Case Series

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Under-reporting by surgical pathologists in tissue removed during revision surgery for metal-on-metal arthroplasties

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Abstract

Although adverse local tissue reactions (ALTR) have been reported for metal-on-metal implants (MoM) requiring early revision surgery, no study has looked at the accuracy of surgical pathologists in diagnosing ALTR. This study aims to investigate the accuracy of reporting adverse local tissue reactions in tissue samples following revision surgery from metal-on-metal implants. The authors reviewed histology glass slides as well as the original pathology reports of tissue processed in revision arthroplasties in 23 cases. These samples were microscopically analyzed for tissue necrosis and cystic degeneration, the presence of metal particles, corrosion byproducts, membrane formation, histiocytic cells, lymphocytic cells, and vascular pathology. The authors' findings were then compared to their corresponding original pathology reports. The authors found consistent under-reporting of the tissue findings. Most importantly, 18 samples showed evidence of metal present compared to 2 samples on original pathology reporting. The authors found that 15 samples showed evidence of pathological membranous tissue compared to just 6 on original pathology reporting. While just 3 of the original pathology reports indicated the presence of areas of predominantly lymphocytic inflammatory cells, the authors found 13 examples of such areas. Although ALTR reactions have been described as a sequala of failed MoM, the authors' data suggest that ALTR may occur more frequently than previously described. Under-reported findings of ALTR deprive both the patient and orthopaedic surgeon of important information that can help guide further follow-up.

Keywords: adverse local tissue reactions, metal-on-metal arthroplasty, metallosis, revision arthroplasty

Introduction

Despite being one of the most significant developments in surgery in the last 70 years, there is still no perfect joint implant to replace the natural joint, so efforts to improve materials and design continue. During the 1990s, there was a renewed interest in metal-on-metal (MoM) implants for hip arthroplasty due to the absence of polyethylene debris and reputed decreased wear rates and dislocations. At one point, MoM implants were used in approximately one-third of all total hip arthroplasties in the United States[1].

HIGHLIGHTS

- Tissue reactions in failed metal-on-metal arthroplasties are often unrecognized.
- As a result, the patient's surgeon may not do the appropriate follow-up.
- If not reported, this can have medical consequences for the patient.

However, over time, it became apparent that many patients were experiencing clinical problems and early failure of the implants, necessitating revision due to factors suspected to be unique to MoM implants[2]. One reason for early failure in MoM implants was found to be adverse local tissue reactions (ALTR), a constellation of pathologic findings in tissue removed during revisions due to the damaging effects of the presence of metal, debris, and corrosion byproducts[3]. Failures have led to premature revision surgeries, FDA warnings, lawsuits, and manufacturing recalls. Given the number of MoMs still implanted in patients, additional cases undergoing surgery may be ongoing for years. Since proper documentation of ALTR by pathologists reviewing tissue removed at the revision surgery is critical for ongoing patient care and monitoring by the patient's physicians, we reviewed our experience with such cases.

Material and methods

The material studied was from the consultation cases of one of the co-authors (V.J.V.). The consultations were initiated by

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litigations involving failed metal-on-metal revision total hip arthroplasties. Both the histology slides from the cases and the original surgical pathology reports from the hospitals where the original revision surgeries took place were retrieved. In each case, the slides were reviewed by a board-certified pathologist with more than 40 years of experience in orthopaedic pathology cases, including in cases with failed revision arthroplasties.

The glass slides that were reviewed had been made at the original hospital pathology laboratory. In each case, we looked for and documented the tissue changes that have been reported in the literature as ALTR in failed MoM arthroplasties (Table 1)[4–13]. Our review took place after the reports by the original surgical pathologist were completed and signed out. We examined the slides blinded from the findings in the original surgical pathology reports. After our microscopic review of the slides, we compared our findings with those reported by the pathologist in the original surgical pathology report. We examined each case for changes including tissue changes, necrosis and cystic degeneration, the identification of metal and corrosion byproducts (Figs. 1 and 2), the presence of membranes (Fig. 3), changes in the membranes such as ulceration or pseudosynovial hyperplasia of the membrane, the presence of histiocytic cells (Fig. 4) lymphocytic cells, and vascular pathology, including necrotic vessels and intravascular thrombi.

Although we realize that changes such as necrosis and cystic degeneration identified in isolation are non-specific, they are relevant in revision MoM cases as they may correlate well with the formation of so-called pseudotumors by MRIs. We documented if tissue changes included the formation of membranous tissue having a superficial lining of cells mimicking synovium.

