Case Report

Periprosthetic Malignancy as a Mode of Failure in Total Hip Arthroplasty

Kieran O’Shea, AFRCSI,* Stephen R. Kearns, FRCS Orth,* Anya Blaney, MB,† Paraic Murray, FRCSI,‡ Hugh A. Smyth, FRCSI,* and John P. McElwain, FRCSI*

Abstract: The presence of periprosthetic malignancy in proximity to arthroplasty implants has been infrequently reported. We present the clinical, radiographic, and pathological features of three patients in whom loosening and failure of total hip arthroplasties occurred secondary to malignant infiltration. They consisted of a 66-year-old man with the first presentation of metastatic gastric carcinoma as a periacetabular lytic lesion, a 64-year-old man presenting with femoral metastases from a previously undiagnosed lung carcinoma, and a 75-year-old woman presenting with a painless discharging thigh sinus around a total hip arthroplasty subsequently diagnosed as immunoblastic lymphoma. Malignant infiltration should be considered part of the differential diagnosis in aseptic and septic loosening of prosthetic implants. Joint aspiration and isotope bone scanning provide useful additional information before surgical intervention. Key words: periprosthetic, malignancy, failure, hip, arthroplasty.

Failure of total hip arthroplasty through septic or aseptic loosening, periprosthetic fracture, or recurrent dislocation is well recognized and understood. We present three cases of an unusual cause of failure of total hip arthroplasty (THA): that of prosthetic loosening secondary to malignant infiltration around components. Our aim is to highlight the potential for malignancy to mimic septic and aseptic loosening and to encourage inclusion of periprosthetic malignancy as a differential diagnosis in the mechanically failing THA.

Case Reports

Case 1

A 64-year-old man, with morbid obesity, who had undergone a right THA 5 years previously, was admitted to hospital with recurrent falls. Nine months previously, he had injured his hip during a fall and had insidious pain since that time. He developed septic symptoms some 6 months later and was being treated conservatively for prosthetic infection with chronic antibiotic suppression. During his hospital stay, he experienced...
severe exacerbation of hip pain and became unable to weight bear. C-reactive protein was normal but his erythrocyte sedimentation rate was elevated at 71 mm/h. Plain radiographs demonstrated marked destruction of the proximal femur and the presence of a surrounding soft tissue mass with calcification (Fig. 1A). Under anesthetic, a biopsy was performed that revealed the presence of a poorly differentiated adenocarcinoma. No organisms were cultured.

Further to this, a thoracic computed tomographic (CT) scan demonstrated a mass measuring 4 × 2 cm adjacent to the right main bronchus with mediastinal lymphadenopathy, thus indicating stage IV non–small cell lung carcinoma.

He proceeded to revision THA using a porous-coated uncemented femoral stem and a cemented acetabular prosthesis (Fig. 1B). After implantation, there was evidence of posterior instability on internal rotation of the lower limb and a posterior lip augmentation device was applied. This is a congruent polyethylene acetabular augmentation with a stainless steel backing plate. It has been shown to be successful in the secondary management of posterior prosthetic hip dislocations in cases where there is no gross malalignment, wear, or loosening of the acetabular component [1]. He received one dose of postoperative radiotherapy of 8 Gy to the right hip. After discharge home, he died approximately 6 weeks postoperatively as a result of disease progression.

Case 2

A 75-year-old woman, 13 years after THA, presented with a painless discharging sinus over the lateral aspect of her right thigh. Plain films showed lysis in Gruen zones 2 and 6 with evidence of periosteal reaction over the lateral femoral cortex. Wound swabs cultured a broadly sensitive *Escherichia coli*. C-reactive protein was 23 (N < 5). A technetium Tc 99m bone scan showed very mildly increased uptake around the right femur in keeping with a low-grade infection. Owing to lack of pain and medical comorbidities, initial treatment was with antibiotic suppression and surveillance.

