

Case Report

Infection or Allergy in the Painful Metal-on-Metal Total Hip Arthroplasty?

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Abstract: Metal-on-metal articulations are increasingly used in total hip arthroplasty. Patients can be sensitive to metal ions produced by the articulation and present with pain or early loosening. Infection must be excluded. Correct diagnosis before revision surgery is crucial to implant selection and operation planning. There is no practical guide in the literature on how to differentiate between allergy and infection in a painful total hip arthroplasty. We present the history, clinical findings and hip scores, radiology, serology, hip arthroscopy and aspirate results, labeled white cell scan, revision-hip findings, histology and clinical results of a typical patient with a hypersensitivity response to a metal-on-metal hip articulation, and how results differ from patients with an infected implant. A practical scheme to investigate patients with a possible hypersensitivity response to an implant is presented. **Keywords:** metal hypersensitivity, painful THA, hip arthroscopy, metal ion levels, imaging, metal allergy, diagnosis metal allergy.
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When a patient presents with a painful total hip arthroplasty (THA), with or without obvious pathology, radiographic osteolysis, and clinical early loosening, diagnosis of the etiology of the pain is crucial in planning further management. Infection must be considered.

There is increasing use of modern metal-on-metal hip articulations, especially in young people, as the volumetric wear over time is less than in metal-on-polyethylene hips, although the number of particles released is higher [1]. Hypersensitivity reactions have been known to occur to the degradation products of metallic biomaterials since the first generation of metal-on-metal hips were implanted [2,3]. Metallic ions are released as metal in contact with biological systems corrodes. These ions can bind with native proteins and become candidate antigens activating the immune system hypersensitivity responses [4]. In the metal-on-metal hip, degradation products are released from the

articulation and also corrosion products can be released in significant numbers from the head neck junction in any metal modular prosthesis [5,6].

Cutaneous metal sensitivity occurs in 10% to 15% of the population [7], but this does not correlate with the incidence of hypersensitivity to orthopedic implants. The triple assay technique of Hallab et al [8] has been shown to highlight individuals potentially susceptible to hypersensitivity reactions, but no levels are given to ascertain what constitutes a hypersensitivity reaction. Also, it is impossible to be certain whether a hypersensitivity reaction may be triggered by the prosthesis in a previously unaffected individual. Patch testing of the skin is reliable for investigating contact dermatitis but not so useful in evaluation of deep tissue metal allergy; furthermore, it has been postulated that the process of patch testing can actually sensitize an individual to certain metals [8,9].

There is a lack of knowledge of the true prevalence of metal hypersensitivity to orthopedic implants, the association between dermal and deep implant sensitivity, and the exact role of hypersensitivity in the pathogenesis of the painful joint.

For the surgeon faced with the practical problem of investigating a patient with a painful metal-on-metal THA, differentiating allergy from infection is difficult because there is not one consistently reliable test generally available at most hospitals [10], but this is crucial in planning further management. Often infected arthroplasties are treated by 2-stage revision, and

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Submitted August 15, 2007; accepted August 30, 2008.

No benefits or funds were received in support of the study.

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0883-5403/08/2300-0000\$36.00/0

