Adverse Soft-Tissue Reactions Around Non-Metal-on-Metal Total Hip Arthroplasty
A Systematic Review of the Literature

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Abstract
Adverse local soft-tissue reactions have been associated with severe osteolysis and implant failure in metal-on-metal total hip arthroplasty (THA). Such a causal relationship has not often been associated with non-metal-on-metal bearing surfaces. The purpose of this study was to assess the literature for cases of adverse soft-tissue reactions in non-metal-on-metal bearings in order to determine if a consistent histological diagnosis existed and if it was bearing-specific.

Methods: A systematic review was performed in Medline® and Embase™ databases, utilizing keyword searches to target reports of soft tissue complications following THA. Strict exclusion criteria were applied to retrieved studies in order to ensure that analyzed papers involved non-metal-on-metal bearing surfaces, had a final histological diagnosis, and had no previous history of periprosthetic infection or neoplastic process. Presenting symptoms, diagnostic work-up, histological diagnosis, and operative treatment were recorded for all reports retained for analysis.

Results: Twenty-seven reports representing 31 cases of adverse soft-tissue reactions for non-metal-on-metal THAs met the criteria for analysis. In the majority of cases, patients presented with painful, limited motion in the affected hip, and radiological evidence of severe osteolysis. Histological examination often revealed a cystic mass, denoted by a granulomatous reaction comprised of histiocytes and giant

The development of alternate bearing surfaces in total hip arthroplasty (THA) has emerged due to the need to decrease prosthetic component wear, to improve component longevity, and to reduce the risk of revision surgery. However, although novel bearing surfaces involving solely metal or ceramic components have been associated with lower in-vivo wear rates, adverse local soft-tissue reactions to particles from such components are rare but carry devastating complications that have been associated with massive osteolysis and subsequent implant failure. Adverse tissue reactions are perhaps best understood in metal-on-metal bearing surfaces, due to their long track record and the advent of hip resurfacing arthroplasty. The first description of a local reaction to metal bearings was provided by Evans and colleagues in 1974 and was believed to be related to a hypersensitivity reaction to cobalt chrome alloys. Since the initial description, metal sensitivity has been further characterized by a predominantly lymphocytic immune response and is histologically described by aseptic lymphocytic vasculitis-associated lesions (ALVAL) in both the presence and absence of excessive metal wear. Clinically, soft-tissue changes due to metal-on-metal hypersensitivity are manifested through effusions or soft-tissue masses referred to as pseudotumors and lead to early osteolysis and failure. Pseudotumor formation has been associated with higher circulating levels of cobalt and chromium and has
recently been linked to increased edge loading and increased combined anteversion.\textsuperscript{11}

Unfortunately, the causal relationship between non-metal-on-metal bearings and adverse local soft-tissue reactions has not been as well-established. Although polyethylene wear debris is considered to be the most common cause of aseptic loosening in THA, its relationship with the development of soft-tissue masses has not been clarified. Furthermore, limited literature exists on the relationship between ceramic bearings and adverse soft-tissue reactions.

Therefore, the purpose of the present study was to provide a comprehensive systematic review of the published medical literature that has dealt with the natural history and therapeutic options for dealing with adverse soft-tissue reactions in non-metal-on-metal THAs. The presence of confounding factors that can cloud the relationship between THA and the de novo formation of a malignant process (such as infection, metabolic disease, social habits, and prior medical history) are beyond the scope of this review and are discussed elsewhere.\textsuperscript{12}

Our primary question was “Is there a consistent histological finding associated with benign soft-tissue masses in non-metal-on-metal THAs and is it bearing-specific?” Secondary questions included 1. What are the spectrums of patient presentations associated with these types of tissue reactions? 2. Is there a consistent diagnostic strategy? and 3. Is revision surgery necessary to prevent local recurrence?

