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Case Report

Post radiotherapy femoral head avascular necrosis ☆,☆☆

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ABSTRACT

Osteonecrosis is the death of bone cells due to insufficient blood supply; radiotherapy for various underlying malignancies is one of the uncommon causes. Microvascular damage or underlying tissue fibrosis, which leads to an ischemic environment and cell death, is a proposed mechanism. Factors influencing risk of radiation induced AVN include type of radiation whether external beam radiotherapy or brachytherapy, age of the patient, included body part and concomitant additional steroid or chemotherapy treatment. In this case report we brought a case of 40-year-old male patient with right proximal thigh leiomyosarcoma who underwent surgical resection and adjuvant radiotherapy, about a year later when Pelvic MR was done for evaluation of surgical bed and tumor progress right femoral head AVN was detected, the patient was asymptomatic. The exact cut-off radiation dose that causes AVN is unknown and varies across studies, necessitating a cautious study of joints included in the radiation field even in asymptomatic patients for early diagnosis and to prevent morbidity associated with delayed diagnosis.

Introduction

Avascular necrosis or AVN is the ischemic death of bone tissue that occurs when there is an insufficient blood supply. It occurs due to different etiologies including trauma, infections, steroid use, alcohol abuse, connective tissue disorders, sickle cell disease and rarely radiotherapy [1,2]. About 75% of femoral head AVN is attributed to trauma, mainly femoral neck fractures and femoral head dislocations [3]. The femoral head is

Abbreviations: AVN, avascular necrosis; GY, gray (SI unit of radiation dose); rad, radiation absorbed dose.

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more susceptible for AVN because it only has limited collateral circulation from the lateral and medial circumflex arteries [4,5]. Other bones like mandible and the sacrum are more susceptible for radiotherapy induced AVN during head as well as pelvic region radiotherapy respectively [6,8].

Incidence of radiotherapy induced AVN widely varies depending on type of radiation, dose, age of patient, and concomitant drugs like chemotherapy or steroid use. A retrospective study assessing pelvic bone complications in cervical cancer patients who underwent radiotherapy and found the incidence of AVN to be only 0.5% out of a total of 510 patients [2]. However, more recent studies on pelvic radiation-induced necrosis found that it happened in between 2.1% and 34% of those patients [6]. A review of 71 hips from patients with gynecologic cancer receiving radiotherapy revealed an incidence of approximately 24% AVN [7].

The clinical manifestations of femoral head AVN range from asymptomatic to intermittent and severe constant pain in the late stages with associated joint stiffness and limping. On physical examination joint tenderness, reduced range of motion, and pain during dynamic maneuvers could be demonstrated [3,9].

Magnetic resonance imaging (MRI) has a higher sensitivity making it the gold standard imaging modality for assessing AVN. It enables early detection of marrow changes as well as determining the extent of pathology. Other imaging modalities like radiographs, skeletal scintigraphy and single-photon emission computed tomography (SPECT) have lower sensitivity and specificity compared to MRI [10].

Case history

A 40-year-old male patient underwent a surgical resection of a low-grade leiomyosarcoma in the medial compartment of his proximal right thigh 12 months ago, with an unknown postresection tumor margin. After surgery, he underwent 2 phases of external beam radiotherapy: 56 gray on phase 1, about 3 months after surgery, and 66 gray on the second phase. Subsequently, a control MRI of the right thigh was performed 6 months apart (Figs. 1 and 2) for follow-up purposes. The patient had no symptoms in the right hip area, such as pain or joint stiffness, and did not receive any chemotherapy or steroids during his treatment. Prior to his right thigh tumor, he had no known chronic illnesses and was not an alcoholic. On physical examination, the patient was comfortable with a non-antalgic gait. His vital signs were normal. Except for a healed surgical scar over his right medial thigh region, the musculoskeletal examination was nonrevealing. Laboratory examinations, including a complete blood count, organ function tests, and erythrocyte sedimentation rate, are normal.

The treatment plan is to use conservative management and the patient is advised to avoid excessive weight bearing and to perform PET (positron emission tomography) scan for re-staging and assessment of the extent of the local recurrence of leiomyosarcoma.