doi:10.1016/j.arth.2008.08.015

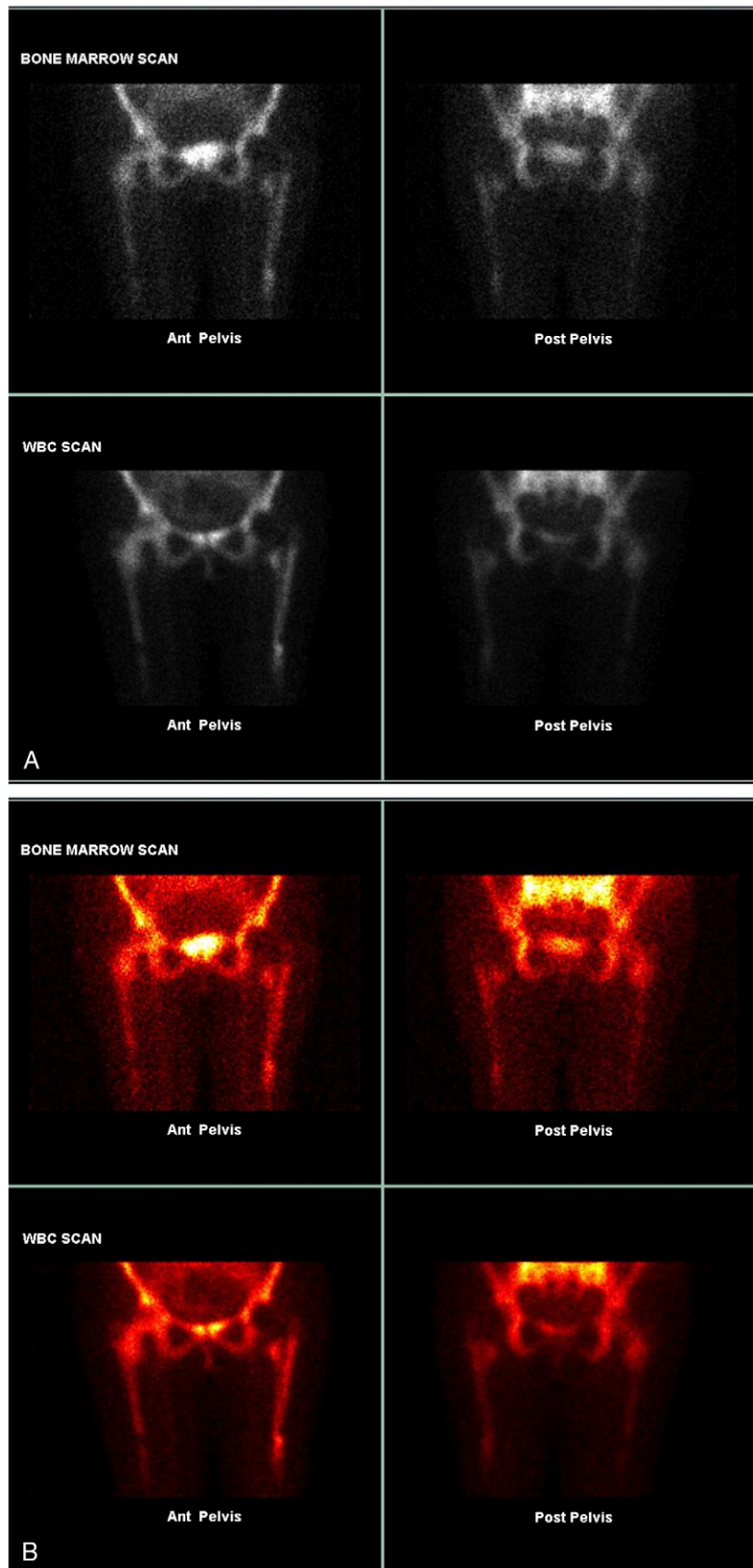


Fig. 1. Technetium Tc 99m stannous colloid-labeled leukocyte scintigraphy demonstrating a matching pattern of distribution of activity between the 2 scans in a patient with a hypersensitivity reaction to the THA prosthesis. There are no criteria for infection, which would give an unmatched distribution of activity and increased uptake around the painful left hip.

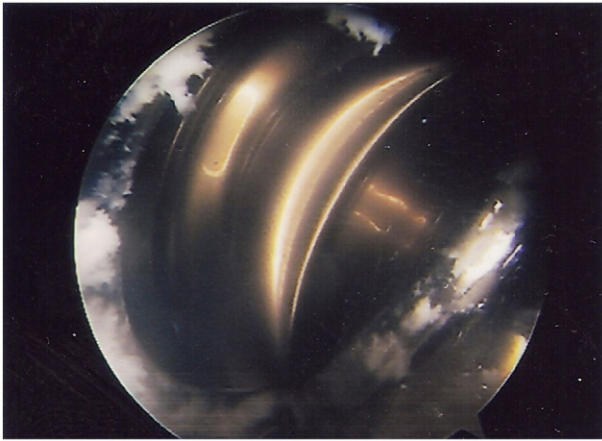


Fig. 2. Arthroscopic appearance of the metal-on-metal articulation showing no significant inflammation of peri-prosthetic tissues.

arthroplasties revised for hypersensitivity can be treated by a 1-stage revision procedure.

