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Avascular necrosis of the hips with increased activity on ^{68}Ga -DOTATATE PET/CT

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Abstract

Prolonged exposure to cortisol is one of the major causes of avascular bone necrosis (AVN). We report on a case of a woman with Cushing's syndrome attributed to ectopic ACTH secreting tumor who was evaluated with whole body PET/CT study using ^{68}Ga -DOTATATE. The scan showed increased activity by both femoral heads, corresponding to the margins of bilateral AVN seen on MRI. The presented data suggests AVN-induced reactive inflammatory alterations adjacent to the necrotic segment of the bone which can be effectively targeted using radiolabeled somatostatin (SST) analogues.

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Figure.

A 55-year-old woman with history of Cushing's syndrome (CS), hypertension and diabetes mellitus was referred to our institute for further work-up. Diagnosis of ectopic ACTH-secreting tumor responsible for CS was established by inferior petrosal sinus sampling (IPSS). On subsequent MR imaging scan, typical features of avascular necrosis in both femoral heads were noted (**Fig. 1A**: Coronal T1-weighted MR image of the hips; red arrows). Bone marrow edema extending to the intertrochanteric area (thick green arrows) and mild subchondral femoral head collapse of the left (open yellow arrow) hip, indicate more advanced-stage osteonecrosis on this side. Since the majority of ectopic tumors causing CS are neuroendocrine tumors (NETs) which are known to over-express somatostatin receptors (SSTRs), they can be effectively targeted and localized using radiolabeled somatostatin (SST) analogues [1, 2]. Therefore, the patient was also evaluated with whole-body PET/CT study using ^{68}Ga -DOTATATE (radiolabeled SST-analogue), which showed increased activity by both femoral heads (SUVmax: 7,17 and 4,2 for the left and right femoral head respectively) localized at the margins between normal and osteonecrotic bone (**Fig. 1B**: Coronal fused ^{68}Ga -DOTATATE PET/CT images of the hips; white arrows). In addition, increased radiotracer activity was noted by the area of bone marrow edema due to the mild femoral head collapse on the left side (thick green arrows). Avascular necrosis (AVN) or ischemic bone necrosis or osteonecrosis, results from interruption of bone vasculature and can lead to significant morbidity and impairment of patient's function. Prolonged exposure to high levels of cortisol either due to excessive endogenous production by the adrenal glands or exogenous administration of glucocorticoids (cortisol-like medication) is the most common non-traumatic cause of AVN [3]. The pathophysiologic mechanism of hypercortisolemia-induced AVN is not fully elucidated. Fat cell hypertrophy, fat embolism, intravascular coagulation and cortisol-induced osteocyte apoptosis are postulated mechanisms which provide the rationale of bone vasculature interruption and subsequent ischemic necrosis. Typically, femoral heads are most commonly affected, although other skeletal sites like knees, shoulders or ankles could also be involved [4].

Early recognition of AVN is critical for the optimal patient management, since progression of bone ischemia limits treatment options. Conventional bone scintigraphy has been

employed in the work-up of AVN although with limited specificity, while MRI has been considered as the imaging modality of choice for the confident and early diagnosis of AVN [5, 6]. The introduction of the ^{68}Ga -DOTA-conjugated peptides into clinical practice has enabled SSTRs imaging with PET and is evolving as the new standard of reference for the detection and characterization of NETs and other SSTR-positive lesions [7, 8]. Expression and upregulation of SSTRs has also been identified on white blood cells including leukocytes and macrophages, suggesting potential application of PET/CT using ^{68}Ga -DOTA-conjugated peptides (SST analogues) in targeting inflammatory processes [9, 10]. The presented data suggests AVN-related cell-surface over-expression of SSTRs at the borders between normal and ischemic bone indicating underlying sterile inflammation.