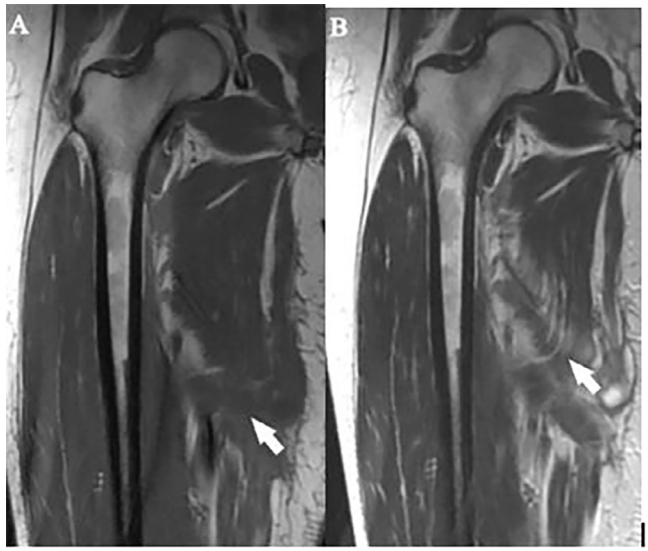

Fig. 1 – The first control MRI in T1W (A) and T2W (B) coronal sequences showed disrupted muscular fibers with T1 hypo and T2 hyperintensity changes within medial thigh compartment (white arrows in A and B). The femoral head was normal.

Discussion

A male patient with recurrent right proximal thigh leiomyosarcoma and assymptomatic radiotherapy-induced AVN of the ipsilateral femoral head was presented.

The development of AVN in cancer patients is considered multifactorial as they are often on multiple drug therapies including systemic steroids, bone-altering drugs such as bisphosphonates or cytotoxic chemotherapies in addition to receiving radiotherapy. As the stated drugs are also potential causes of AVN, it is difficult to pinpoint the exact cause of AVN in this group of patients [1]. Other contributing factors in cancer patients include metastatic infiltration, hypercoagulability, and the congenital absence of the ligamentum teres artery [1].

On a cellular level, the pathophysiology of radiotherapy-induced AVN is not clearly understood, but there are many theories, including macrovascular damage with endothelial dysfunction, which can lead to thrombosis and underlying tissue necrosis [6,11,12,13]. Other theories suggest radiation-induced fibrosis, which occurs due to underlying endothelial damage leading to the accumulation of fibroblasts and macrophages, contributing to an ischemic environment and tissue damage [11–13].

The type of radiotherapy also determines the AVN risk. Conventional external beam radiotherapy, like in our case, carries a higher risk of AVN compared to brachytherapy, which places the radiation capsules close to the target tumor cells [14,15].

There are two categories of biological radiation effects namely deterministic and stochastic. When expected complications occur, deterministic effects follow a threshold dose and their severity is directly proportional to the dose. However, the stochastic effect does not have a threshold dose level

