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Original Article

The Diagnosis of Infection in Metal-on-Metal Hip Arthroplasties

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ABSTRACT

Background: Distinction of aseptic from septic hip arthroplasty failure can be challenging. Some studies report an increased incidence of septic failure with metal-on-metal (MoM) hip arthroplasties. The Musculoskeletal Infection Society (MSIS) have formulated criteria to facilitate the diagnosis of periprosthetic joint infection (PJI). In this study, we determined the prevalence and histologic features of septic MoM hip failure.
Methods: Overall, 104 cases of failed MoM hip arthroplasty, classified as septic or aseptic by MSIS microbiological criteria, were analyzed. The overall prevalence of septic failure was determined and the nature of the causative organisms noted. The extent of the neutrophil polymorph (NP) infiltrate in periprosthetic tissue in all cases was analyzed by hematoxylin-eosin and chloroacetate esterase staining.
Results: The prevalence of septic MoM hip arthroplasty failure was 6.7%. Infective organisms were coagulase-negative *Staphylococcus* in 4 cases; *Staphylococcus aureus*, *Streptococcus*, and *Propionibacterium* species were isolated in the remaining cases. Chloroacetate esterase staining facilitated identification of NPs. All cases of PJI contained more than 5 NPs per high-power field (HPF) on average. Four cases of aseptic MoM implant failure contained scanty or scattered NPs (less than 5 per HPF on average).
Conclusion: The prevalence of PJI as a cause of MoM hip arthroplasty failure was relatively high compared to other hip bearing combinations; however, the organisms responsible were similar. Histologically, a minority of aseptic MoM implant failures contained some NPs, but the MSIS criteria for the histologic diagnosis of PJI (>5 NPs/HPF) correctly identified all microbiologically confirmed cases of septic failure.

Periprosthetic joint infection (PJI) is a relatively uncommon complication of hip arthroplasty; it has been reported to occur in approximately 1%-2% of primary total hip arthroplasties in most specialist orthopedic centers, although epidemiologic studies suggest that the incidence may be higher [1-5]. The diagnosis of PJI can be challenging, particularly in cases of delayed or late loosening, which are usually due to pathogens of low virulence, mainly coagulase-negative *Staphylococcus* (CNS) [2,6]. Additional laboratory investigations, such as determination of the erythrocyte sedimentation rate, C-reactive protein, and isotope bone scans and histopathology are commonly used to distinguish septic from aseptic implant failure [6-10]. The Musculo-Skeletal Infection Society (MSIS) have formulated clinical, microbiological, and histologic criteria for the diagnosis of PJI [8].

Metal-on-metal (MoM) hip arthroplasty was extensively used in recent years, especially in young patients with hip arthritis. Although MoM implants are associated with less volumetric wear, the number of nanosized cobalt–chrome (Co–Cr) particles released is higher [11-13]. Deposition of these particles in periprosthetic tissues results in extensive necrosis, a heavy foreign body macrophage response, as well as a pronounced, cell-mediated specific immune response characterized histologically by the presence of a prominent, often perivascular lymphoid infiltrate termed aseptic lymphocyte-dominated vasculitis-associated lesion (ALVAL) [14-16]. The effect of these profound inflammatory and necrotic changes in MoM periprosthetic tissues on the likelihood of

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developing PJI is uncertain. There are several case reports documenting MoM implant failure and pseudotumours being associated with infection [17-20]. In one small case series of 9 MoM total hip arthroplasties undergoing revision for local soft tissue reactions, 3 were found to be concomitantly infected [21]. In a larger study of 124 MoM hip arthroplasty cases, the rate of infection was 5.6% [22]. Other studies, however, have not reported an increased incidence of infection associated with MoM hip arthroplasties [23-27].

To determine more accurately the prevalence of MoM hip implant failure, we used microbiological criteria to identify cases of PJI in 104 cases of failed MoM hip arthroplasties undergoing revision for presumed aseptic modes of failure. We also investigated whether the organisms causing septic MoM hip implant failure are similar to those seen with other (non-MoM) types of hip implant and determined whether the nature of the infecting organism was associated with specific histologic findings. Periprosthetic tissues associated with MoM hip implant failure often show significant necrosis and contain a heavy inflammatory infiltrate. We therefore analyzed histologic findings in both septic and aseptic MoM hip implant failures with regard to the number of neutrophil polymorphs (NPs) in periprosthetic tissues to determine if the histologic criteria previously described are valid in this context.

