Case report

Metastatic endometrial carcinoma invading bilateral total knee arthroplasties

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Article info

Article history:
Received 3 March 2015
Received in revised form 8 April 2015
Accepted 8 April 2015
Available online 23 June 2015

Keywords:
Metastasis
Arthroplasty
Endometrial carcinoma
Total knee
Tumor
Loosening

Abstract

We present a case of a 64-year old female with bilateral knee pain several months after undergoing staged bilateral TKA. Radioluencies surrounding the keels of bilateral tibial components were found to represent metastatic poorly differentiated endometrial carcinoma. PET scan showed adrenal, pulmonary and tibial foci consistent with metastatic disease. No other cases of bilateral periprosthetic metastasis of endometrial carcinoma have been described in the literature. Metastases around orthopedic implants are a rare occurrence. The possibility of periprosthetic metastasis should remain in the differential diagnosis for any patient with a painful total joint arthroplasty, especially in the setting of a patient with a known diagnosis of cancer elsewhere in their body.

Introduction

Pain after total knee arthroplasty has several etiologies, which are often categorized as intra-articular or extra-articular. The most common causes include infection, loosening, instability, patellar mal-tracking, or osteolysis [1]. Routine work-up includes plain radiographs, WBC, ESR, CRP, aspiration of the joint and occasionally bone scan. Rarely, however, has metastatic disease been reported as a source of pain after total joint arthroplasty [2].

We report the case of a patient who presented to our clinic with bilateral knee pain several months following total knee arthroplasty. It was noted the month prior that she developed a vague radiolucency around bilateral tibia prostheses of her total knee arthroplasties. One month later the radiolucent area had drastically worsened. Coincidentally, she was scheduled for robotic assisted laparoscopic hysterectomy and lymph node dissection for endometrial carcinoma four days after her clinic visit. During her stay, CT guided biopsy was performed of the radiolucent area of the left proximal tibia, which demonstrated metastatic poorly differentiated carcinoma, morphologically similar to the patient’s known endometrial carcinoma. The patient gave verbal consent for the use of the data concerning her case for publication.

Case history

A 64 year-old Egyptian female with bilateral knee osteoarthritis underwent bilateral staged total knee arthroplasty (TKA) with cemented, posterior stabilized implants (Vanguard PS; Biomet, Warsaw, Indiana). Cementation was performed by coating the implants and pressurizing the tibia using Biomet Cobalt cement with gentamycin. The left side was performed in March 2012. Her initial post-operative course was complicated by multiple deep venous thromboses (DVT), in the operative extremity, and bilateral pulmonary emboli, in June of 2012. She was diagnosed having Factor V Leiden and Methylene tetrahydrofolate reductase (MTHFR) mutations, which resulted in her coagulopathy. These were treated with Heparin bridged to Coumadin, and she has been followed in our anticoagulation clinic. With regards to her TKA, she did extremely well with very little knee pain on the left side, and wished to proceed with the right TKA approximately 18 months later. She was seen by her primary care physician and cleared for surgery. Her increased risk for surgery was discussed at length with the patient, and she elected to...
undergo right total knee arthroplasty in September 2013. Meanwhile, in March of 2014, the patient presented to her primary care physician with complaints of approximately seven months of postmenopausal bleeding. An endometrial biopsy, done in April 2014, showed endometrial carcinoma with serous type features, and she was referred to the Gynecologic-Oncology (Gyn-Onc) service for further management. Their team recommended robotic assisted total laparoscopic hysterectomy, bilateral salpingo-ophorectomy, omentectomy, and lymph node dissection. She was amenable to this and scheduled for surgery in late April 2014.

Her initial post-operative course was uncomplicated, and she continued to progress very well with minimal right knee pain until April of 2014, when she presented to the Orthopaedic clinic complaining of new onset left knee pain and worsening right knee pain (7 months post-operative from her right side, 25 months post-operative from her left). Serologic laboratory tests were ordered, which showed a slight elevation of the C-reactive protein (CRP) 2.6 mg/dL, (ref range 0.0–0.3 mg/dL) with a normal white blood cell count and erythrocyte sedimentation rate. She returned to the Orthopaedic clinic for follow up on her serologic tests 4 days before her planned Gyn-Onc procedure. Radiographs were obtained during that visit which showing a large area of radiolucency with cortical destruction surrounding both tibial components (Figs. 1 and 2). This demonstrated a drastic change from her prior radiographs of her left and right knees performed three months and eleven months prior (Figs. 3 and 4). Her left knee was aspirated at that clinic visit to rule out infection. A cell count of the synovial fluid showed a white blood-cell count of 518 cells/cm² with 20% polymorphonucleocytes. Further analysis of the fluid demonstrated: no crystals identified, and negative aerobic, anaerobic, fungal cultures and with negative AFB stain. Given the results of her arthrocentesis, we recommended that she undergo bilateral computed tomography (CT)-guided tibial bone biopsies to rule out the possibility of metastasis during the same hospital stay as her gynecologic surgery. She underwent robotic total laparoscopic hysterectomy, bilateral salpingo-oophorectomy, sentinel lymph identification and biopsy, complete pelvic, common iliac, and periaortic lymphadenectomy, omentectomy, extensive lysis of adhesions with Gyn-Onc service. Pathology showed Grade 3 serous carcinoma confined to the uterus with clear margins and no involvement of ovaries, fallopian tubes, omentum, or any of the multiple lymph nodes sent (Fig. 5). During the same hospital stay, a CT-guided tibial bone biopsy was performed. This biopsy demonstrated “metastatic poorly differentiated carcinoma, morphologically similar to the patient’s known previous endometrial carcinoma” (Fig. 6). Given the rarity of this condition, the specimens were sent to the Mayo clinic for further review. Their assessment supported the diagnosis, “metastatic adenocarcinoma with morphologic features similar to those present in the patient’s hysterectomy specimen.” The tumor cells were also positive for cytokeratin AE1/AE3 and negative for S100 and Melan A, which further supported the diagnosis of metastatic carcinoma.