Table 1

Composite of tissue findings

	Original report	Our findings
Tissue changes		
Necrosis	1	17
Cystic degeneration	0	3
Metal		
Metal identified	2	18
Corrosion byproducts	0	12
FBGCR	0	3
Membranes		
Membranes identified	6	15
Pseudosynovial hyperplasia	1	10
Ulceration	0	10
Metal present	0	3
Histiocytic cells		
Histiocytic cells identified	11	17
Infiltrating pattern	3	9
Intracytoplasmic metal	3	15
Inflammatory cells		
Predominantly lymphocytes	3	13
ALVAL like pattern	2	10
Multinucleated giant cells	4	4
Vascular pathology		
Endothelial cell hyperplasia	0	2
Necrotic vessels	0	5
Intravascular thrombi	0	4

Comparison of incidence of findings in original pathology reports and our analysis.
ALVAL, aseptic lymphocyte-dominant vasculitis associated lesion; FBGCR, foreign body giant cell reaction.

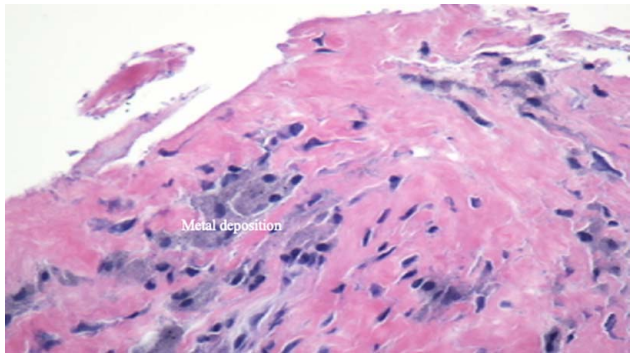

Figure 1. Histiocytes infiltrating fibrous tissue. Intracytoplasmic black metal flecks can be seen. (hematoxylin and eosin stain, magnification 400×).

Such membrane formation has been a well-documented tissue feature in MoM revisions, often described as "pseudosynovial". In many such cases, the pseudosynovial membranes demonstrated villous projections, fibrin deposition, and, most significantly, ulceration and bleeding. We also recorded whether histiocytic cells or lymphocytes were present as classification of the histologic changes in revision MoM cases run the gamut from predominantly one of histiocytic infiltration to one with a predominantly lymphocytic infiltration to cases with both present[4,13]. We recorded if lymphocytes were present in a perivascular pattern as this pattern was found in early descriptions of tissue in MoM revisions, which led to the term ALVAL (Aseptic Lymphocyte Vasculitis Associated Lesion). We refer to such findings in our review as "ALVALISH" (Fig. 5). This case series has been reported in line with the PROCESS Guideline.

Results

We found consistent under-reporting of the tissue findings associated with failed MoM arthroplasties. Our tissue findings and the findings in the original surgical pathology reports are

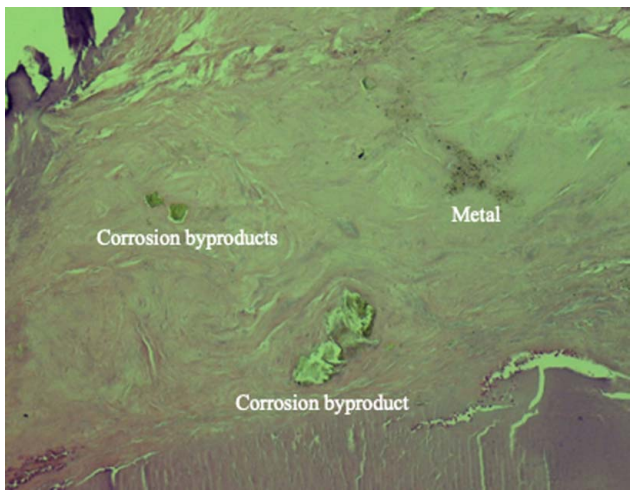

Figure 2. Corrosion byproducts appear as yellowish green deposits. Aggregates of dark black flecks of metal are seen. (hematoxylin and eosin stain, magnification 200×).

