Microcalcified Hepatic Metastases Incidentally Detected on F-18 NaF PET/CT in a Patient with Prostate Cancer

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Received: 7 March 2016 / Revised: 20 May 2016 / Accepted: 27 May 2016 / Published online: 17 June 2016
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Abstract F-18 NaF PET/CT evaluation has gained importance in recent years. Achievements from F-18 NaF PET/CT are: higher sensitivity of positron imaging, higher target background ratio with higher tracer accumulation in bone hydroxyapatite and higher specificity through CT correlation. These properties have also given directions to new research fields based on imaging microcalcifications, very recently. A limited number of cases have reported the F-18 NaF uptake in macrocalcified soft tissue metastases. Although the presence of microcalcification was not proved; accumulation

of F-18 NaF in the metastatic brain lesion with no visible calcification on the CT, in a patient with ductal breast carcinoma has also been reported. Herein we present a patient with microcalcified hepatic metastasis of prostate cancer incidentally detected on F-18 NaF PET/CT which was confirmed with histochemical staining.

Keywords Calcification · Imaging · Metastasis · Positron-emission tomography · Prostate · Sodium fluoride

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Fig. 1 A 62-year-old patient with adenocarcinoma was treated with radical prostatectomy and radiotherapy to the prostate bed initially in 2008. He has been followed-up as disease free since the initial treatment. Although there was not any patient complaint, free prostate-specific antigen (f-PSA) was determined as 30 ng/ml (normal range: 0–0.934) and his alkaline phosphatase (ALP) was 173 U/L (normal range: 45–129) in his latest laboratory evaluation. Because of the biochemical recurrence, the patient was referred for F-18 fluoride positron emission tomography/computed tomography (F-18 NaF PET/CT). Multiple

skeletal metastatic sites were seen on the maximum intensity image (a); multiple heterogeneous uptake regions on *right upper* quadrant region of abdomen on axial PET (b) and F-18 NaF PET/CT fusion image (d) corresponding to hepatic hypodense metastatic lesions (Arrows) on CT (c) were incidentally detected. He was referred for a tru-cut biopsy and the histopathologic evaluation of the liver biopsy revealed metastasis of the prostatic adenocarcinoma with positive PSA in histochemical assessment

Fig. 2 The histopathologic evaluation of the liver biopsy revealed metastasis of the prostatic adenocarcinoma with comedo necrosis and intracellular calcifications (**a**: H&E X 100, **c**: H&E X 400). Further evaluation with histochemical staining with von Kossa exhibited intracellular *black-brown* colored accumulations (*Arrows*); resembling calcifying particles in tumor cells, in the walls of small capillaries and in areas of comedo necrosis (**b**, **d**: von Kossa histochemical stain X 400). The accumulation of bone-seeking radiopharmaceuticals in benign or malign soft tissue structures has been associated with altered extracellular fluid, capillary permeability due to tumor neovascularization and high calcium content of centrally laminated psammoma bodies, and usually enhanced with the presence of macrocalcification. F-18 NaF uptake in soft tissues, with macrocalcification of the lesions shown on CT images, were reported in intracranial meningiomas, in metastases of a patient with ovarian carcinoma, a patient with an infiltrating ductal carcinoma of the breast, and a patient with osteosarcoma [1–4]. Although presence of microcalcification was not proved; accumulation of F-18 NaF in the metastatic brain lesion with no visible calcification on the CT in a patient with ductal breast carcinoma has also been reported [5]. The multiple hypodense metastatic lesions detected on CT images in our case were also not macrocalcified. We confirmed the microcalcification with histochemical staining with von Kossa. This propensity of F-18 NaF accumulating in microcalcifications of remodeling and necrotic tissues has been gaining importance in studies on the prediction of high-risk coronary atherosclerotic plaques. It has been shown that F-18 NaF uptake is associated with necrosis, greater positive remodeling and more microcalcification [6, 7]. Recently, Irkle et al. has shown that F-18 NaF PET/CT imaging can distinguish between areas of macro and microcalcification. They determined that F-18 NaF uptake co-

localized with both underlying calcium deposits and regions with no apparent calcification on CT. They histologically demonstrated that the PET signal was binding to microcalcifications below the detection limit of clinical CT and micro-CT [8]. Consistent with this knowledge, no calcification was detected on CT images corresponding to F-18 NaF accumulations detected on PET in our case. Histochemical staining with von Kossa exhibited intracellular calcifying particles in tumor cells, in the walls of small capillaries, and in areas of comedo necrosis (Figs. 1 and 2b and d). Calcifications in the metastatic lesions may also be seen as a result of radiotherapy or systemic chemotherapy. However, in this case there were no other treatment in the patient's history, except the radiotherapy that he had received to the prostate bed after the radical prostatectomy and he has been followed up as disease free since the initial treatment. The specificity of F-18 NaF PET/CT showing microcalcifications has also recently been proposed to specifically target type 2 microcalcifications that have been shown to be produced by malignant cells. Wilson et al. suggested that, early detection of microcalcifications with F-18 NaF PET imaging before calcium deposits observed on the CT scan could be useful in early breast cancer diagnosis [9]. Microcalcifications are also associated with other disease processes and prostate cancer. Although it is beyond the scope of this paper, utility of F-18 NaF PET/CT in evaluating many disease processes, in early detection of microcalcifying tumors and their metastases even when invisible on other imaging techniques seems to be a likely topic for investigation. With the spreading use of F-18 NaF PET/CT in oncology, cautious, detailed interpretation of benign and malignant extraosseous lesions and incidental findings contributing to the staging, treatment, as well as osseous lesions on F-18 NaF PET/CT scans will gain importance

Compliance with Ethical Standards

Conflict of Interest Authors; Gul Ege Aktas, Ali Sarıkaya, Nuray Can and Selin Soyuluoglu Demir declare that they have no conflict of interest.

Ethical Statement All procedures performed were in accordance with the ethical standards of the institutional review board and with the 1964 Helsinki declaration and its later amendments. All subjects in the study gave written informed consent or the institutional review board waived the need to obtain informed consent.

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