Lubricin and α-Smooth Muscle Actin-Containing Myofibroblasts in the Pseudomembrane Around Loose Hip and Knee Prostheses


1VA Boston Healthcare System, 2Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, 3Rush University Medical Center, Chicago, IL

e-mail address: mspector@rics.bwh.harvard.edu

Introduction

Aseptic prosthetic loosening continues to be a challenging problem despite the advances in implant technology and surgical technique in patients undergoing hip and knee replacements. Since the first description of the tissue around loose prostheses as a “synovial-like membrane”, it has been appreciated that an understanding of its composition may inform therapeutic approaches to its management. We hypothesized that the pseudomembrane around loose hip and knee prostheses would: 1) bind and express lubricin, the lubricating and anti-adhesion glycoprotein, like the synovial membrane of joints; and 2) contain contractile α-smooth muscle cell actin (SMA)-expressing myofibroblasts like other scar tissues. Expression of both lubricin and SMA is stimulated mechanically and by transforming growth factor (TGF)-β, which is known to be elevated in the pseudomembrane, providing further rationale for the hypothesis; and these proteins have been found in the tissue around loose noncemented glenoid components. That the presence of these proteins in the pseudomembrane could be expected to promote loosening underscores the importance of their identification in periprosthetic tissue. The objective of this study was to immunohistochemically evaluate the presence and distribution of lubricin and cells containing SMA in tissue around loose hip and knee prostheses.

Methods

Periprosthetic tissue resected at revision arthroplasty of aseptic, loose hip (8 pts.) and knee (4 pts.) implants was obtained with IRB approval. The implant-tissue surface of the pseudomembrane was marked at the time of resection. Micronotomated sections of formalin-fixed, paraffin-embedded tissues were stained with monoclonal antibodies to lubricin and SMA. Immunohistochemical negative control sections were labeled with nonspecific immunoglobulin instead of the antibody.

The presence of lubricin was evaluated as the % of: 1) surface displaying a discrete layer of the protein; 2) extracellular matrix (ECM) containing lubricin; and 3) cells expressing the protein intracellularly (IC). The % of SMA-containing cells was also assessed. The grading of the % staining was determined as follows: 0: No staining; +: 1-25% of the surface, ECM, or cells staining; ++: 26-50% staining; +++: 51-75% staining; ++++: 76-100% staining. For statistical analysis, Grades 0, +, and ++ were taken together as “low-grade” staining and Grades +++ and ++++ were taken as “high-grade” staining. For distribution of the proteins, the above analyses were performed in the following 3 zones: 1) within 300 µm of the edge of the implant-tissue interface; 2) between Zones 1 and 3; 3) within 300 µm of the resected edge.

Results

On histologic examination, a distinct synovium-like layer was not identified in any of the samples at the implant-tissue interface; the periprosthetic tissue contained areas of metaplasia, inflammation, and fibrosis. None of the immunohistochemical negative control sections showed lubricin or SMA staining.

Lubricin was consistently seen as a discrete layer on the surface of human articular cartilage positive control samples. Fresh cut surfaces of the pseudomembrane samples, produced during trimming of the samples in preparation for paraffin embedment, did not stain for lubricin indicating the absence of edge-artifact staining.

The presence of lubricin was evident in all the pseudomembrane samples: as a discrete layer on the implant-tissue interface (black arrows, Fig. 1A); within the ECM (Fig. 1A); and IC (Fig. 1B). The majority of the implant-tissue interface of all samples displayed high-grade lubricin staining as a discrete layer a few µm thick. Zone 1 had significantly higher ECM lubricin staining than Zone 3. There was strong correlation between the IC and ECM grading of lubricin (R²=0.83-0.96), suggesting that the cells comprising the pseudomembrane were the source of at least some of the lubricin in the ECM and on the implant-tissue surface. Lubricin was found in pseudomembrane cells of morphologies consistent with macrophages (Fig. 1B) and spindle-shaped fibroblastic cells (Fig. 1B), as previous reported.

Discussion

SMA staining was present in smooth muscle cells and pericytes surrounding vessels in the pseudomembrane tissues, and in human skin controls. SMA in nonvascular cells was predominantly found in cells of fibroblast morphology (Fig. 2A), often with a crimped appearance. Positive staining was also seen, however, in macrophages and undifferentiated mesenchymal cells (black arrows). SMA staining was present in smooth muscle cells and pericytes surrounding vessels in the pseudomembrane tissues, and in human skin controls. SMA in nonvascular cells was predominantly found in cells of fibroblast morphology (Fig. 2A), often with a crimped appearance. Positive staining was also seen, however, in macrophages and undifferentiated mesenchymal cells (black arrows). SMA staining was present in smooth muscle cells and pericytes surrounding vessels in the pseudomembrane tissues, and in human skin controls. SMA in nonvascular cells was predominantly found in cells of fibroblast morphology (Fig. 2A), often with a crimped appearance. Positive staining was also seen, however, in macrophages and undifferentiated mesenchymal cells (black arrows).

Discussion

The presence of a lubricating and anti-adhesion protein in the pseudomembrane at the interface with loose hip and knee prostheses might explain why the fibrous capsule offers little stability to the implants, and why loose prostheses can be so “loose.” The presence of lubricin on the surfaces of tissue folds within the pseudomembrane would be expected to interfere with integration of the layers, which may be a prerequisite for remodeling. While the source of the lubricin could be the joint fluid in the periprosthetic “effective joint space,” there was ample evidence of lubricin expression in cells within the pseudomembrane. Myofibroblasts within the peri-implant may be responsible for contracture and densification of the fibrocollagenous tissue. This may contribute in part to both the stability of the pseudomembrane and instability of the prosthesis.

Significance

These findings deepen our understanding of the tissue response to prostheses and the process of loosening, and may inform therapeutic approaches for management of loose implants.

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References


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