Unusual Soft Tissue Uptake of F-18 Sodium Fluoride in Three Patients Undergoing F-18 NaF PET/CT Bone Scans for Prostate Cancer

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Abstract Three males aged 71 to 80 years with known stage IV metastatic prostate cancer underwent F-18 sodium fluoride (NaF) PET/CT to assess osseous metastatic disease burden and stability. In addition to F-18 NaF avid known osseous metastases, each patient also exhibited increased F-18 NaF activity in soft tissues. The first patient exhibited multiple F-18 NaF avid enlarged retroperitoneal and pelvic lymph nodes on consecutive PET/CT scans.

The second patient demonstrated an F-18 NaF avid thyroid nodule on consecutive PET/CT scans. The third patient exhibited increased F-18 NaF activity in a hepatic metastasis.

Keywords F-18 NaF · Sodium fluoride · PET/CT · Soft tissue · Prostate cancer

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Fig. 1 F-18 NaF contrast-enhanced CT (a, d), PET (b, e), and fused PET/CT images (c, f) through the kidneys demonstrate an enhancing, non-calcified NaF avid aortacaval lymph node (long arrow, images a–c) and a less-avidly enhancing NaF avid retrocaval lymph node (long arrow, images d–f) which is separate from physiologic NaF activity seen in the right ureter (short arrow, images d–f; ureteral uptake in (f) is misregistered slightly such that it overlies the psoas muscle). These nodes and NaF avid iliac chain nodes were present in a 71 year old male with a stable prostate cancer metastasis to the acetabulum, not on androgen deprivation therapy, and with slowly rising PSA (10.1 ng/mL at time of the first scan). The nodes' NaF activity increased on subsequent scans, for example the retrocaval node SUVmax was 7.6 in September 2013 (10.7 mCi F-18 NaF, uptake time 58 min), and SUVmax 12.6 in February 2014 (10.7 mCi F-18 NaF, uptake time 61 min). Both scans were performed

according to established guidelines [1]. NaF activity was significantly higher than background blood pool, liver, and spleen activity (SUVmax 1.8, 0.79 and 0.95 respectively) [2]. It is conceivable that malignant infiltration of a lymph node could result in increased NaF deposition due to increased perfusion, as may sometimes be seen with Tc99m methylene diphosphonate bone scans. A follow-up F-18 FDG PET/CT was suggested to assess for hypermetabolic lymph node metastases but was not pursued by the referring oncologist, likely due to patient's overall clinical stability. Sheth et al. reported NaF uptake in a mediastinal node in a renal cell carcinoma patient and speculated that the etiology may be related to presence of microscopic calcifications [3]. It has been shown that F-18 NaF activity can be elevated in the blood pool and coronary arteries from atherosclerosis and inflammation. However, the true significance of NaF uptake in lymph nodes remains unknown [4]

Fig. 2 F-18 NaF CT (a, d), PET (b, e), and fused PET/CT images (c, f) through the thyroid gland were obtained on a 80 year old male with stage IV prostate cancer and stable osseous metastases, on androgen deprivation therapy. Images B and C depict increased NaF activity (SUVmax 6.1) in a thyroid nodule (long arrow) demonstrating rim calcification within an enlarged right lobe. Tracer uptake is demonstrated along this calcification, as expected, but there is also diffuse uptake in the soft tissue attenuation portion of the nodule. A PET/CT performed 5 months later with contrast-enhanced CT (images e, f) demonstrated stable NaF tracer avidity in the nodule with SUVmax 7.5 and enhancement similar to the

adjacent parenchyma. Although the patient passed away before ultrasound could be undertaken, which might have demonstrated microcalcifications responsible for the diffuse NaF uptake, the presence of rim calcifications on CT in this patient may be an adverse feature, with Yoon et al. reporting a sensitivity of 47 % and specificity of 87 % of rim calcification for malignant histology [5]. While focally increased thyroid activity on F-18 FDG PET/CT correlates with primary or metastatic thyroid malignancy, whether or not thyroid nodule F-18 NaF uptake correlates with malignant etiology is unknown [6, 7]

Fig. 3 F-18 NaF contrast-enhanced CT (**a**) and PET (**b**), T1-weighted post-contrast MRI (**c**), diffusion-weighted MRI (**d**), and fused PET/CT images (**E**-axial, **F**-coronal) through the liver of a 77 year old male with stage IV prostate cancer, known osseous and nodal metastases, and a rising PSA (127 ng/mL). The scan showed a new hypoattenuating, non-calcified liver lesion on CT (**a**) with subtle F-18 NaF uptake on PET (long arrow, **b**). Liver MRI showed heterogeneous contrast enhancement (long arrow, **c**) and restricted diffusion (**d**) along with numerous other liver lesions. Biopsy revealed adenocarcinoma, negative for TTF-1 and PSA. Basu et al. [8] and Swietaszczyk et al. [9] reported intense NaF uptake in hepatic metastases from breast and neuroendocrine cancers, respectively.

However, the lesions reported by both of these authors were densely calcified, in keeping with NaF's mechanism of direct incorporation into the hydroxyapatite crystal [10]. It is not clear why the non-calcified metastasis in our patient would demonstrate tracer avidity, although a plausible explanation exists. F-18 NaF kinetic studies have shown that NaF activity in the soft tissues, blood pool, and solid organs is highest early after injection, rapidly clears during the first 20 minutes, and then gradually diminishes thereafter [11–14]. The heterogeneous enhancement of the metastasis on MRI suggests that altered vascular perfusion may have prolonged clearance of NaF from this lesion, thereby accentuating the intensity of uptake.

Compliance with Ethical Standards

Conflict of Interest Andrew Hawkins and Brandon Howard declare that they have no conflict of interest relevant to the work described herein.

Ethical Statement This report of three patients did not constitute human subjects research according to the standards of the Duke Institutional Review Board (IRB) (<https://irb.duhs.duke.edu/policies-and-regulations/policies>) and was exempt from IRB review.

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