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Case Report

Joint Arthroplasty Wear Debris-Associated Pathologies Simulating Malignancy (Sheep in Wolves Clothing): A Report of Two Cases

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Abstract

We report 2 cases of joint arthroplasty wear debris associated pathologies that simulated malignancy. In one case wear debris associated osteolysis radiographically simulated an osteolytic metastasis. In the second case wear debris associated lymphadenopathy simulated metastatic carcinoma to a lymph node. We discuss the pathogenesis of wear debris associated pathologies, noting pathologic differences in the two cases reported.

Keywords: *Total Joint Arthroplasty (TJA); Malignancy; Wolves Clothing*

Introduction

Total joint arthroplasty (TJA) is one of the most clinically successful, cost effective surgical interventions in all of surgery. They are highly successful for alleviating pain, improving ambulation and function for end stage arthritis. However, TJA implants undergo wear of the bearing surfaces, generating a variety of wear debris which contribute to prosthetic joint loosening and periprosthetic osteolysis [1]. Aseptic loosening by periprosthetic osteolysis is the leading cause of failure in TJA [2] with incidents rates as high as 70% [3]. It is projected that by the year 2030, 572,000 primary total hip arthroplasties (THA), 97,000 THA revisions, and 3.48 million total knee arthroplasties will occur [4]. As more TJA are performed on increasingly younger patients, the rate of TJA failure will only increase as young age is a known risk factor for osteolysis [5]. Thus, the future societal and economic impact of TJA is staggering.

The pathology of total joint arthroplasty can have a variety of manifestations. Systemic dissemination of wear debris from prosthetic joints can include polymers such as polyethylene (PE) and polymethylmethacrylate, metals and ceramics. These debris are phagocytosed by macrophage, osteoclast precursor cells, osteoblasts, fibroblasts, and lymphocytes. Molecular responses include activation of MAP kinase pathways, transcription factors (including NFkB), and suppressors of cytokine signaling. This results in up-regulation of proinflammatory signaling and inhibition of the protective actions of antiosteoclastogenic cytokines such as interferon gamma. Thus, the homeostatic coexistence between the implant and the surrounding musculoskeletal tissues is altered [6].

The systemic dissemination of wear debris of TJA has been well described but the long term ramifications of this dissemination have not been fully clarified. There are numerous benign and reactive pathologic processes reported to masquerade as malignant disease. Examples of wear debris-associated pathologies include wear debris associated lymphadenopathy [7,8] and wear debris associated osteolysis [9,10]. We report 2 additional cases of patients with wear debris associated pathology, wear debris associated lymphadenopathy and wear debris associated osteolysis, where at the time of clinical presentation, there was a high clinical suspicion for malignancy. We report these cases to draw further attention to these "pseudo-malignant" processes (sheep in wolves clothing).

Case Reports

Case 1: A 47-year-old woman presented with a PET/CT scan demonstrating right inguinal and external iliac lymphadenopathy with hypermetabolic activity. The enlarged inguinal lymph node was also demonstrated on ultrasound studies (Figure 1). The patient had a complex medical history which included a history of osteosarcoma 31 years previously which was treated with limb salvage resection and right total knee replacement followed by chemotherapy. 23 years previously the patient was diagnosed with papillary carcinoma of the thyroid which was successfully resected. One year prior to admission the patient underwent a right upper lobe of lung resection for pulmonary adenocarcinoma. The pulmonary adenocarcinoma was found to have an ALK gene rearrangement and there was no evidence of lymph node metastasis at the time of resection. The PET/CT scan was performed as part of the patient's follow-up for her lung cancer resection. There was clinical concern for metastatic carcinoma as an etiology for this lymphadenopathy. Subsequent to the patient's scan, an ultrasound directed needle core biopsy of the right inguinal lymph node was performed. The lymph node biopsy showed dilated sinusoids filled with enlarged histiocytes with eosinophilic granular cytoplasm. Examination with polarized light revealed birefringent foreign material consistent with wear debris (metallosis). Numerous plasma cells were noted in this lymph node. Kappa and lambda ISH studies showed no evidence of light chain restriction (polyclonal plasmacytosis). There was no evidence of metastatic carcinoma. The histologic features are characteristic of wear debris lymphadenopathy (Figure 2).

