

Case Report

Acetabular Insufficiency Fractures in the Setting of Graft vs Host Disease: A Report of Two Cases

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ABSTRACT

We report a case series of 2 patients with unilateral acetabular insufficiency fractures who received allogeneic peripheral blood stem cell transplantation for hematologic malignancies complicated by chronic graft vs host disease. These were managed with uncemented cup and cage total hip arthroplasty and stabilization of posterior column with plating. Osteonecrosis of the acetabulum is an uncommon musculoskeletal complication of chronic graft vs host disease. The orthopedic impact of this disease should not be overlooked. Surgical intervention with this construct can provide necessary stability to improve patient function.

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Introduction

Graft vs host disease (GVHD) can manifest with multisystemic effects. GVHD can occur after allogeneic peripheral blood stem cell transplantation (PBSCT) and can have orthopedic implications such as osteonecrosis. The incidence of osteonecrosis after allogeneic stem cell transplantation is 4–19% [1–4], and the risk is increased in patients with GVHD [5]. Most studies described involve the femoral head [1–4,6–12]. Osteonecrosis of the acetabulum, although rare, can lead to significant complications. These include interruption of the articular surface, insufficiency fracture, and protrusio acetabulum. Osteonecrosis of the acetabulum presents particular difficulty in fixation; poor bone quality can impact long-term patient outcomes and implant survivorship. Implant survivorship of THA in patients with allogeneic peripheral stem cell transplantation at 5 years is up to 93% [11], although it can be as low as 74.8% at 10 years [13]. Therefore, THA and fracture fixation in this setting require an approach that combines primary and revision arthroplasty skills to enable immediate weight bearing and pain relief. We present 2 cases of allogeneic PBSCT complicated by GVHD, with resultant

acetabular osteonecrosis leading to acetabular insufficiency fracture and the surgical reconstruction that followed.

Case histories

Case 1

Case 1 is a 60-year-old woman with a history of diffuse large B-cell lymphoma who underwent 8 cycles of R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin [vincristine], and prednisolone). Her disease recurred and was treated with radiolabeled tositumomab with maintenance on rituximab. Relapse occurred once more, and she received salvage chemotherapy with R-ICE (rituximab, ifosfamide, etoposide, carboplatin) followed by autologous PBSCT. She underwent human leukocyte antigen (HLA)-matched allogeneic PBSCT after fludarabine-melphalan conditioning for relapse involving the central nervous system. This was complicated by GVHD, primarily affecting the gastrointestinal tract, that improved with 20-mg prednisone BID (0.5 mg/kg/day). After several dose escalations and relapses, she was tapered off prednisone three times, but after two severe episodes of pericarditis in the absence of steroids, she remained on 10-mg prednisone daily.

She presented to orthopedics with 1 month of acute, “aching” left-sided groin pain, global left hip weakness, difficulty ambulating (newly required a four-wheel walker), and ecchymosis in her inguinal crease. Physical examination revealed severe pain with hip internal and external rotation, as well as adduction and abduction. She could

Statements of informed consent were obtained from patients and family members of deceased patients.

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conduct passive hip flexion to 90 degrees but had pain with resisted hip flexion. Magnetic resonance imaging (MRI) of the pelvis and hip was obtained by her primary care provider before orthopedic referral, and AP of the pelvis was obtained as seen in Figure 1. Initial radiography in Figure 1 and MRI demonstrated comminuted minimally displaced fracture of the acetabulum involving the anterior and posterior columns with acetabular protrusio fracture and superior displacement of the femur of 3.5 cm. Interruption of the anterior and posterior columns is better visualized on iliac oblique and obturator oblique views seen in Figures 2 and 3.

Owing to severe disability and pain, and acetabular insufficiency (pathologic) fracture and joint collapse, posterior THA and posterior column stabilization was undertaken. Posterolateral approach was taken to optimize exposure of acetabular fracture and perform THA. Complex THA was performed using a cage construct. Pelvic side thwarted the use of a cup and cage construct. Findings include fragmentation of medial acetabulum with transverse-type insufficiency or pathologic fracture. Acetabular pathologic fracture was repaired, or stabilized, with 8-hole reconstruction plate bent for the left posterior column. Morselized femoral head autograft was placed at the base of the protruded acetabulum. Dome screws of anti-protrusio cage were placed before ilium cage screws, and 5 mL of synthetic bone graft and 30 mL of cancellous bone allograft was injected behind cage. Postoperative x-ray is demonstrated in Figure 4. Her postoperative activity restrictions included posterior hip precautions, and weightbearing as tolerated with an assistive device, with weaning as she was able.