Materials and Methods

Methods of the analysis and inclusion criteria were specified prior to literature review. An online literature search was conducted using Medline\textsuperscript{®} and Embase\textsuperscript{™} bibliographic databases, utilizing the following keyword searches: “total hip arthroplasty” and “soft-tissue reaction,” “soft-tissue mass,” “pelvic mass,” “thigh mass” and “pseudotumor.” Titles and abstracts of articles retrieved from the search were then appraised for adherence to predetermined exclusion criteria. Exclusion criteria included 1. inadequate description of types of articular bearing surfaces utilized; 2. use of primary metal-on-metal total hip prosthesis; 3. use of a resurfacing prosthesis; 4. negative indications of active periprosthetic infection; 5. previous patient history of local or metastatic malignancy; 6. lack of histological diagnosis achieved through fine needle or open biopsy; and 7. basic science study involving non-human subjects. The translated abstracts from reports published in foreign languages were also considered for analysis. Once relevant studies were identified, their citation lists were perused in order to ascertain additional articles. Furthermore, the most recent Proceedings of the American Academy of Orthopaedic Surgeons (March 2010) was reviewed in order to identify any recent case series or presentations of non-metal-on-metal soft-tissue reactions.

Within each relevant article, information regarding the type of bearing surface, presenting symptom(s) secondary to soft-tissue mass, timing of symptom(s) since initial surgery, diagnostic investigations undertaken, status of surrounding prosthetic components and bone stock, final histological diagnosis, and type of revision procedure, if necessary, were recorded. Initially, attempts were made to divide outcomes according to the bearing surface utilized in the relevant study. However, due to the paucity of literature related to soft-tissue reactions to ceramic wear and the relative abundance of metal-on-polyethylene literature, results were summarized in order to answer pre-analysis questions.

Results

Twenty-seven published articles representing 31 cases of adverse soft-tissue reactions in non-metal-on-metal THAs met the exclusion criteria and were retained for analysis. All of the articles were case reports and were retrospective in nature. Of the 31 identified cases, 28 involved primary metal-on-polyethylene bearing surfaces,\textsuperscript{13-36} one cemented metal-on-poly revision following ceramic head fracture,\textsuperscript{37} one primary alumina ceramic on metal,\textsuperscript{38} and one primary alumina ceramic on polyethylene.\textsuperscript{39} Of the primary metal-on-polyethylene cases, 14 involved at least one cemented component and 14 were cementless.

Is There the Presence of a Consistent Histological Diagnosis?

Histological characteristics of soft-tissue masses were consistent among the cases involving metal-on-polyethylene bearings. Twenty-seven of the 29 cases were histologically described as being cystic in nature, with specific features of an external fibrotic, necrotic capsule (6/29) containing a cell population made-up of histiocytes (16/29), giant cells (14/29), and foamy cells (8/29). Positive birefringence indicating polyethylene debris was described in 20 of the 29 cases. Two cases, both uncemented metal-on-polyethylene bearings, described synovial cysts containing polyethylene debris but consisting of few inflammatory cells.\textsuperscript{14,15} There was also one case of a periprosthetic extra-cranial meningioma.\textsuperscript{31}

Specific mention of metallic debris, including cobalt, chromium, and molybdenum fragments, was found in five cases.\textsuperscript{16,23,27,30,37} Interestingly, although metal debris is mentioned in five cases, lymphocytes were histologically absent from the soft-tissue mass in four of the five cases. The only finding of lymphocytic involvement in a metal-on-polyethylene bearing surface was found in a study performed by Svensson and coworkers,\textsuperscript{27} who described the presence of a pseudotumor-like soft-tissue mass containing an extremely high-amount rate of metal debris, due to taper corrosion. Despite these unique findings, at no point were plasma cells described in studies involving metal-on-polyethylene bearing surfaces.

Cases involving alumina ceramic-on-polyethylene\textsuperscript{39} and alumina ceramic-on-metal\textsuperscript{16} exhibited similar findings to those seen with metal-on-polyethylene, with a thick fibrous
Is There A Consistent Spectrum of Presenting Symptoms?

Ipsilateral leg pain (21/31), presence of a mass (17/31), and impaired ambulation (19/31) were the most consistent complaints described in all patients suffering from adverse local tissue reactions in non-metal-on-metal THAs. Asymptomatic presentations were described in two cases.\(^{19,23}\) Specific identification of an enlarged iliopsoas bursa was described in two cases.\(^{24,30}\) Furthermore, depending on the size and location of the soft-tissue mass, additional symptoms due to compression of surrounding structures were also reported. Neurological deficits secondary to sciatic nerve compression\(^{16}\) and femoral nerve neuropathy\(^ {33}\) were reported. Femoral vein occlusion leading to proximal deep vein thrombosis was described in two cases.\(^ {30,35}\) Ureteral obstruction and hydronephrosis as well as vaginal and rectal symptoms were described secondary to a large intrapelvic soft-tissue mass.\(^ {17}\)

With regard to the interval between insertion of the THA and presentation secondary to adverse soft-tissue reactions, a clear difference was noted. Primary metal-on-polyethylene bearings had a mean interval of 11.4 years, ranging between 3 and 26 years since surgery. The single alumina ceramic on polyethylene had a 13-year interval. The revision metal-on-polyethylene following ceramic fracture presented only 9 months following surgery. The ceramic-on-metal implant presented only 6 months following surgery.