We present an illustrative case study and evaluation of investigations commonly available to orthopedic surgeons to differentiate between a patient with a hypersensitivity reaction to a metal-on-metal prosthesis or infected hip arthroplasty.

Case Study

A healthy 64-year-old woman presented to our unit as a tertiary referral from her original surgeon. Thirteen months previously, she had undergone primary left THA for osteoarthritis using an uncemented SROM stem and uncemented Pinnacle Sector acetabular component with a metal-on-metal articulation using a size 36-mm femoral head (DePuy, Warsaw, IN).

The hip had “never felt right” postoperatively; there was a severe deep aching pain in the groin and buttock that radiated down the anterior thigh to the knee. The patient also complained of general malaise. Her physical examination was unremarkable, except global hip discomfort with all movements of the hip, not only at the extremes of range. Serial blood analysis of erythrocyte sedimentation rate, C-reactive protein, and full blood count and differential were within normal limits. Plain radiographs revealed a well-positioned prosthesis with no evidence of migration or osteolysis. A bone scan showed no significant abnormality.

Table 1. Level of Cobalt and Chromium in the Serum and Synovial Fluid 19 Months After Primary Metal-on-Metal THA

Sample Collected 19 Months After Primary THA	Cobalt, nmol/L (Reference Range)	Chromium, nmol/L (Reference Range)
Serum	45 (2-7)	53 (1-26)
Synovial fluid	52,211	11,080

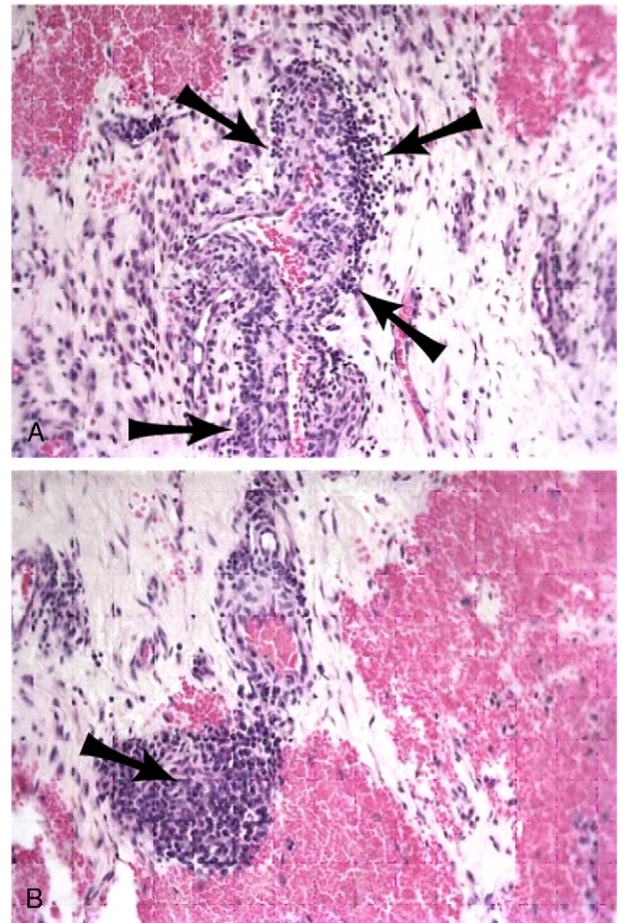


Fig. 3. Histology of the periarticular soft tissue pseudocapsule. (H & E $\times 10$) demonstrating (A) vasculitis and dense perivascular cuffs of lymphocytes (arrow) and (B) perivascular cuff of mature plasma cells.