At her 3-month follow-up visit, she was able to fully weight bear on her left lower extremity without pain or assistive device. Imaging obtained at that time is seen in Figure 5. At 5 months postoperatively, she underwent right total knee arthroplasty because of osteoarthritis present before the acetabular osteonecrosis and was progressing very well with physical therapy. Unfortunately, 16 months after complex left THA, she succumbed to complications of diffuse large B-cell lymphoma and GVHD.

Case 2

Case 2 is a 51-year-old woman with a history of acute myelogenous leukemia (AML), secondary myelodysplastic syndrome (MDS), GVHD,



Figure 1. AP pelvis x-ray upon initial presentation showed displaced acetabular fracture and interruption of the femoroacetabular joint space.



Figure 2. Left obturator oblique better demonstrates insufficiency fracture of the posterior wall and anterior column.

steroid-induced diabetes, and restrictive pulmonary disease. Autologous PBSCT was undertaken for AML 9 years before presentation. Matched unrelated donor PBSCT was conducted 1 year before presentation, after fludarabine-melphalan conditioning. GVHD characterized by gastrointestinal symptoms and florid skin rash complicated PBSCT 4 months before presentation. Steroid dosage during GVHD was started at 1 mg/kg/day (60 mg BID) with rapid resolution of symptoms leading to taper of steroids down to 0.5 mg/kg/day after 1 week. She developed recurrence of pulmonary symptoms and gastrointestinal symptoms with tapering and was restarted on 1 mg/kg/day.

She presented to orthopedics with 2 months of right hip pain, primarily in her deep inguinal crease. She required a walker for ambulation and was limited to very short distances because of pain.



Figure 3. Left iliac oblique further demonstrates osteonecrosis of the acetabulum and fracture extending through the posterior column.



Figure 4. Day 0 postoperative AP pelvis x-ray. THA with cage construct and iliac plating.

The examination was remarkable for BMI = 44, anasarca, and painful and limited right hip rotation with only 10 degrees of passive external and internal rotation. Radiographs taken at that time are seen in [Figure 6](#). MRI performed at that time showed hypointensity of the supra-acetabular ilium with some T2 hyperintensity measuring 2.5 cm transverse \times 2.4 cm AP suggestive of osteonecrosis, although without collapse. There was also osteonecrosis of the left femoral head, without collapse. Given significant comorbid conditions including bilateral lower extremity edema and severe open-leg ulcerations, surgery was not initially recommended.

Given ongoing severe pain and disability, she underwent medical optimization taking 13 months, although during that time, she developed progressive osteonecrosis of the acetabulum. The progression of this can be seen in [Figures 7 and 8](#) obtained 1 month later. Her fracture initially demonstrated disruption of the right iliopubic line with sclerosis of the supraacetabular ilium with superior displacement of the femoral head into the ilium consistent with protrusio fracture. This was further evaluated with a CT of the



Figure 6. AP right hip obtained upon initial presentation to PCP with right hip pain. Revealing subchondral lucency of the right femoral head. No acetabular involvement noted.

pelvis, which demonstrated comminution of anterior and posterior columns and 14 gapping of articular surface along anterosuperior acetabulum and medullary sclerosis of the surrounding ilium. Follow-up radiography seen in [Figure 8](#) demonstrated increased displacement of anterior and posterior columns with medial acetabular wall displacement measuring 8 mm. [Figure 8](#) was ultimately used for templating her implants. Iliac oblique and



Figure 5. Three months postoperative AP pelvis. Revealed intact cage hardware, posterior column plating, and THA. Interval ileum healing was perceived.

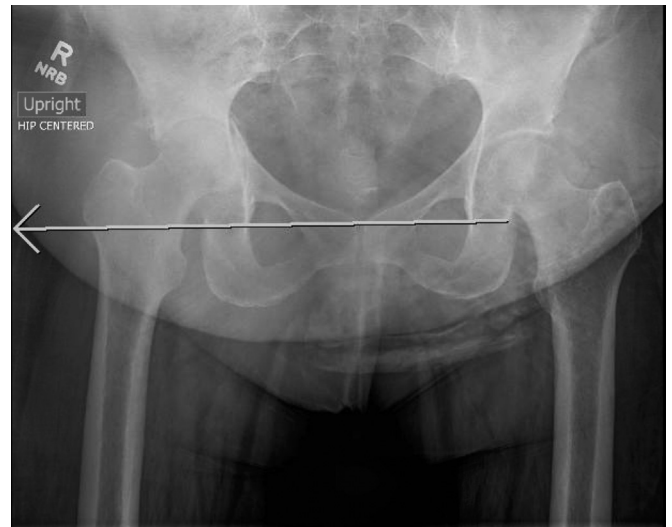


Figure 7. AP pelvic x-ray 6 months since onset of symptoms and 10 months preoperatively. Revealing displaced healing right acetabular fracture. Disruption of the right iliopubic line and sclerosis of the right supra-acetabular ilium. Sclerosis of the right femoral head was also observed.