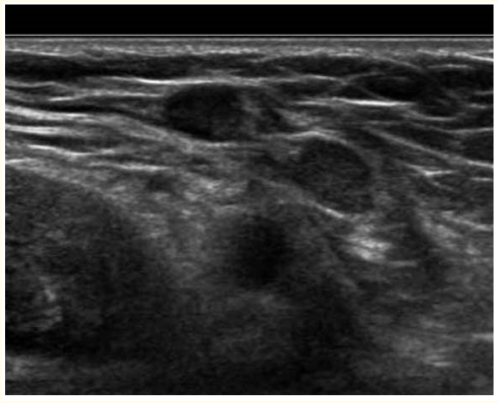

Figure 1: *Ultrasound of right inguinal canal demonstrating enlarged inguinal lymph node.*

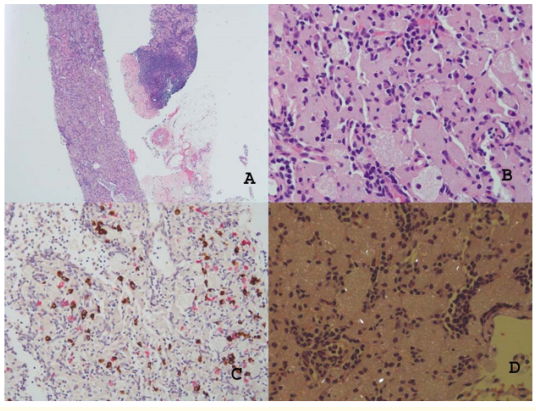

Figure 2(A-D): *A) Lymph node with histiocytic infiltrate (hematoxylin and eosin; 2 X), B) wear debris histiocytes with lymphoplasmacytic infiltrate (hematoxylin and eosin; 400X), C) Kappa (brown) and Lambda (red) light chain in situ hybridization tains demonstrating a polyclonal plasmacytosis (ISH stain, 400X), D) Birefringent wear debris demonstrated by polarized light examination (hematoxylin and eosin; 400X).*

Case 2: An 80-year-old woman presented with increasing left hip pain. A PET/CT scan showed a lytic lesion in the inferior pubic ramus ischial tuberosity region (Figure 3). However, the lesion did not appear hypermetabolic. Radiologic review of the lytic lesion raised the possibility of metastatic carcinoma. A chest X-ray demonstrated a right lower lobe of lung lesion. The lung lesion was biopsied and found to be an adenocarcinoma. In addition, within a month prior to her presentation with left hip pain, the patient had undergone a colectomy for colonic adenocarcinoma. The adenocarcinoma showed invasion into the muscularis propria without lymphovascular space involvement and resected regional lymph nodes showed no evidence of metastatic carcinoma (pT2 N0). It was noted that the patient had undergone a total left hip arthroplasty 25 years previously for degenerative joint disease. Because of the concern for an osteolytic metastasis to the bone, a radiology directed needle core biopsy of the lytic lesion was performed. The biopsy tissues showed fragments of bone and hyalinized fibrocollagenous tissues with a marked histiocytic infiltrate. The histiocytes had eosinophilic granular cytoplasm with small amounts of birefringent foreign material consistent with cytoplasmic wear debris and the histologic features were consistent with arthroplasty related changes. No lymphoplasmacytic infiltrate was identified. The histiocytes were found to be strongly positive for Cathepsin K (Figure 4). No atypical cells were seen and a keratin stain for occult microscopic metastatic carcinoma was negative. Subsequently, the patient underwent a right lower lobe of lung resection for pulmonary adenocarcinoma. There was no evidence of lymph node involvement by carcinoma (pT1b N0).

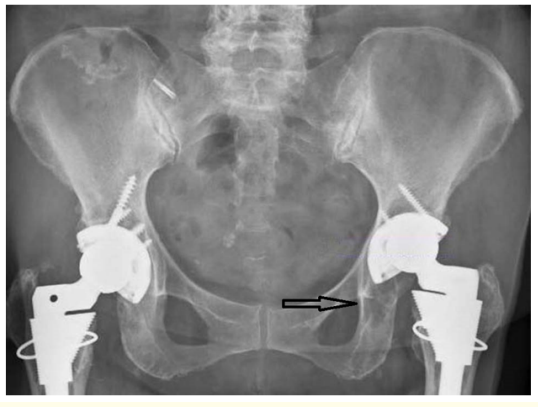

Figure 3: *Pelvic radiograph demonstrating left hip prosthesis and areas of a lytic lesion (arrow).*

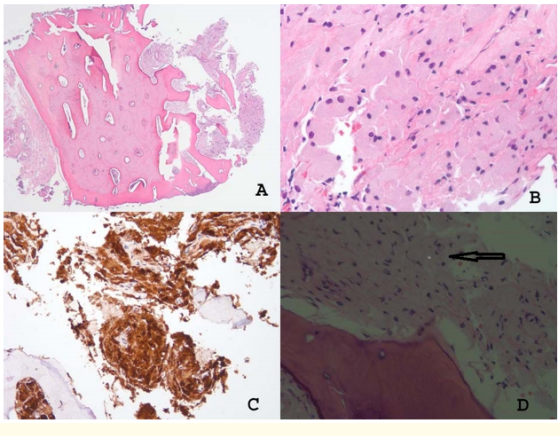

Figure 4(A-D): *A) Reactive bone with histiocytic infiltrate (hematoxylin and eosin; 40X), B) Wear debris histiocytes without inflammatory infiltrate (hematoxylin and eosin; 400X), C) Cathepsin K immunohistochemistry stain demonstrating strong positive staining in wear debris histiocytes (hematoxylin and eosin; 400X), D) Rare fragment (arrow) of birefringent wear debris demonstrated by polarized light examination (hematoxylin and eosin; 400X).*

