sequences
 - Increasing frequency encoding gradient strength
 - Using fast spin echo with a long echo train and short echo time rather than GRE
 - Reducing voxel size
 - Using a higher-resolution matrix
 - Using thinner imaging sections
 - Selectively orienting the frequency and phase encoding gradients
 - Aligning the primary magnetic field with the longitudinal axis of the components
 - Artifacts most easily reduced by increasing the amplitude of the frequency encoding gradient either by increasing the receiver bandwith or decreasing the pixed size
 - Increasing the bandwidth can result in >90% artifact reduction

MRI grading system

- Various MRI grading systems have been proposed to attempt to stratify the severity of periprosthetic pseudotumors
 - Size, composition, cyst wall thickness, and regional tissue abnormalities, etc
- Prognostic significance remain to be validated
- Maximal synovial thickness (Median 13.6 mm/12 mm) and synovial volumes (Median 62778 mm^3/50428 mm^3) determined on MRI correlated with high ALVAL scores and severe intraoperative tissue damage
 - 94% sensitivity, 87 % specificity for detecting ALVAL
 - 90% sensitivty, 86% specificity for quantifying intraoperative tissue damage

Differential Diagnosis of Periprosthetic Masses

- ALTR/AMRD
- Infection
- Tumor

CASE: Status post MoM THA 8 years ago with recurrent hip pain and swelling worsening over the last couple of weeks radiating to the right scrotum. Recently on steroids for polymyalgia rheumatica.



Courtesy of Dr. Evelyne Fliszar

CASE: Status post MoM THA 8 years ago with recurrent hip pain and swelling worsening over the last couple of weeks radiating to the right scrotum. Recently on steroids for polymyalgia rheumatica.



MoM... is this another case of ARMD???

Courtesy of Dr. Evelyne Fliszar

CASE: Status post MoM THA 8 years ago with recurrent hip pain and swelling worsening over the last couple of weeks radiating to the right scrotum. Recently on steroids for polymyalgia rheumatica.





LARGE ABSCESS with osteomyelitis ASPIRATION: ~ 240 mL of brownish, purulent, foul smelling fluid. >300,000 WBC's.

CASE: Status post cementless revision right THA 21 yrs ago presents with hip pain.





7 months later

European Journal of Radiology 2011 77, 43-50DOI: (10.1016/j.ejrad.2010.08.015)

Missed diagnosis of angiosarcoma ultimate resulting in patient's death.



- Periprosthetic malignancy such as primary sarcoma or metastatic cancer is a very rare yet reported event in the setting of previous hip replacement.
- Delay in diagnosis will likely leading to catastrophic consequences when not diagnosed in a timely manner.

TREATMENT

- Symptomatic pseudotumors candidate for revision
- Management of smaller lesions that are asymptomatic is less clear
- Depends on source of wear or corrosion
 - − MoM bearing wear \rightarrow MoP or CoM
 - Head-Neck interface corrosion → Ceramic femoral head or removal of femoral stem to provide a virgin femoral trunnion
- Avoid Co and Cr revision components as ARMD typically arise from reactions to Co and Cr debris.
 - Use Ti alloy and CoC or CoXLP bearing surfaces
- Outcomes for revision are generally poor, particularly if associated with extensive tissue destruction.
- Early revision should be considered in symptomatic patients to limit extent of soft tissue destruction
TEACHING POINTS

- Terminology is confusing. Know your referrers to make sure that you are using the same language.
- ARMD can be both related to metal reactivity and metal sensitivity
- ALTR often do not have signs of osseous abnormality or hardware failure especially if related to metal sensitivity.
- Look at ST WINDOW on XR!!!
- Don't forget infection and neoplasm as differentials.

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