Figure 8. AP pelvis x-ray 13 months since onset of symptoms and 1.5 months preoperatively. Showing comminuted displaced right acetabular transverse fracture also involving the posterior and medial acetabular walls. Right femoral head is also eroded and aspherical. This film was used for templating.

obturator oblique views at this time seen in [Figures 9 and 10](#) better demonstrate involvement of the anterior and posterior column, medial protrusion of the acetabulum. She was no longer able to ambulate with a walker and was wheelchair bound. Her steroid dose then was 5 mg, 5 days per week, and 10 mg, 2 days per week. Treatment options discussed with patient included Girdlestone resection, THA, and THA with antiprotrusion cage or cup and cage construct. Reconstruction was preferred by patient over Girdlestone resection as she was hoping to resume ambulation and activities of daily living (ADLs). Surgery was pursued with posterior THA, with cage construct and posterior column plating. This fixation was used as the size of the pelvis was not large enough to facilitate a cup/cage construct. Medial acetabulum bony deficiency with both columns, or transverse-type insufficiency fracture or pelvic discontinuity variant, was encountered. After femoral neck cut was made, A 7-hole pelvic reconstruction plate was contoured,

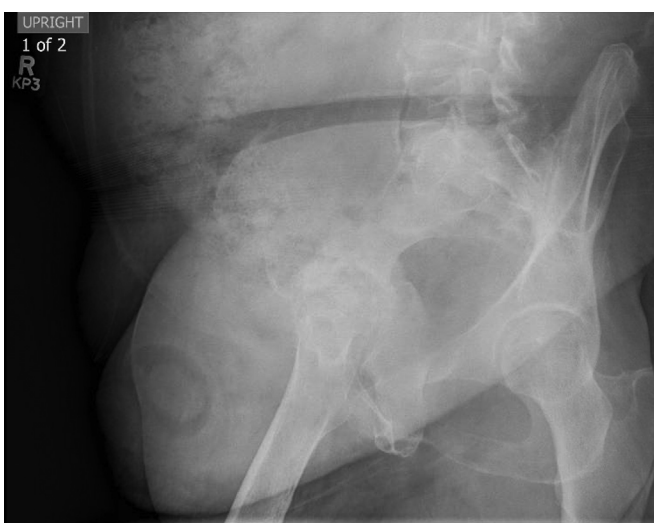


Figure 9. Right iliac oblique x-ray 13 months since onset of symptoms and 1.5 months preoperatively demonstrating transverse plus posterior acetabular wall fracture with 1.5 cm medial displacement of medial acetabular wall.



Figure 10. Right obturator oblique x-ray 13 months since onset of symptoms and 1.5 months preoperatively. Further demonstrating comminuted posterior acetabular wall insufficiency fracture, aspherical and eroded femoral head, and some bony callus.

and a posterior column plated from ischium to ileum with good fixation using 4 small fragment screws. After the cage was placed, 10 mL of synthetic bone graft with 30 mL of allograft cancellous chips was placed posteriorly to cage. There were no intraoperative complications, and she was discharged home after 2 days. Two weeks postoperatively, she had a 2-day admission for viral gastroenteritis. She also underwent kyphoplasty for three (T9, T11, L1) vertebral compression fractures 2 months postoperatively. There were no readmissions or emergency department visits for postoperative complications.

One-month postoperatively, her pain was decreasing, and function with ADLs increased, although she required a walker because of back pain and deconditioning. Her gait was smooth, not antalgic, with the walker. Two views of AP pelvis performed at that time are seen in [Figure 11](#). One-year postoperatively, her pain had resolved, she still required a walker, and she was noted to have Trendelenburg gait. AP pelvis 1 year postoperatively, seen in [Figure 12](#), showed