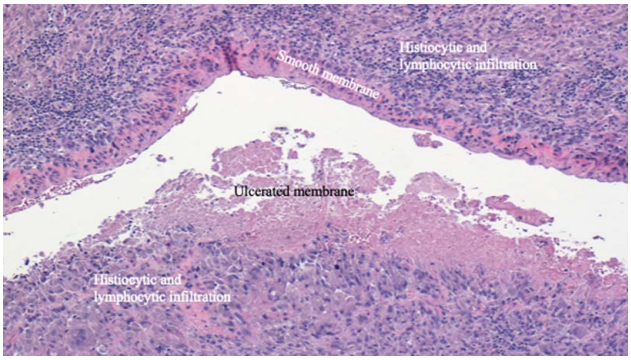

Figure 3. The formation of membranous tissue shows both smooth surfaced membranes (top) and ulcerated membranes (bottom). Below the surface lining cells marked histiocytic and lymphocytic infiltration can be seen. (hematoxylin and eosin stain, magnification 100×).

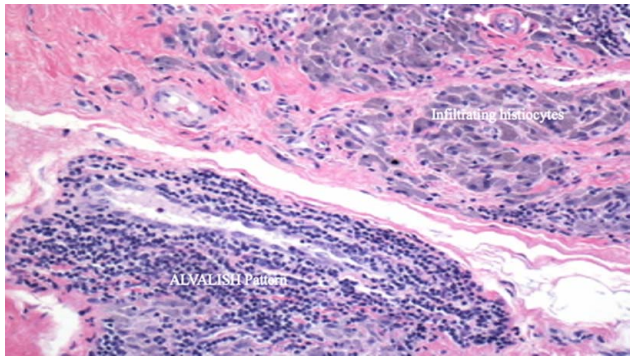

Figure 5. Perivascular lymphocytic infiltration is demonstrated in the bottom of the photo and histiocytic infiltration in the top. (hematoxylin and eosin stain, magnification 200×).

tabulated in Table 1. The most frequently under-reported findings are listed in Table 2. We note that some findings, such as tissue necrosis, are non-specific. But under-reporting of pathologic findings more specifically relevant in revision surgeries of MoM, such as the presence of metal, corrosion byproducts, and tissue infiltration by histiocytes often with engulfed metal, is of importance as the potential toxicity of increased cobalt and chromium in the human body is well documented[14].

Discussion

Introduced by Sir John Charnley in England in the 1960s, joint replacement surgery of the hip is a very commonly performed procedure worldwide. In the United States, it is projected to reach over 600,000 surgeries by 2030[15]. Charnley's original implants were made of stainless steel, but since that time, many different materials and designs have been introduced. Currently, most implants contain cobalt and chromium metal.

Although most implants are expected to last at least 20 or more years, complications that are associated with clinical symptoms will eventually occur over time, requiring revision surgery. Since revision surgeries are also associated with greater expense, prolonged and more difficult procedures, and poorer clinical outcomes[5], understanding the associated tissue pathology findings is important in guiding further management.

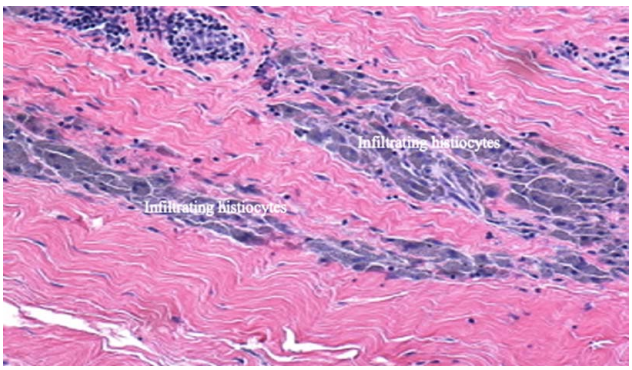

Figure 4. Histiocytes are infiltrating the tissue and are darkened due to intracytoplasmic metal (hematoxylin and eosin stain, magnification 200×).

Given the expected increase in arthroplasty surgeries in the future, it is prudent to understand and avoid implants that are more prone to failure. It is equally prudent that the pathologic changes in the tissue removed at revision surgeries be accurately documented in the final pathology report by the surgical pathologist evaluating the tissue that was removed.