Materials and Methods

Cases Examined

Overall, 104 cases of MoM hip implant failures, revised over a 3-year period (January 2012-December 2014), in our tertiary referral center (Nuffield Orthopaedic Centre, Oxford, UK) were analyzed, in this institutional review board–approved study. The age range of the patients was 34-89 years. There were 46 males and 58 females. In all cases, the original arthroplasty was carried out for osteoarthritis. Hundred of the 104 (96%) cases were primary cases and 4 were conversions of resurfacings to large head total hip arthroplasty for periprosthetic fracture. Thirty-six (35%) had the index MoM arthroplasty performed at our institution. Implant details are shown in Table 1. Clinical and operative findings were noted in cases of septic implant failure. Reasons for revision included pain and a pseudotumour (confirmed by both preoperative imaging and intraoperative findings) around the hip in 82 cases (79%), component loosening in 6 (6%), and pain only in 16 (15%). None of the cases were thought to be PJIs before revision. All the cases were consented for research.

Microbiological and Histologic Analysis

We have used microbiological criteria [8] (isolation of a pathogen from microbiological cultures in at least 2 separate tissue samples) to establish a diagnosis of definitive PJI in the cases studied. For microbiological investigation, samples of periprosthetic tissue were cultivated by direct and enriched methods as previously described [28]. The nature of the infecting organism was documented.

Specimens from the joint capsule and from the femoral and acetabular pseudomembrane of hip revision arthroplasties were submitted for histologic analysis. The tissues were fixed in formalin and 5-μm paraffin sections cut and stained with hematoxylin-eosin and chloroacetate esterase enzyme histochemistry as previously described [29]. A histologic finding of more than 5 NPs per high-power field (HPF) on average provides supportive evidence for the diagnosis of PJI [8]. Accordingly, we examined at least 5 HPFs (1.55 mm^2) in 5 different areas of each histologic section (ie, 25 HPF) and counted the number of NPs in these 5 areas. From this the average number of NPs per HPF (×400 magnification) was calculated. Gram staining was also carried out on all hip revision arthroplasty cases, which contain NPs in samples of periprosthetic tissues.

Table 1
Surgical Details of Implants Revised.

Surgical Details	Number
Implant survival, y (range)	7 (2-13)
Index performed at our center	36
Implant type	
HRA (%)	62 (60%)
THA (%)	42 (40%)
Implant name	
BHR	35
ReCap	4
CONSERVE	16
CORMET	5
ASR	2
CPT	5
ASR	3
CORAIL/Pinnacle	3
Not available	31
Head size/mm (range)	48 (42-54)

THA: Smith & Nephew, Leamington Spa, UK; ReCap and CPT: Biomet, Warsaw, IN; CONSERVE: Wright Medical, Arlington, TN; CORMET: Corin, Cirencester, UK; and ASR, ASR, and CORAIL/Pinnacle: DePuy, Warsaw, IN.
BHR, Birmingham hip resurfacing; HRA, hip resurfacing arthroplasty; THA, total hip arthroplasty.

Results

Seven of the 104 cases in this study were diagnosed as PJI. Clinical and microbiological details of these cases are shown in Table 2. The organism isolated in 4 cases was CNS; *Staphylococcus aureus*, *Streptococcus sanguinis*, and *Propionibacterium* species were isolated in each of other 3 cases (Table 2).

Histologic Analysis

Histologic analysis of periprosthetic tissues from all microbiologically confirmed cases of septic implant failure showed that they contained a heavy NP (>5 NPs per HPF on average) infiltrate (Fig. 1A). This was confirmed by chloroacetate esterase staining, which facilitated identification of NPs (Fig. 1B). There were no specific differences in the nature of the acute inflammatory infiltrate with regard to the type of infecting organism. In addition to numerous NPs, these cases of septic MoM hip arthroplasty failure showed extensive tissue necrosis (Fig. 1C) and contained a macrophage response to Co–Cr wear particles (Fig. 1C). A scattered lymphocyte and plasma cell infiltrate was noted, and there were perivascular lymphoid aggregates (Fig. 1D). In most cases of aseptic MoM hip arthroplasty failure, NPs were absent but, in 3 cases, scanty NPs (less than 1 per HPF on average) were noted; in 1 case, 4 NPs per HPF on average was noted (Fig. 2). No organisms were identified on Gram staining in any of the cases analyzed.

Discussion

The MSIS has formulated criteria whereby clinical, microbiological, histologic, and other laboratory findings are used to define the presence or absence of a PJI [8]. We applied the previously described microbiological criteria for the diagnosis of PJI to presumed aseptic cases of MoM hip implant failure and found that 6.7% of these cases were infected. One of the supportive criteria for the diagnosis of PJI, the histologic finding in periprosthetic tissues of >5