While remaining constitutionally well, she began to develop pain and swelling of her right thigh, and at review 6 months later, plain radiographs showed a moth-eaten destruction of the lateral femoral cortex (Fig. 2). A further technetium Tc 99m bone scan showed marked increase in uptake over the proximal femur. She was scheduled for a staged revision procedure. At the first stage, a bone defect measuring 4 × 2 cm at the lateral...
cortex extending to the cement mantle was noted. Histological analysis of intraoperative sections revealed extensive infiltration with malignant immunoblastic lymphoma. She received local palliative radiotherapy consisting of 20 Gy over 5 fractions. Chemotherapy was administered consisting of cyclophosphamide, vincristine, and prednisolone. She remained an inpatient in hospital due to recurrent episodes of neutropenia and ultimately died 20 weeks after excisional arthroplasty due to neutropenic sepsis. With regard to her hip, as she died 20 weeks after excisional arthroplasty due to recurrent episodes of neutropenia and ultimately died 20 weeks after excisional arthroplasty due to neutropenic sepsis, With regard to her hip, as she remained medically unfit, it was not possible to proceed to a reimplantation procedure.

Case 3
A 66-year-old man underwent sequential bilateral THAs for osteoarthritis. After the second THA, he developed dysphagia and odynophagia. At gastroscopy, a moderately differentiated adenocarcinoma was diagnosed, further staged as T3N1M0 based on celiac nodal involvement at endoscopic ultrasound and the absence of visceral metastases in the abdomen and thorax at CT. Treatment was with chemoradiotherapy. At 1 year, follow-up gastroscopy showed no residual tumor mass.

He returned 4 months subsequently complaining of pain and stiffness in his left hip and difficulty in weight bearing. Pelvic radiographs demonstrated a large lucent area in the dome of his left acetabulum with gross loosening of the acetabular component (Fig. 3). Technetium Tc 99m bone scan showed increased uptake in the region of the acetabular component, suggestive of infection rather than any secondary pathology.

An arthrogram was performed and 10 mL of hemorrhagic fluid was with withdrawn for analysis. No organism was cultured. Cytological analysis revealed a “cellular aspirate containing clusters of malignant epithelial cells in keeping with metastatic carcinoma from a primary site in the stomach.” Further workup revealed no evidence of metastatic disease elsewhere. After a discussion of the available treatment options, the decision was made to proceed to a Girdlestone resection arthroplasty, as a one-off definitive procedure was preferred by the patient. At revision, operative bone and capsular/soft tissue specimens confirmed the presence of metastatic disease thus indicating stage IV gastric carcinoma. After a short period of bed rest, he was fitted with a shoe orthosis for his limb length discrepancy and was discharged mobilizing pain-free with the aid of two crutches. An 8-Gy single dose of radiotherapy was administered to his left hip. Two months after discharge from hospital, he was admitted to a hospice for palliative care and died while an inpatient 10 weeks later.

Discussion
To date, there have been four reports in the literature documenting the occurrence of metastatic disease in proximity to orthopedic implants [2-5]. These consisted of a non-Hodgkin lymphoma spreading to the periprosthetic region of a THA [2], a bronchogenic carcinoma metastasizing to the femur of a patient with a THA [3], and a gastric carcinoma presenting with a synovial metastasis to a total knee arthroplasty [4]. Allain et al [5] reported a squamous cell carcinoma of the lung metastasizing to the neosynovium of a THA and presenting as pain and femoral loosening. At revision, all 6 bony specimens showed no involvement by tumor. The patient had multiple visceral metastases in both the liver and lung on CT.

In contrast, primary malignant tumors occurring in proximity to prosthetic implants have been more widely reported. Troop et al [6] described 12 cases of malignant fibrous histiocytoma associated with orthopedic implants: 4 in association with THAs, 1 in association with a total knee arthroplasty, and 7 in association with plates and screws. Other reports include isolated occurrences of undifferentiated sarcomas [7], synovial cell sarcomas [8], and squamous cell carcinomas [9]. It has been postulated that a strong association exists between these soft tissue tumors and the presence of implants, but the relative infrequency of these cases makes demonstration of a causal relationship difficult.

