Soft Tissue Histology Around Metal-On-Metal Hips

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ABSTRACT INTRODUCTION:
Metal-on-metal bearings were introduced to reduce the volume of wear debris and the subsequent histiocytic reaction in the periprosthetic tissues and the osteolytic reaction in the bone. While clinical results have been generally satisfactory, recent reports of pseudotumor formation in and around painful hips implanted with metal-on-metal joint replacements have raised new concerns. The etiology of these soft tissue masses has been attributed to either a reaction to high implant wear levels, or to a hypersensitivity reaction to low or normal amounts of wear (1). This interpretation was largely based on the histological appearance of lymphocyte aggregates in the some of the tissues. We have had the opportunity to examine a number of metal-on-metal total hip replacements bearings that were revised for suspected metal sensitivity and for component malpositioning which can cause high implant wear. We have noted features of aseptic vasculitis associated lesions (ALVAL, 2) in both, which can lead to difficulty diagnosing the cause of this lymphocyte dominated response. The aim of this study was to characterize the histopathological and clinical features of both groups of patients and to determine what criteria, if any, could be used to differentiate the cause for their pain.

METHODS:
Group 1: eight cases were revised for pain from suspected metal sensitivity; this group comprised 3 total hip replacements with large diameter metal-on-metal bearings and 5 hip resurfacings from 3 male and 5 female patients at average 2 years post-op (range 12 – 36 months). Typically these patients reported ongoing groin pain within the first 6 months of the original surgery.

Group 2: eight cases were revised at average 24 months (range 10-39) because of pain, swelling and/or high serum ion levels associated with implant malpositioning or suspected high wear. This group comprised 1 male with a total hip replacement and 7 female patients with hip resurfacings. One hip resurfacing obtained at autopsy after 77 months was found to have a mass (pseudotumor) within the joint.

Group 3: the following tissues were included for comparison: capsule tissue from a revised metal-on-polyethylene hip with marked metallosis, primary tissue from an osteoarthritic hip, and tissues from 2 metal-on-metal hip replacements with mechanical impingement but without high wear revised at 4-15 months.

None of the patients had clinical signs of infection and no positive cultures were obtained from intra-operative cultures.

The implants were removed and submitted for retrieval analysis, including wear measurement by coordinate measuring machine. Periprosthetic tissues included capsule and enlarged bursas. Tissues were fixed in formalin, paraffin embedded, sectioned and stained with hematoxylin and eosin. Serial sections were stained using standard immunoperoxidase techniques with markers for B and T lymphocytes, plasma cells and macrophages. All staining was performed at a specialized facility and positive and negative controls were included in each batch. The slides were reviewed in a blinded fashion and key histological features and predominant cell types were noted. An ALVAL score was applied by ranking the number of lymphocytes from 0 to 3+ and the degree of tissue involvement from 0 to 4 for a total of 12. The results of these analyses were reviewed with clinical variables, radiographs and implant retrieval findings.

RESULTS SECTION:
There was often considerable variation within the histology of each case but the following trends were observed. Tissues with an ALVAL score of more than 6 from both groups 1 and 2 typically contained large numbers of macrophages and lymphocytes but the arrangement of the cells and the predominant lymphocyte type was often different. In Group 1 revised for suspected metal sensitivity, lymphocytes were usually arranged away from the surface, often as large, dense perivascular aggregates behind a wide layer of necrotic tissue lined by fibrin. These aggregates included CD3 and CD20 positive lymphocytes in variable proportions (Fig 1), and often contained plasma cells. Macrophages often were located around these aggregates or interposed between the lymphocytes and the surface. The typical synovial surface features were often replaced by adhered, organizing fibrin. By contrast, in Group 2, smaller perivascular lymphocyte aggregates, which were predominantly CD20 positive, and scattered macrophages were both distributed throughout the tissue, and the synovial surface was usually preserved. The histology of the pseudotumor was consistent with other cases in Group 2 and the wear measurements confirmed high wear (77 microns femoral wear depth). Group 3 tissues contained very few lymphocytes and the ALVAL scores were low. There was no clear relationship between the results of wear measurements, or implant factors and the immunohistopathology when the ALVAL score was <6.

DISCUSSION:
Diagnosing the cause of a painful hip replacement involves eliminating the obvious causes (infection, aseptic loosening, mechanical impingement) and this can often be achieved through a combination of radiographic and other imaging techniques and clinical lab tests. Differentiating a tissue reaction to high wear from metal sensitivity in the absence of blood ion levels, the appearance of metallosis in the tissues or component wear measurements can be difficult. We often noted considerable variation in the cellular features from site to site within each hip unless the reaction was very pronounced in which case there was better consistency from site to site. Immunohistochemical staining also was helpful as there was a clear tendency for the lymphocyte aggregates in metal sensitivity cases to contain a mixture of CD3 and CD20 positive lymphocytes while there was a strong tendency for CD3 positive cells to be reduced when the reaction was associated with higher levels of wear. Further study of additional samples is needed to verify these observations and to provide surgeons and pathologists with better guidelines for the interpretation of soft tissue reactions around metal-on-metal hip replacements.

Fig 1. Low power micrograph of CD 20 stained B lymphocytes (Brown)

Fig 1b. Low power micrograph of CD 3 stained T lymphocytes (Brown). The density of staining, the mix of T and B cells, and low implant wear suggested that this patient had a metal allergy response.