Is There A Consistent Diagnostic Strategy?

In addition to radiographs, computed tomography (CT) of the pelvic region was almost universally utilized (25/31) during the diagnostic process. Biopsy of the soft-tissue mass either through percutaneous or open means was performed in 12 of the 31 cases. Ultrasound visualization (7/31), duplex venography (5/31), arthrography (4/31), magnetic resonance imaging (MRI) (3/31), and bone scanning (2/31) were also utilized, depending on the presenting symptoms.

Is There A Consistent Therapeutic Strategy?

The choice of operative versus nonoperative interventions was dependent on the presence or absence of loosening secondary to osteolysis at the time of presentation. Aseptic loosening was described in 27 of the 31 cases, and revision of at least the loose component was offered to the patient in all cases. Two patients refused revision arthroplasty.\(^ {17,23}\) Of the remaining cases, where no loose components were initially identified, eventual operative intervention occurred. Exchanging of the polyethylene liner occurred in two cases,\(^ {22,32}\) while revision to alternate bearing surfaces took place in the other two remaining cases.\(^ {36,37}\)

Only one case of attempted nonoperative management through repeated drainage of the soft-tissue mass by percutaneous incisions was found. Regis and associates\(^ {35}\) noted that in the presence of a soft-tissue granuloma secondary to a metal-on-polyethylene recurrence of the soft-tissue mass and associated symptoms occurred twice following drainage and only completely resolved following revision arthroplasty.\(^ {35}\)

Discussion

Results from the present analysis suggest that adverse local soft-tissue reactions are a clinically important entity in non-metal-on-metal THAs that, when suspected, warrant a diagnostic work-up and consideration for component revision. Such reactions usually present as symptomatic pelvic cystic masses and consist of a granulomatous reaction that appears to emerge secondary to polyethylene wear debris. As has been seen in metal-on-metal bearings, adverse soft-tissue reactions in non-metal-on-metal THAs often involve an aggressive osteolytic process and likely lead to implant failure if left untreated.

The major limitation affecting this study involves limited reports of alternate bearing surface wear soft-tissue reactions. Traditional metal-on-polyethylene THAs comprised over 90% of the cases that were qualified for analysis, permitting few conclusions to be drawn about soft-tissue reactions secondary to ceramic bearings, which were only represented in two cases. Fortunately, two recent retrieval studies involving mechanically loose ceramic-on-ceramic bearings revealed that periprosthetic tissue changes in response to ceramic wear exhibited multiple histiocytes and tissue fibrosis,\(^ {40}\) with little to no plasma cells or lymphocytes,\(^ {41}\) suggesting a similar soft-tissue immune reaction as seen with metal-on-polyethylene wear.

Recent investigations have indicated that soft-tissue reactions may be more common than previously suspected in mechanically loose THAs. Hisatome and colleagues\(^ {19}\) report two cases of hidden intrapelvic granulomas in loose non-metal-on-metal bearing surfaces that would have been missed during revision surgery had it not been for adequate preoperative imaging. Furthermore, soft-tissue changes secondary to particle wear were found on MRI in 33% of non-metal-on-metal THAs at a minimum of 12 months following surgery.\(^ {42}\) Further study is warranted to determine the clinical sequelae of these changes.

Conclusion

The present analysis indicates that adverse local soft-tissue reactions in non-metal-on-metal THAs are a potential cause of destructive osteolysis and implant failure. Within the presence of loose components, biopsy of the affected area should be performed to identify the inciting wear particle and revision to alternate bearing surfaces should be considered as a definitive intervention. Taper corrosion is a rare cause of adverse soft-tissue reaction in non-metal-on-metal THA.
and can be addressed through revision to a noncorrosive ceramic interface.

**Disclosure Statement**

John Antoniou, M.D., is a consultant for Depuy, Johnson & Johnson. None of the other authors have a financial or proprietary interest in the subject matter or materials discussed, including, but not limited to, employment, consultancies, stock ownership, honoraria, and paid expert testimony.

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