By the mid-2000s, MoM arthroplasties came under scrutiny due to patient complaints of pain and soft tissue reactions secondary to the release of cobalt and chromium metal particles and corrosion byproducts being deposited into the surrounding hip tissue and bloodstream. Initially considered isolated anomalies in case reports, registry reports such as that of the Australian Orthopaedic Association National Joint Replacement Registry documented a more substantial number of cases[16]. MoM hip implants have since been recalled from the market or de-commercialized by device manufacturers who have had, in some cases, compensated billions to patients who have had these implants[17]. Nonetheless, many patients still have these implants in their bodies, and the surveillance of complications that arise from them continues[18–20]. In current practice and the literature, the term ALTR or adverse reaction to metal debris (ARMD) have been increasingly used as terms that encompass the various changes in local tissue that can be seen due to the release of metal particles and the ensuing cascade of tissue damage. Since ALTR in MoM arthroplasties has been shown to be a negative predictor of implant survival[21], documentation of ALTR in tissue removed at revision surgery is of paramount importance. Our findings

Table 2

Most notable under-reported tissue findings

Feature	Instances in original path reports	Instances in our findings
Metal identified	2	18
Intracytoplasmic metal	3	15
Corrosion byproducts identified	0	12
Membranes present	6	15
Pseudo synovial membranes	1	10
Ulceration	0	10
Necrosis	1	17
Infiltrating patterns of histiocytes	3	9

A selection of some frequently under-reported tissue findings between original pathology reports and our analysis.

document that surgical pathologists often under-report ALTR in tissue removed in revision MoM arthroplasties (Table 2). Of particular concern is the under-reporting of the presence of metal and corrosion byproducts. Metal particles such as cobalt and chromium from implants can circulate systemically via the lymphatics and bloodstream to lymph nodes, bone marrow and the liver and spleen and, if systemically circulating in the blood at high levels, can lead to toxicity of tissue organs[14]. In addition, metals degrading and undergoing oxidation can lead to oxidized corrosion byproducts such as chromium phosphates, which can cause multinucleated foreign body type giant cell reactions that can contribute to the formation of pseudotumors, which, if large, can cause local tumour-like effects in the patient. Under-reporting of such findings by surgical pathologists in revision MoM arthroplasties has potential detrimental ramifications for both the patient and the orthopaedic surgeon. It deprives both of knowing the extent of pathologic findings, which would help dictate appropriate clinical surveillance. If metal is present and not reported, the surgeon may not consider a more cautionary degree of follow-up for the potential damaging effects of local and disseminated cobalt and chromium, for which cut-offs for concern and algorithms to monitor the adverse effects have been proposed[22–32].

Under-reporting also deprives the ability of radiologists to retrospectively correlate MRI findings with the subsequent tissue findings, MRIs currently being the best cross-sectional imaging modality to evaluate and classify ALTR in MoM cases[31,33,34]. Inadequate documentation of ALTR can also deprive patients of appropriate compensation for their pain and suffering in litigated cases. There are several possible reasons for surgical pathologists to underreport ALTR. They may not be familiar with the tissue findings in ALTR. The submitted tissue and paperwork from surgery may not alert the pathologist to the reason for the submission of the tissue or request the pathologist to look for ALTR. In most instances of tissue submitted from a revision arthroplasty, the pathologist is looking for evidence of a prosthetic joint infection or osteolysis due to a reaction to polyethylene or cement debris. In light of the MoM experience, efforts are underway for a more careful evaluation and introduction of new devices as it is now clear that inadequate investigation of new devices potentially exposes both patients and their physicians to catastrophic consequences[35].

Although invaluable, surgical pathology reports on tissue submitted from revision MoM arthroplasties are not the only factor used to monitor a patient's treatment and follow-up. The surgeon's clinical impression and judgement, any available serum cobalt and chromium blood metal levels, including surveillance by published algorithms monitoring such levels[29,31–34], and radiographic findings, including MRIs, should be taken into account. It is our experience that surgical pathologists need more training in identifying and recording tissue findings in ALTR revision cases. These findings of ALTR or ARMD, terms used for the constellation of findings that may be found in such cases, are well documented in this and other publications[4,6,8,10,12,13] and can form a core curriculum in residency training programs in pathology.

Ethical approval

Ethics clearance was not needed as the study was based on the review of archived tissue slides from the biopsied tissue. Patients were not identified in the study.

Consent

This is not applicable as we studied archived tissue samples.

Source of funding

Not applicable.

Author contribution

A.V. and V.V., S.P., E.B. all contributed to study design, data collection, data analysis and interpretation and writing the paper.

Conflicts of interest disclosure

A.V. gave expert testimony in the past and received eight payments from Weitz and Luxenburg Law Firm. Otherwise NA.

Research registration unique identifying number (UIN)

We did not recruit patients for this study. It was based on archived tissue samples.

Guarantor

Vincent Vigorita.

Data availability statement

Data are available upon reasonable request.

Provenance and peer review

Not applicable.

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