She gave a clear history of cutaneous metal sensitivity for many years before her hip arthroplasty operation; she was unable to wear a watch or ring. She had noticed

Table 2. Clinical Scores and Serum Metal Analysis Pre-Revision Surgery and 1 Year After Revision Surgery

	Pre-Revision of Metal-on-Metal Articulation	1 y Post Revision to Ceramic-On-Ceramic Articulation
Harris Hip Score [12]	49	75
SF12 [13] physical component	32.43	30.55
SF12 mental wellbeing component	32.54	59.25
WOMAC [14] (the lower the score the better the outcome)	80	70
Serum chromium nmol/L (NR 1-26)	53	6
Serum cobalt nmol/L (NR 2-7)	45	12

SF12, short form 12; WOMAC, Western Ontario and McMaster Universities osteoarthritis index; NR, normal range.

no rashes or irritation around the hip, or any other cutaneous reaction.

She had no other significant medical history.

We performed a white blood cell/colloid scintigraphy study. This investigation revealed uptake around the hip joint (Fig. 1). No evidence of infection was apparent on the scan.

An ultrasound-guided aspirate of the hip joint was performed. The fluid obtained was milky in color and consistency. There were pus cells present in the aspirate, but no organisms were seen, and none grown on enrichment cultures.

A hip arthroscopy was undertaken (Fig. 2); the milky fluid was seen again. The gray rubbery necrotic soft tissue sometimes observed around an infected arthroplasty was not seen; there was also absence of the severe inflammatory response Hyman et al [11] described at arthroscopic evaluation of infected THAs. There were no visible metallic particles, although there was evidence of

soft tissue debris in the joint. The head appeared macroscopically undamaged.

Periarticular soft tissues were arthroscopically biopsied and sent for histologic analysis. Fluid from the joint was sent for analysis of cobalt and chromium levels. The patients' serum was also analyzed for cobalt and chromium levels.

There was no bacterial growth from the synovial fluid. Results are shown in Table 1.

From these investigations, a hypersensitivity reaction to the hip seemed the likely cause of the patients' pain, so a 1-stage revision procedure was planned. At revision surgery, the soft tissues did not appear necrotic or significantly inflamed; tissue planes were easily identifiable. Both the femoral and acetabular components were well positioned and well fixed. The appearance of the articulation was macroscopically normal. Some minor scuffing of the taper was noted; corrosion at the head/neck interface is known to occur in some patients [5]

Table 3. Investigations Used to Differentiate Infection from Hypersensitivity in A Painful THA

Investigation	Result in Early Infected Arthroplasty	Result in Hypersensitivity to Arthroplasty
History	Pain, malaise, "hip doesn't feel right"	Pain, malaise, "hip never felt right"
ESR	Usually raised; mean ESR in infected hip, 46 (range, 5-103) [15]	Unknown in hypersensitivity; mean ESR in loose but not infected hips, 12.8 (range, 2-34) [15]
CRP	Peaks on day 2-3, but normal after 3 wk in uninfected THA [16]; raised in infection [17]	Normal in our patient; Unknown in hypersensitivity; normal in patients with mechanical loosening but no infection [17]
White blood cell count	Normal or raised [15]	Normal in our patient; Unknown in hypersensitivity; normal for patients with mechanical loosening but no infection [17]
Plain radiograph	Normal, or with lucent lines around the prosthesis	Normal in our patient; Normal, or with lucent lines around the prosthesis
Technetium Tc 99m bone scan	Early infection indistinguishable from loosening of other etiology [15] but gallium more useful; Positive predictive value in infection 30% and negative predictive value 87.5% [18]; sensitivity 100%, specificity 64%, diagnostic accuracy 73% [19]	Unknown in hypersensitivity; positive if associated with loosening
Combined white cell sulfur colloid scan	Positive; Sensitivity 70%, specificity 100%, diagnostic accuracy 93% [19]	Negative
Hip aspirate	Sensitivity 83%, specificity 100%; more useful in patients who have had their prosthesis less than 5 y [20]; positive predictive value 93.6% [18]	Not recorded in the literature; pus cells and no growth in our patient
Hip arthroscopy appearance	Moderate to severe inflammation [11]	Not recorded elsewhere in the literature; minimal inflammation in our patient
Histology of periarticular soft tissues	Lymphocyte and macrophage infiltration more than polymorpholeukocytes [21]	Aseptic lymphocyte-dominated infiltration; droplike inclusions in the cytoplasm of macrophages [22]
Serum cobalt and chromium	Unknown in infection; in noninfected metal-on-metal hips, 5- to 10-fold increase in blood cobalt [23]; 10-fold increase in chromium [24]	Unknown; Case study serum level cobalt 45 nmol/L (NR 2-7) and chromium 53 nmol/L (NR 1-26)