A number of theories regarding the pathoetiology of metastatic disease occurring in relationship to implants have been expounded. Roques et al [10] felt that abnormalities in blood flow as a result of surgical injury and the healing process may predispose to the development of metastases around surgical implants. Enneking [11] showed that metastases had a predilection for bone where there is an abnormal increase in blood supply. The inflammatory reaction to metastatic tumor includes the presence and activation of macrophages, giant cells, and leukocytes and is associated with necrosis of bone. The activation of these inflammatory cells may be an important mechanism in the development of aseptic loosening. However, in contrast, it has been postulated that synovial metastases occur relatively infrequently due to the large concentration of immune cells in synovial tissue, which may be important in controlling metastatic seeding [5].
In most cases, the diagnosis of malignant disease is made at histology after revision for either presumed infection or aseptic loosening. Two patients (case 1 and case 2) in this series were initially treated for infection. Technetium bone scanning and serum inflammatory markers often yield nonspecific results. Joint aspiration and arthrography as part of the preoperative workup for revision surgery are useful for cytological detection of malignancy.

Two of the three patients in this series (case 2 and case 3) did not proceed to prosthetic reimplantation. Performing a Girdlestone resection arthroplasty as a primary intervention for acetabular malignancy has been shown to yield only modest results [12]. However, our patient managed effectively with this treatment, mobilizing independently and remaining pain-free. The second patient was not fit for a revision procedure because of disease progression and complications of chemotherapy. Revision in the third patient (case 1) involved the use of an extensively porous-coated uncemented femoral stem and a cemented acetabular prosthesis. Active administration of chemotherapy and radiotherapy is considered a relative contraindication to the use of proximally porous-coated femoral implants [13]. Both Konski et al [14] and Chin et al [15] have demonstrated in animal models that therapeutic doses of radiation can inhibit osseointegration over a porous-coated prosthesis. Hence, in the setting of primary arthroplasty for metastatic disease around the hip, it is advisable to use only cemented components [16]. However, in a revision setting, the proximal femur is often a poor environment for cementation [17]. Owing to the extensive proximal femoral bone loss, we elected to use an extensively coated implant with the aim of achieving primary distal fixation. An alternative would have been to use a proximal femoral arthroplasty with cemented distal fixation such as a Kotz or similar tumor endoprosthesis.

The three cases described in this report illustrate well the potential for secondary malignant disease to mimic both septic and aseptic loosening. With regard to the patient with gastric malignancy, this is the first reported case of metastatic carcinoma presenting in isolation as loosening of an acetalular component of a THA. Similarly, there have been no previous reports of the occurrence of immunoblastic lymphoma in relation to orthopedic implants. As for the patient with lung carcinoma, the first presentation leading to diagnosis was the periprosthetic metastasis, that is, he presented with stage IV disease. As the number of patients with in situ endoprostheses grow in tandem with increased survival from malignancy, it is likely that orthopedic surgeons will become more exposed to such cases.

**Conclusion**

One should maintain a high index of suspicion and consider metastatic disease as a differential diagnosis in cases of aseptic loosening, particularly when there is rapid progression of symptoms, the history is atypical, or the patient has a history of malignant disease. Equally, in the setting of infection, marked osteolysis or periosteal changes with associated soft tissue swelling should arouse suspicion of the possibility of an additional process. A bloodstained aspirate from a joint should specifically arouse suspicion of the potential presence of a primary or metastatic tumor [9]. Aspiration fluid should be routinely sent for cytological analysis as well as standard microbiological culture and sensitivity. A preoperative diagnosis of malignancy, in the setting of revision surgery, will significantly alter the management plan.

**References**
