Systemic Avascular Necrosis Following Steroid Administration for Acute Graft Versus Host Disease in a Post-Bone Marrow Transplant Adolescent – A Case Review
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Introduction:
With increased survival rates for pediatric leukemia, greater emphasis has been focused on the adverse effects of leukemia treatment. One of the most debilitating side effects is avascular necrosis (AVN), also known as osteonecrosis. Incidence rates for AVN following treatment for acute lymphoblastic leukemia are between 5 and 10\%\textsuperscript{1,12} with recent studies showing an increased incidence of AVN as high as 23.8\% in patients treated with high dose steroids following bone marrow transplant.\textsuperscript{12} For those pediatric patients with AVN, 60\% remain symptomatic three years later. Of these individuals, 20\% have symptoms that ultimately affect their activities of daily living and quality of life.\textsuperscript{2,12} Today, there are many different treatment options for AVN, however very few are effective, and ultimately the best way to decrease morbidity is prevention and early diagnosis.

Case Report:
A 13 year old male presented to his family physician’s office with a two day history of diffuse lymphadenopathy, fatigue, and malaise. CBC was notable for a WBC count of 131,000 with 52\% blasts. The patient was referred to Connecticut Children’s Medical Center for further evaluation including a bone marrow aspiration and biopsy. A diagnosis of biphenotypic leukemia was made, and a chemotherapy regimen including cytarabine, etoposide and daunorubicin was initiated. Once in full remission, the patient received a bone marrow transplant from an older sibling at Boston Children’s Hospital. Three weeks later, he developed a skin rash consistent with acute graft versus host disease (GVHD) and was started on high-dose steroids. Several weeks into steroid treatment, the patient noted bilateral knee pain. MRI demonstrated multifocal areas of abnormal signal within the femoral head and condyles. The steroids were immediately tapered. Six months later, repeat MRI revealed extensive AVN involving multiple joints. The patient was made non-weight bearing, began bisphosphonates and started hyperbaric oxygen therapy. Subsequent surgical procedures over a three-year period included microfracture, core decompression with stem cell infusion, iliac crest bone grafting, and finally, an osteochondral allograft of the right knee. Despite multiple modalities of treatment, there has been little improvement in pain and function of the patient’s right knee and the patient has continued to experience diffuse joint pain.

Discussion:
The pathophysiological mechanism of AVN following steroid therapy is still not fully elucidated, however most theories point to compromised bone vascularization.\textsuperscript{1} Recent studies show that specific risk factors are associated with an increased incidence of AVN. These include age >10 and age <20, female gender, high BMI and genetics.\textsuperscript{1,5} Although there are differing research results regarding the incidence of AVN in regards to the use of steroids, most studies point to a higher incidence of AVN in those patients receiving higher cumulative doses, increased daily dosing and oral steroid administration versus parental administration.\textsuperscript{5,6}

In assessing AVN, the clinician needs to recognize the early signs and symptoms of joint pain in a patient with AVN risk factors and begin a non-weight bearing regimen immediately. Both medical and surgical treatments need to be utilized and a stepwise approach to management should be followed in order to leave options for future treatment. The ultimate treatment goal is to prevent irreversible subchondral collapse. Despite the many treatment modalities available, there is currently no cure for AVN. At this time, the best medicine physicians can provide for their patients with risk factors for AVN is to practice prevention and detect disease early in its course.
References:

1. Ducassou S., Perel, Y. Curing Acute Lymphoblastic Leukemia and Avoiding Osteonecrosis, Can’t We Have It All?. Pediatric Blood Cancer 2013; 60: 713-714.