Immunohistopathology Of Tissues From Hips Revised For Suspected Metal Sensitivity

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Introduction: The histopathology of tissues from hips with failed metal-on-metal implants sometimes includes unusual lympho-plasmacytic accumulations not previously seen in tissues from metal-polyethylene implants [1,2]. Total joint replacement failures attributed to metal sensitivity have been described in association with older generation hips or knees using stainless steel (which contained the common allergen nickel), or cobalt-chromium (CoCr) metal-on-metal designs, which typically produced high wear. A small number of total hip replacements with modern generation, low-wearing CoCr metal-on-metal bearings have been revised for suspected metal sensitivity and lymphocytes were noted in those tissues. With the accumulation of over 200 failed metal-on-metal hip resurfacing specimens in our laboratory, the aim of this study was to describe the immunohistopathology of tissues from hip resurfacings revised for suspected metal sensitivity.

Materials and Methods: Because of the difficulty diagnosing metal sensitivity, cases submitted with implants, tissues and clinical details after revision for unexplained pain were studied. Retrieval analysis was performed by sectioning the femoral heads, and the analysis was used to exclude bone-related causes for the pain, such as avascular necrosis, fracture or loosening. Only cases in which infection had been excluded by the absence of cultured organisms from multiple surgical samples were studied. Periprosthetic tissues accompanying all failed implants were routinely formalin fixed, paraffin embedded, sectioned and stained with hematoxylin and eosin. A subset of cases with unusual lymphocytic infiltrations were serially sectioned and stained using standard immunoperoxidase techniques with markers for lymphocytes (CD20, CD3, CD4) and macrophages (CD68); iron was demonstrated with Perl’s stain and proliferating cells were stained with Ki67. All staining was performed at a specialized facility and positive and negative controls were included in each batch. The results of these analyses were reviewed with clinical variables, radiographs and implant retrieval findings.

Results: Sixteen resurfacings were revised for unexplained pain; retrieval analysis was unable to exclude the possibility of a bone-related cause in 9 cases (2 heads had extensive proximal osteonecrosis, 7 heads were found to be loose - median time to failure was 24 months). In this group, the soft tissues typically contained minimal lymphocytes, often arranged perivascularly and scattered throughout the tissue. One case with femoral loosening showed extensive lymphocytic infiltrates. In contrast, 4 of the remaining 7 pain cases had extensive infiltrates of lymphocytes and plasma cells in the periprosthetic tissues. Immunological staining showed that the lymphocytes included both B and T cells and were often accompanied by macrophages and fibrin deposits but proliferating cells were not abundant. Typically, the cells were arranged both perivascularly and diffusely and were separated from the surface by a thick band of necrotic tissue, often lined with thick fibrin. Although the macrophages often contained granular or globular material, it did not stain positively by Perl’s stain. In this group of 4 suspected metal sensitivity cases, the median time to failure was 34.5 months. In the remaining 3 cases, no mechanical cause for pain could be found. In two cases the periprosthetic tissues contained only small numbers of lymphocytes arranged both perivascularly and diffusely with minimal necrosis. There were only occasional lymphocytes in the large fibrous mass that was the reason for the revision of the remaining case. The measured component wear in all of these 3 cases was low.

Discussion: The pattern of inflammation in tissues from metal-on-metal hips has been described as lymphocytic vasculitis and the term ALVAL (aseptic lymphocytic vasculitis associated lesions) has been coined to describe these particular histopathological features [1]. Clinically, as well as histologically, patients with metal sensitivity differ from patients with failed metal-on-metal total hip replacements with wear debris. However, there is likely to be a “spectrum of effects” and the manifestations of metal sensitivity may differ among individuals. It is also possible that metal sensitivity can occur in conjunction with mechanical problems, or high wear, further complicating diagnosis. When all other causes for their pain have been eliminated, a diagnosis of metal sensitivity should be considered, especially when the tissues show extensive ALVAL. Timely revision should then be performed to avoid progressive local tissue damage.


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