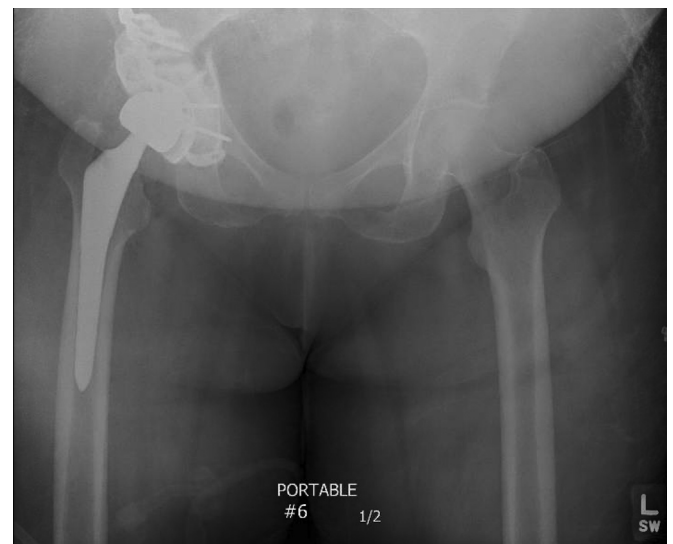


Figure 11. Portable pelvis x-ray 1-month postoperatively. Intact cup and cage construct implants, near anatomic alignment of acetabular fracture.



Figure 12. AP pelvis x-rays 1-year postoperatively. Interval acetabular healing was seen. Diffuse osteopenia but no evidence of implant failure.

well-positioned THA with no lucencies or subsidence. Unfortunately, 3 years postoperatively, she died of causes related to her MDS and GVHD.

Discussion

Patients with hematologic malignancies are having increased remission and survivorship after autologous and allogeneic hematopoietic stem cell transplantations [14,15]. Allogeneic stem cell transplantation is unique as opposed to autologous transplant as it can lead to GVHD. GVHD is a systemic immune reaction by donor cells against host cells [16]. Several studies have demonstrated the increased risk of osteonecrosis because of GVHD [5,9,11,17,18]. GVHD is thought to cause osteonecrosis because of an inflammatory process in the intraosseous vasculature. Sixou et al. [19] found histologic evidence of vasculitis attributed to GVHD. This vasculitis exacerbates risk factors associated with osteonecrosis inclusive to patients with hematologic malignancies including systemic glucocorticoids, chemotherapeutics, and irradiation [5].

Unique to the presented cases is osteonecrosis of the acetabulum and the timeline to develop osteonecrosis. Case 1 took 5 years for manifestation of acetabular osteonecrosis after initiation of steroids for GVHD. Case 2 took 13 months until acetabular osteonecrosis began after onset of GVHD. In 11 patients (19 hips, 8 patients with bilateral osteonecrosis) studied by Schulte and Beelen, onset of osteonecrosis after allogeneic stem cell transplant ranged from 5 to 57 months, with an average of 25 months [9,18]. However, all these cases were of the femoral head, and the hematologic malignancies were AML, MDS, CML, and ALL. It is unclear in the presented cases what circumstances led to osteonecrosis of the acetabulum. Location and timeline could be attributed to age. Bizot et al. [17] had 16 patients with osteonecrosis secondary to GVHD, although the oldest patient was 47 years old at the time of surgery (average age 13 ± 8 years). The patients presented were 60 and 52 years old at the time of surgery.

Several other studies have identified osteonecrosis risk factors in hematologic malignancies; Schulte and Beelen demonstrated that the most impactful risk factors were chronic GVHD and cumulative steroid intake, followed by female gender, younger age, and conditioning therapy before transplant. Advanced disease stages, bone mineral density, and body composition did not have a

significant impact on osteonecrosis [9,18]. The disease process of lymphoma itself may contribute; Chalmers et al. showed that lymphoma was the underlying diagnosis in 33% of THAs in patients with a history of stem cell transplant. However, not all of these patients had a history of GVHD [13].

In these cases, owing to the insufficiency fractures of the acetabular with effective pelvic discontinuity (PD) and the tenuous vascular supply of surrounding bone, THA was conducted with cage construct and bridge plating of the posterior column. This construct has shown efficacy in cases with PD and severe acetabular bone loss in revision THA [20–23]. Plating is primarily studied in revision arthroplasty cases with PD [24,25]. Plating was chosen to restore continuity, optimize contact of viable bone, and add stability to the reconstruction. This fixation technique of posterior column plating with antiprotrusion cage placement led to stability with improved ADLs, restoration of ambulation with full weightbearing, and resolution of pain at 1 year for both cases. Certainly, the perioperative risk of significant surgical or medical complications is high for patients with GVHD; therefore, this technique should be considered in situations with tenuous blood supply and insufficiency fractures in the setting of hematologic malignancy and GVHD.

Summary

These cases are unique reports of osteonecrosis focal to the acetabulum, in patients with history of stem cell transplant and subsequent GVHD. The impact of this disease process should not be overlooked in patients with hematologic malignancies and GVHD. Surgical treatment with multifaceted construct, in these cases with an antiprotrusion cage bolstered by posterior column plating, can relieve pain and improve mobility.

Conflict of interest

Dr. Schabel obtains research support from Zimmer Biomet, unrelated to this work. She is also a board member for the Oregon Association of Orthopaedists.

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