Discussion

We report two cases of reactive/inflammatory wear debris associated pathologies where a clinical concern for malignancy was raised. In the case of wear debris associated lymphadenopathy, the joint replacement was quite remote from the presentation of a PET positive lymph node in a patient with multiple malignancies. Although the long interval between joint replacement and presentation with the enlarged lymph node may appear to be unusual, review of the literature indicates that these delayed presentations are common for this condition [8,15]. Both regional lymph node spread of wear debris [7,12,16] as well as systemic spread of wear debris has been documented [11,17]. Most cases of wear debris associated lymphadenopathy affect lymph node groups in the most proximal lymphatic drainage of the joint prosthesis. This suggests a possible dose-response relationship and that the lymphadenopathy requires a significant threshold dose of wear debris. The marked plasmacytosis associated with this lymphadenopathy suggests a hypersensitivity type reaction to the wear debris particles.

Wear debris associated osteolysis have been reported to be extensive enough to simulate osteolytic metastases [13]. However, wear debris associated joint loosening is a more common manifestations of wear debris associated osteolysis as compared to large overt radiologic lytic lesions. Wear debris associated osteolysis is often asymptomatic and undiagnosed until late in the course of the process when there is need for revision surgery. In the patient we report, there was already a large lytic lesion adjacent to her prosthesis at the time of presentation. The pathogenesis of wear debris associated osteolysis has been well investigated. The aseptic release of fragments from the surface of prosthetic joints activates an immune response that leads to bone destruction and ultimately results in loosening and failure of the joint. Unlike the pathology of the wear debris associated lymphadenopathy, a reactive plasmacytosis is not a typical feature of wear debris associated osteolysis. This suggests that a hypersensitivity type reaction does not play a significant role in osteolysis. We have identified strong positive staining of the eosinophilic granular histiocytes with Cathepsin K in this case. Cathepsin K is a strong proteolytic enzyme and has been implicated in other disease processes, including pulmonary lymphangioleiomyomatosis.

Previously proposed strategies to modulate the chronic inflammatory reaction to orthopedic wear particles include: 1) interfering with monocyte/macrophage migration, 2) conversion of pro-inflammatory M1 type macrophages to anti-inflammatory pro-tissue healing M2 type macrophages, 3) diminishing the production and release of pro-inflammatory cytokines activated macrophages and/or walking the activity of these cytokines [14]. Given the strong positive staining we have demonstrated in the histiocytes associated with the osteolytic process, an agent capable of inhibiting/blocking the activity of Cathepsin K might also be a potential strategy to attenuate the osteolytic process.

The two cases we present highlight examples of wear debris associated pathologies which may simulate malignancy. Total joint arthroplasty has been successful in long-term improvements patient quality-of-life. TJA's are being performed at an increasing rate with revision burden for total hip replacements projected to be 14.5% in 2030 [4]. We anticipate a continued increase in the number of cases where wear debris associated pathologies present with unusual clinical appearances including those which suggest malignancy. Given the prevalence of total joint arthroplasty and the long periods of time patients survive with these prosthetic joints, it is common that patients with these prosthetic joints also have or will develop a variety of malignancies. In the setting of malignancy, unexpected lymphadenopathy and osteolytic bone lesions will always raise the clinical suspicion for metastatic malignancy. However, awareness of the possibilities of wear debris associated lymphadenopathy and osteolysis will expand the differential diagnosis for these lesions and potentially decrease patient anxiety while they are waiting for definitive studies.

Conclusion

The two cases we present highlight examples of wear debris associated pathologies which may simulate malignancy. Total joint arthroplasty has been successful in long-term improvements patient quality-of-life. TJA's are being performed at an increasing rate with revision burden for total hip replacements projected to be 14.5% in 2030 [4]. We anticipate a continued increase in the number of cases where wear debris associated pathologies present with unusual clinical appearances including those which suggest malignancy. Given the prevalence of total joint arthroplasty and the long periods of time patients survive with these prosthetic joints, it is common that patients with these prosthetic joints also have or will develop a variety of malignancies. In the setting of malignancy, unexpected lymphadenopathy and osteolytic bone lesions will always raise the clinical suspicion for metastatic malignancy. However, awareness of the possibilities of wear debris associated lymphadenopathy and osteolysis will expand the differential diagnosis for these lesions and potentially decrease patient anxiety while they are waiting for definitive studies.

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