Clinical note

Metabolic and osteogenic pattern of prostate cancer bone metastases


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Abstract

The current protocols include the bone scintigraphy and choline PET/CT to localize recurrence in patients having elevated serum PSA after treatment for prostate cancer. Both methods show good agreement in the diagnosis of bone metastases; however, conflicting results can be found. We present three cases in which a PET/CT was performed with 18F-fluoride due to disagreement between the bone scintigraphy and 11C-choline PET/CT. The 18F-fluoride PET/CT was capable of confirming the existence of bone metastasis in all of them, so it may be an alternative to the MRI as a tracer of second bone imaging modality, although its use is limited by cost and availability.

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Introduction

Bone metastases are a very frequent complication of prostate cancer since around 65–75% of the patients with advanced disease present metastatic bone disease.1,2

Bone scintigraphy continues to be the screening test used in bone metastasis in patients with prostate cancer because of its availability, low cost and extensive clinical experience. However, the specificity of this test in the differentiation between benign and malignant skeletal processes is not very good. The addition of tomographic studies (SPECT) improves its diagnostic precision, and integrated SPECT/CT increases the specificity of the technique.1

The use of PET studies with 18F-FDG has been introduced in oncology in the last years. However, this tracer shows low affinity for differentiated tumors which are frequent in prostate cancer.2

The use of tracers such as 11C-acetate and choline marked with 11C or 18F have therefore been implemented with promising initial results in prostate cancer, especially in the management of biochemical relapse. The mechanism of choline uptake in prostate cancer is related to the increase in phospholipidic consumption by tumoral cell proliferation and the dysregulation in choline-kinase activity.2,3

The mechanism of uptake of the PET tracer 18F-fluoride is similar to that of the tracers used in bone scintigraphy, being related to regional bone perfusion and osteogenic/blastic activity. Preliminary studies have demonstrated a higher sensitivity with PET with 18F-fluoride than that of bone scintigraphy due to the better resolution of the PET cameras and also, perhaps, to some pharmacokinetic advantage of 18F-fluoride. As occurs with SPECT, PET/CT adds morphological information which increases the specificity of the technique.1,4

In clinical practice bone scintigraphy and PET/CT with choline are performed in patients suspected of biochemical relapse of prostate cancer in order to locate the recurrence. Although there is good concordance between the two techniques in the diagnosis of bone metastases, a problem has arisen with the reports of some discordant results.2,3

We present 3 cases in which we performed PET/CT with 18F-fluoride as a second method of bone imaging after presenting discordance between the results of bone scintigraphy and PET/CT with choline.

Clinical cases

The three patients underwent bone scintigraphy and PET/CT with 11C-choline within a period of less than one month. All the
patients presented discordant findings between the two methods and thus, underwent PET/CT with $^{18}$F-fluoride one week later.

After the administration of 740 MBq of $^{99m}$Tc-HDP, a whole body planar study was performed in a double-head gamma camera. $^{11}$C-choline was synthesized in a cyclotron located in the same installation as the PET/CT tomograph according to the method of Hara et al. All the patients had undergone 6 h of fasting prior to the study and signed informed consent. The patients were placed in the bed of the PET/CT Gemini (Philips) tomograph. Following intravenous injection of 656 ± 119 MBq of $^{11}$C-choline whole body images were acquired 5 min after the injection, beginning at the pelvis in a caudal-cranial direction.

The synthesis of $^{18}$F-fluoride was performed in the same cyclotron. After intravenous administration of 185–259 MBq of $^{18}$F-fluoride, the acquisition was carried out at 2 min per bed in a caudal-cranial direction including the skull at 50 min post injection.

Interpretation of the images was visual and performed together by 2 specialists in Nuclear Medicine and one specialist in Radiodiagnosics.

The uptake, localization and the presence of morphological changes of all the bone images were characterized. The final diagnosis was obtained by other imaging techniques, post-treatment follow up or histology.

Case 1

A 72-year-old patient diagnosed with adenocarcinoma of the prostate, T3N1, Gleason 4+3 was treated by prostatectomy and pelvic lymphadenectomy one year previously. He presented an evaluation in serum PSA level, 6-month doubling time, and the current serum PSA value was 1.7 ng/mL.

Bone scintigraphy did not show images of uptake suggestive of bone metastasis. The PET/CT study with $^{11}$C-choline showed an abnormal tracer deposit in the T3 vertebral body suspicious of metastatic infiltration. The PET/CT study with $^{18}$F-fluoride showed active images with marked intensity, in the cervical column and left shoulder with a greater degree of uptake than in the bone scintigraphy, attributable to an arthrodigenerative process by CT. These changes were not visible with $^{11}$C-choline. Uptake was also observed in the T3 vertebral body with greater intensity probably in relation to the marked inflammatory activity in the remaining lesions (Fig. 2). A MR was finally performed which also labeled the lesion as metastatic.

Case 2

A 69-year-old patient was diagnosed with adenocarcinoma of the prostate, T4N0, Gleason 4+4 and treated with prostatectomy 2 years previously. He presented an elevation of serum PSA levels, with a 4-month doubling time and a current PSA value of 3.0 ng/mL.

The bone scintigraphy was negative for malignancy, showing arthrodegenerative changes of cervical predominance as well as in the shoulders. The PET/CT study with $^{11}$C-choline showed an abnormal tracer deposit in the T3 vertebral body suspicious of metastatic infiltration. The PET/CT study with $^{18}$F-fluoride showed active images with marked intensity, in the cervical column and left shoulder with a greater degree of uptake than in the bone scintigraphy, attributable to an arthrodigenerative process by CT. These changes were not visible with $^{11}$C-choline. Uptake was also observed in the T3 vertebral body with greater intensity probably in relation to the marked inflammatory activity in the remaining lesions (Fig. 2). A MR was finally performed which also labeled the lesion as metastatic.

