CASE REPORT

Solitary Increase of $^{11}$C-Choline Uptake in an Enchondroma Patient with Biochemical Recurrence of Prostate Cancer

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Abstract We report the case of a 72-yr-old prostate cancer patient with biochemical failure (PSA = 2.8 ng/mL) after radical prostatectomy in whom both bone scintigraphy and $^{11}$C-choline PET/CT detected an isolated focal pathological activity in the proximal diaphysis of the left tibia. Surgery was performed and histological analysis revealed enchondroma. The finding is discussed on the basis of the specificity of radiolabeled choline for prostate cancer vs. other tumors or inflammation processes. Particularly, proliferation or concomitant inflammatory processes associated with bone remodeling in enchondroma are discussed and related to $^{11}$C-choline uptake.

Keywords: $^{11}$C-choline PET/CT; enchondroma; prostate cancer

INTRODUCTION

A 72-yr-old prostate cancer patient with biochemical failure was referred to bone scintigraphy because of a biochemical recurrence (prostate specific antigen, PSA = 2.8 ng/mL). The patient had been treated with radical prostatectomy five years earlier owing to prostate cancer (pT2 pN0 cM0, Gleason 3 + 3 = 6). Bone scan revealed an isolated hot spot in the proximal diaphysis of the left tibia (Figure 1).

No lesions were visible in the pelvis or in the spine, which made the isolated finding in the tibia unlikely to be related to prostate cancer. The traditional whole body $^{11}$C-choline PET/CT, conducted from the cranial basis to the midthigh, did not reveal any pathological uptake site of $^{11}$C-choline (Figure 2).

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Figure 1. Anterior (right) and posterior (left) view of whole body bone scintigraphy. Increased $^{99m}$Tc-methylenediphosphonate activity is observed in the proximal diaphysis of the left tibia.
However, since the sensitivity of $^{11}$C-choline positron emission tomography/computed tomography (PET/CT) is higher in comparison to bone scintigraphy and also because of the capability of PET/CT to investigate local recurrence and lymph node metastases, the patient underwent subsequent $^{11}$C-choline PET/CT to further exclude macroscopic disease.

The CT component of the PET/CT revealed an area of sclerosis (Figure 3B). Fusion imaging demonstrates that the increased metabolic activity localizes to the sclerotic area (Figure 3C).

Figure 2. Coronal view of fused $^{11}$C-choline PET/CT showing physiological distribution of the tracer. No pathological $^{11}$C-choline uptake sites could be detected.

Physiological uptake was seen in the right axillary vein, in the liver, in the spleen, in both kidneys, in the small bowel and in the bladder. In the additional static acquisition centered on the knees, a pathological increase of $^{11}$C-choline uptake was seen in the proximal diaphysis of the left tibia which corresponded to the scintigraphic finding (Figure 3A).

Figure 3A. Coronal view of PET (A) of the inferior limb at knee height. There is a region of increased uptake of $^{11}$C-choline in the area of bone thickening evident in the CT scan.

Figure 3B. Coronal view of CT (B, bone window), of the inferior limb at knee height. There is a region of increased uptake of $^{11}$C-choline in the area of bone thickening evident in the CT scan.

Figure 3C. Coronal view of and fused $^{11}$C-choline PET/CT images (C) of the inferior limb at knee height. There is a region of increased uptake of $^{11}$C-choline in the area of bone thickening evident in the CT scan.
The patient decided to undergo surgery. Histological analysis revealed enchondroma (Figure 4A and Figure 4B).

Figure 4A. Typical enchondroma: hypocellular tumor with abundant hyaline cartilage matrix without necrosis and mitosis (e.e. 20x).

Figure 4B. Chondrocytes with finely granular eosinophilic cytoplasm is often vacuolated with small nuclei (e.e. 20x).

**DISCUSSION**

Enchondroma is a benign bone tumor, which results from the continued growth of residual benign cartilaginous rests that are displaced from the growth plate. The tumor growth occurs in the medullary cavity of bone [1]. Overall, they are particularly frequent in the phalanges and commonly in the pediatric and young adult age groups, but may also occur in the diaphysis of femur and tibia. This is being recognized in 1.7% of femura at autopsy [2,3]. Enchondromas usually present as a painless bony mass, and radiographically often ovoid in shape with endosteal scalloping; displaying occasionally chondroid type matrix mineralization and do not induce periosteal reactions [4,5]. Bone scintigraphy shows a variable increase of tracer uptake in the skeletal phase whilst the perfusion phase and the blood pool phase are normal [1,2,4]. Malignant transformation into chondrosarcoma is rare but may occur, especially in the diffuse form of multiple enchondromatosis [5,6].

PET/CT with $^{11}$C-choline is frequently used for restaging prostate cancer in patients with biochemical failure. Several studies have shown that recurrent disease can be imaged for low PSA values [7-9], that PET/CT with radiolabeled choline might be more accurate than conventional imaging for the detection of lymph node and skeletal metastases [8,10-12], and that several clinical and pathological factors can be used to identify patients who have a higher risk of positive PET/CT [13-15].

Studies indicated that radiolabeled choline accumulates in several malignancies other than prostate cancer or physiological variants, including lung cancer, brain tumors, bladder cancer, meningiomas, as well as inflammatory arthritis disease, Paget’s disease, thymus hyperplasia, benign prostate hyperplasia [16-22]. Increased $^{11}$C-choline uptake has also been observed in the pelvic and retroperitoneal lymph nodes of prostate cancer patients with biochemical failure and no histological evidence of disease. This was attributed to lymph node hyperplasia [23]. A simple diffusion mechanism, in addition to an energy-dependent specific transport, regulates the uptake of choline in mammalian cells [24]. Therefore, it is possible that, at least in some of these cases, nonspecific uptake might represent the cause of the false positive.

An alternative hypothesis is that uptake of $^{11}$C-choline reflects increased proliferation of cell membranes or of some of their components [25]. It is unknown whether $^{11}$C-choline uptake in enchondroma reflects cell proliferation or a concomitant inflammatory process associated with bone remodeling and/or inflammation [26]. The relation between tracer uptake and cellular proliferation is however complex. In humans, the extent of uptake of $[^{11}]$C-choline in the prostate tumor is not related to the cell proliferation rate, as estimated by Ki67 [27].

Nevertheless, in various tumor cells, there was a significant correlation between choline uptake and cell proliferation, as reflected by the incorporation of $[^{3}H]$methyl-thymidine into DNA [28]. Al-Saedi et al. found that the concentration of concentration of the water-soluble product phosphocholine was higher in breast cancer MCF-7 cells than in control cells [29]. In the same cells, methyl-$[^{3}H]$choline incorporation was found to be related to the fraction of cells in the S-phase as well as to the incorporation of [methyl-$[^{3}H]$thymidine into DNA [30].

**CONCLUSION**

In summary, this case report highlights the necessity of keeping in mind enchondroma in the differential diagnosis of $^{11}$C-choline uptake in the skeleton of patients undergoing $[^{11}]$C]choline PET/CT.

**CONFLICTS OF INTEREST**

The authors report no conflicts of interest.
REFERENCES

Key References: 1, 4, 15, 26