ESR indicates erythrocyte sedimentation rate; CRP, C-reactive protein.

with hypersensitivity reactions to implants. Further samples of periarticular soft tissue was collected for histologic analysis; the results are shown in Fig. 3.

The decision was taken not to revise the well-fixed femoral component. The metal liner of the acetabular component was removed. A ceramic-on-ceramic BioloX (DePuy) articulation was inserted. A ceramic articulation was selected despite the concern that a ceramic head may have a small increased risk of fracture on a taper that has already had one head upon it.

Immediately after her revision operation, the patient reported absence of the deep aching pain in the hip and a general feeling of wellness compared with her pre-operative condition.

At 1 year after revision, her hip scores were as shown in Table 2, and repeat serum analysis for chromium and cobalt revealed greatly reduced levels.

Discussion

When investigating the painful metal-on-metal hip, several investigations are available to the orthopedic surgeon in a standard district hospital setting. The expected results in each condition based on a review of the literature are summarized in Table 3.

Other more complex investigations also exist [8,10], but these are not generally available in most hospitals. There is not one single test that definitively differentiates between infection and allergy; the surgeon must evaluate the clinical presentation and the investigations. Based on the results obtained from our patient and a review of the published literature, it appears that the labeled white blood cell/colloid scan, the hip aspirate, and the hip arthroscopy with biopsy analyzed histologically were the most useful tests in our attempt to differentiate between infection and hypersensitivity as a cause for a painful THA in our patient.

The technetium Tc 99m white blood cell/colloid study provides an image of the distribution of reticuloendothelial elements in the bone marrow. If there is an infection, then the main cellular infiltrate is composed of polymorphonuclear cells, which are labeled by the technetium Tc 99m colloid and therefore gives a relatively unmatched distribution. In hypersensitivity, the main cellular infiltrate is composed of lymphocytes, which are not labeled by the technique; hence, there is a completely matching pattern of distribution of activity between the 2 scans and no criteria for infection. This technique has been shown to be 70% sensitive and 100% specific for diagnosing infection in orthopedic implants [19].

Hip aspirate is one of the most useful investigations for infection as the cause of the painful THA, with a sensitivity of 83% and specificity 100% [20]. The positive predictive value is 93.6% [18] in infection. The aspirate can also be analyzed for metals. It is not known how the synovial fluid level of metallic products

varies in patients whose metal-on-metal hips are asymptomatic, infected, or eliciting a hypersensitivity response. However, a level of 52 211 nmol/L obtained from our patient is very high and likely to be abnormal. Hip arthroscopy allows the surgeon a direct view of the articulation and surrounding soft tissue; it also allows for biopsy and subsequent histology examination of the specimens obtained. Characteristic histologic appearance of the surrounding soft tissues in hypersensitivity reactions to metal-on-metal hip prostheses has been described [22,25,26]. Lymphoplasmacytic infiltrates predominate, and droplike inclusions in the cytoplasm of macrophages may occur. This appearance in a biopsy specimen obtained at hip arthroscopy may help the surgeon reach a diagnosis of hypersensitivity as a cause of the painful THA. Conversely, the appearance of bacteria on histology may lead to the diagnosis of infection.

The diagnosis of infection or hypersensitivity as a cause of a painful THA is difficult but important in planning further surgery. In a standard hospital, a technetium Tc 99m white blood cell/colloid study, hip aspirate, and arthroscopic biopsy are useful investigations.

Acknowledgment

The authors thank Dr Rema Oliver for preparation of the histology slides.

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