Case 3

A 75-year-old patient had been diagnosed with adenocarcinoma of the prostate, T3N0 Gleason 4+4 and treated with prostatectomy 6 years before. He presented local recurrence diagnosed by MR 4 years previously and underwent radiotherapy and hormone therapy until 3 years ago. Serum PSA levels were elevated, with a doubling time of 2 months and the current PSA serum level was 17.0 ng/mL.

Bone scintigraphy showed intense increased uptake of the tracer in the left hip involving the acetabular region and part of the ischium and iliac branch, being compatible with a metastatic bone process. A focal increased uptake was also observed in the axillary line from the fourth rib of the right hemithorax. The PET/CT study with $^{11}$C-choline showed pathological uptake in these 2 lesions. In addition, 2 other hypermetabolic foci were found in the left glenoid region and in the L5 vertebral body. The PET/CT with $^{18}$F-fluoride showed anomalous uptake of greater intensity in the 4 metastatic lesions described (Fig. 3). During the follow up the patient presented progression of the metastatic bone dissemination.

Discussion

Together with lymph node disease bone metastases are the most frequent form of disease recurrence in patients treated with radical prostatectomy or radiotherapy. In addition, 90% of the patients who die due to prostate cancer present bone metastasis thereby supporting the need for early diagnosis of bone recurrence.
Fig. 2. Negative bone scintigraphy. Abnormal deposit of \(^{11}\text{C}\)-choline in the T3 vertebral body demonstrated with \(^{18}\text{F}\)-fluoride, albeit with lesser uptake, labeled as metastasis by MR. The PET/CT study with \(^{18}\text{F}\)-fluoride also showed active images of marked intensity in the cervical spine with a greater uptake than in the bone scintigraphy, attributable to an arthrodegenerative process by CT without significant findings with \(^{11}\text{C}\)-choline. Red arrows: active pathological images shown in the interpretation of the study with choline and fluoride. Blue arrows: review of active pathologic images shown in the interpretation of the study with choline and fluoride. Blue arrows: bone scintigraphy revision after images with choline and fluoride.

Fig. 3. Bone scintigraphy showing pathological increased uptake of the tracer in the left hip, multifocal as well as an active focus in the axillary line of the fourth rib of the right hemithorax. The PET/CT study with \(^{11}\text{C}\)-choline confirmed the metastatic origin. In addition, two other hypermetabolic foci were observed in the left glenoid region in the L5 vertebral body. The 4 metastatic lesions described show greater uptake with \(^{18}\text{F}\)-fluoride. During the follow up the patient presented progression of the metastatic bone involvement. Red arrows: active pathological images shown in the interpretation of the study with disphosphonates, choline and fluoride.

Wide experience reported in the literature sustain the use of bone scintigraphy in the detection of bone metastases in patients with biochemical relapse of prostate cancer.\(^5\) However, recent studies have suggested the use of PET/CT with choline as a diagnostic alternative. Indeed, Beheshti et al. have reported a sensitivity, specificity and diagnostic precision of 79, 97 and 84%, respectively, for \(^{18}\text{F}\)-choline.\(^6\) Riera et al. described a concordance of 58/61 patients with PET/CT with \(^{11}\text{C}\)-choline and bone scintigraphy (15 positive and 43 negative). In 3 patients PET/CT with \(^{11}\text{C}\)-choline identified lesions attributable to bone metastasis with a negative bone scintigraphy.\(^7\)

In cases involving discordance between these two procedures MR is usually utilized.\(^8\) Nonetheless, we believe that the use of \(^{18}\text{F}\)-fluoride may be an alternative to the use of MR. Even-Sapir et al. described an increase in the sensitivity of PET/CT with \(^{18}\text{F}\)-fluoride over whole body SPECT which showed higher sensitivity than planar scintigraphy (100, 90 and 70%, respectively).\(^9\) In the cases we present SPECT was not performed because the first technique carried out was bone scintigraphy and the findings of the planar study do not allow selection of the tomographic area studied (or because it was negative or did not show undetermined lesions).

Thus, although the performance of tomographic studies in bone scintigraphy may raise the sensitivity of the technique, the use of whole body SPECT/CT is not carried out in clinical practice since it requires a much longer study time than the acquisition of PET/CT.

This greater sensitivity of \(^{18}\text{F}\)-fluoride should, a priori, produce a lower specificity compared with bone scintigraphy. Morphologic characterization of the lesions is, therefore, important in both the SPECT and PET studies to thereby avoid erroneous interpretations.\(^3\)

Nonetheless, at present the main limitation of the use of \(^{18}\text{F}\)-fluoride is its precision in comparison with bone scintigraphy, and thus it may only be considered cost-effective in view of the discords with other diagnostic techniques such as those used in our cases.

In the few comparative studies reported, greater specificity is described with \(^{18}\text{F}\)-choline than \(^{18}\text{F}\)-fluoride (99% vs. 93%), albeit...
with a slightly lower sensitivity (74% vs. 81%), with the main advantage of choline being the absence of uptake in arthrodegenerative lesions. Other studies, however, have described the presence of uptakes of choline in benign processes such as inflammatory processes or traumatic lesions. Further, larger studies are, therefore, needed to know the precise specificity of choline in the detection of bone metastasis.

In the cases presented the use of $^{18}$F-fluoride in view of the discordances between the bone scintigraphy and PET/CT with $^{11}$C-choline corroborated the presence of bone metastasis and may, therefore, be an alternative to MR as a tracer of a second method of bone imaging.

References