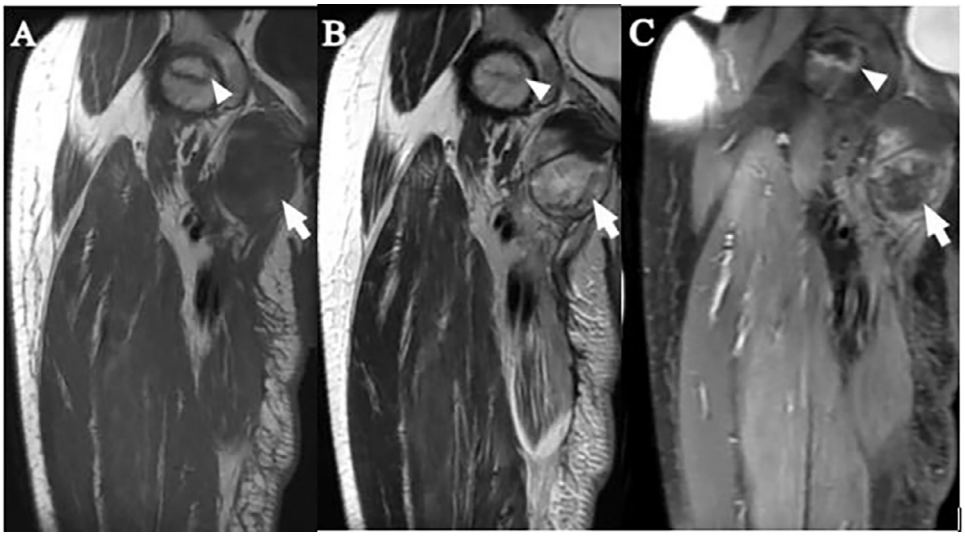

Fig. 2 – After 6 months, T1W (A), T2W (B), T1 FS Postcontrast (C) coronal MR showed a round right femoral headT1 and T2 hyperintense lesion with a circumferential dark rim. The lesion has avid rim enhancement with a nonenhancing center(white arrowheads in A-C). There was also a round well defined T1 isointense, T2 heterogeneously hyperintense lesion with irregular peripheral enhancement (white arrows in A-C).

rather, the received radiation dose directly influences its probability of occurrence [16]. Radiotherapy-induced AVN is believed to have a stochastic effect because it is present in a wide range of radiation exposures occurring at doses as low as 15.4 Gy or 1540 rad [17,18]. Furthermore, it is unclear why patients who received similar doses of radiotherapy might experience AVN complications inconsistently or why unilateral femoral head AVN can develop after bilateral radiation [1].

Even though radiotherapy and systemic chemotherapies/steroids consort to cause AVN, our patient who received 2 phases of external beam radiotherapy for a total of 122 Gy was affected by radiotherapy-associated AVN; his cumulative dose is well above the standard tolerance doses which state a 5% risk of AVN with 52 Gy and significantly rises to 50% with 65 Gy administration [1].

The exact rate of asymptomatic AVN varies across studies. A study among 79 patients with systemic lupus erythematous and antiphospholipid syndrome without history of steroid use found the rate to be 20%. They emphasized the important role of MRI as an earlier identifier of disease. In their cohort, young age was associated with higher AVN incidence [19]. Another study by **Kang et al.** reviewed 68 asymptomatic AVN patients (among which 12/68 with undetermined cause) and determined 55.9% developed symptoms at an average of 2.27 years. We did not come across any studies that looked at incidence of asymptomatic radiation induced AVN [20].

The diagnosis of radiation induced AVN is challenging due to the uncommon nature, nonspecific history, and physical examination sometimes like our case they may be asymptomatic which leads to delayed diagnosis and treatment resulting in increased morbidity. The role of imaging includes detection of AVN as well as ruling out other differential diagnosis like bone metastasis, subchondral insufficiency fracture, idiopathic osteoporosis of hip, infectious and inflammatory arthritis. MRI is preferred imaging modality for early detection of AVN which is characterized by marrow edema which is nonspecific findings and couldn't differentiate among the differential diagnosis stated above. On Intermediate stage, its characterized by T2 hyperintense line separating normal and dead marrow named as "double line sign" which is pathognomonic and on final stages resulting in subchondral bone fracture, bony collapse, T1/T2 hypointensity representing sclerotic dead bone as well as secondary osteoarthritic changes. Radiography and CT even though they are reliable they are insensitive for detection of early osteonecrosis which results in delayed diagnosis and management [21].

Currently, there is a lack of evidence with regards to effective pharmacologic interventions to prevent radiotherapy-related bone complications [22]. Nonsurgical interventions include physiotherapy, weight protection, the use of crutches, and nonsteroidal anti-inflammatory drugs for pain and inflammation are recommended. The cornerstone of AVN treatment is surgery with different options available for each stage of the disease [6,17].

In conclusion, radiotherapy-induced AVN is a rare occurrence and is affected by the type and dose of radiation as well as types of medication like chemotherapeutic agents and steroids. It is important to keep in mind that like in our case, it can be asymptomatic and meticulous assessment of images is needed to look for osteonecrosis even if the purpose of the image is to assess local recurrence of tumor.

Ethical consideration

Written informed consent was taken from the patient and confidentially is ascertained.

Patient consent

Written informed consent was obtained from the patient for anonymized patient information to be published in this article.

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