The patient was presented to our tumor board, and a unanimous recommendation was to obtain a positron emission tomography (PET) scan to identify possible additional metastatic disease to gain further insight into her prognosis. The PET scan demonstrated further adrenal, pulmonary, and tibial foci concerning for further metastatic disease. Unfortunately, the PET scan was performed at an outside facility and the patient is now out of the country and unable to consent to obtaining these images. Collaboration with our Gyn-Onc, Medical Oncology and Radiation Oncology colleagues allowed us to discern that our patient’s prognosis is approximately 6 months. Given her additional comorbidities, extensive reconstruction is not a likely alternative in this case and palliative treatment was discussed with our patient and her family. Measures that were discussed included extensive curettage with cementation around bilateral tibial components versus local radiation therapy. The patient and her

![Figure 1. AP and lateral X-rays 7 months post-operative following right total knee arthroplasty demonstrating a radioluency about the distal portion of the tibial component.](image-url)
family elected to proceed with local radiation. At 1 month following the initiation of medical therapy, the patient has started chemotherapy with mild symptomatic improvement in bilateral knees. She was recommended to use a wheelchair, but allowed to perform transfers. The patient then returned to her country of origin and was lost to clinical follow up. In the case of prolonged survival or periprosthetic fracture, our plan would be proximal tibia replacement with endoprosthesis or amputation given the lack of proximal tibial bone stock.

Discussion

The etiology of a painful total knee arthroplasty can often be identified using a systematic approach [1]. A thorough history and physical exam, appropriate lab and radiographic evaluation often leads to a definitive diagnosis. Metastatic disease, however, is an infrequent cause, and has only been reported in a few instances. The most common primary carcinomas to metastasize to bone are breast, lung, prostate, kidney, thyroid and the axial skeleton is the most common
site to receive metastases. Early detection of metastatic bone lesions leads to improved patient survival with current treatment modalities.

A review of the literature demonstrates a small number of cases of periprosthetic metastases to total hip arthroplasties including non-Hodgkins lymphoma, malignant fibrous histiocytoma, immunoblastic lymphoma and carcinomas of the lung. To our knowledge metastases to total knee implants are even more uncommon [3–9]. This is the first case of simultaneous metastases to bilateral total knee implants to be reported.

Our patient received staged bilateral total knee arthroplasties 18 months apart, and reported no problems until 25 months after the left and 7 months after the right TKA consistent with radiographic findings of more aggressive bony destruction of the left proximal tibia. Her primary diagnosis of serous endometrial adenocarcinoma was thought not to have distant metastases, and underwent hysterectomy with lymph node dissection 4 days after tibial lucencies were identified in clinic. Biopsies obtained after hysterectomy demonstrated metastatic poorly differentiated carcinoma, morphologically similar to patient’s known endometrial carcinoma. In this case, aspiration of the knee was negative for infection, but our specimen was not sent for cytology. Given the aggressive changes in the proximal tibia over a month’s time and her known scheduled hysterectomy for endometrial cancer, we felt that a biopsy was warranted despite the rarity for metastases. The incidence of bone metastases of endometrial cancer is <1% in gynecologic oncology literature, and has not been reported around total joint implants [10]. Prognosis after identifying metastatic disease to implants is poor, and treatment for endometrial carcinoma metastasizing to bone involves a multimodality approach [4,7,11]. A prior report of 21 patients in gynecologic oncology literature reported an overall survival of those patients with bone metastases at primary diagnosis to be 17 months [11].

![Figure 4. AP and lateral X-rays 14 months post-operative following left total knee arthroplasty.](image)

![Figure 5. Endometrial biopsy with H&E stain at 40× magnification.](image)

![Figure 6. Left proximal tibia biopsy with H&E stain at 40× magnification.](image)
bone involvement and extraosseous dissemination were associated with poor prognosis [10]. It has been reported there may be an association between soft tissue tumors and the presence of implants [7]. Several theories have been postulated regarding factors that may predispose to periprosthetic metastatic disease. Enneking reported that areas with abnormal increases in blood flow (post-surgical sites) had a predilection to attract metastases [12]. Roques et al. also felt that surgical insult, resultant abnormal blood flow, and healing response may predispose these areas to metastatic disease [13]. Total joint literature regarding nuclear bone scans following total joint arthroplasty suggest increased metabolic activity and therefore blood flow about total joint replacements up to 2 years following surgery.

Summary

In conclusion, we should maintain a high index of suspicion and consider possible metastatic disease in our differential of a painful total knee arthroplasty. A known diagnosis of a primary soft tissue malignancy in the setting of periprosthetic pain, marked osteolysis or periosteal changes should prompt evaluation for possible metastases. It is prudent in an atypical presentation such as this to include cytology along with microbiological cultures/sensitivities with our routine aspiration studies. Pre-operative diagnosis of malignancy around total joint components significantly influences the treatment strategy and surgical plan.

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