



Physiological FAP-activation in a postpartum woman observed in oncological FAPI-PET/CT

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Fibroblast activation protein (FAP) is a type II transmembrane serine protease overexpressed by cancer-associated fibroblasts [1]. However, high expression can also be observed in non-malignant processes associated with tissue remodeling such as wound healing and diseases leading to fibrosis [2].

Our image presents a 29-year-old female patient with adenoid cystic carcinoma in the right parapharyngeal space with skull infiltration. The tumor was first diagnosed in 12/2018 and subsequently histologically confirmed with an initial classification of cT4 cN0 cM0. Within the scope of planning radiation therapy, a (⁶⁸Ga-FAPI-46) PET/CT was performed presenting a clear finding of the adenoid cystic carcinoma (*a*) with a SUVmax of 17.3, respectively. Surprisingly, the parenchyma in both breasts was well depicted with a SUVmax of 4.1 in the right and 3.5 in the left, respectively (*b*). The endometrium remarkably demonstrated a SUVmax of 25.7 as highlighted in *c*. Uptake in the thyroid (SUV 6.3) was also increased.

We hypothesize that the presented high FAP-uptake in the hormone-sensitive organs such as breast parenchyma and

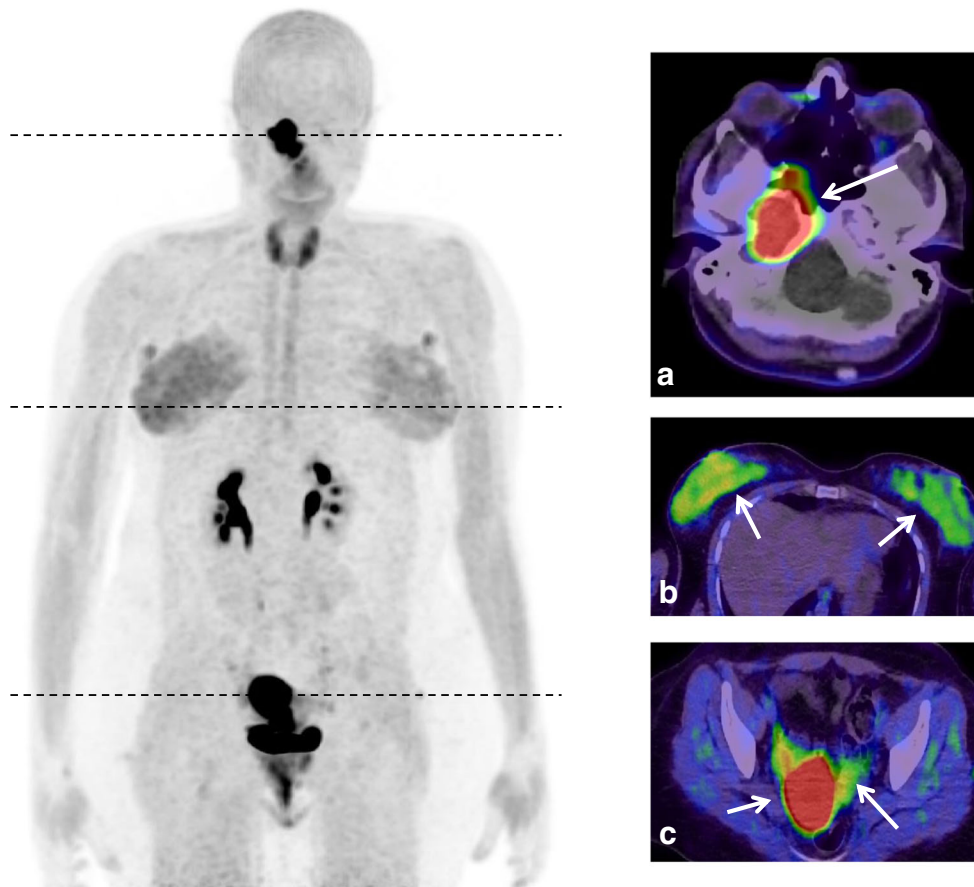
endometrium is a physiological mechanism due to the fact that the presented patient is currently breastfeeding after giving birth 5 months ago. Post-partum thyroiditis is often asymptomatic, thus underdiagnosed and reflects chronic inflammation [3]. Breast parenchyma is characterized by low FAP expression in normal tissue, but high expression in breast cancer [4, 5]. Furthermore, the density of breast and fibro-glandular tissue depends on dynamic physiologic processes based on endogenous and exogenous hormonal fluctuations. During lactation, the cessation of progesterone secretion leads to the release of prolactin, enabling cell vacuolization and secretory changes resulting in the production of milk [6]. Therefore, an increased parenchymal breast density can be seen [7] with an increased FAP expression as a functional correlate.

This case demonstrates that a physiologic increase in FAP expression in hormone-sensitive organs such as the breasts and uterus may occur in the post-pregnancy period and breastfeeding.

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Compliance with ethical standards

Ethics approval and consent to participate The radiopharmaceutical was used on an individual patient basis according to German Pharmaceuticals Act §13(2b). The patient gave written informed consent to receive the novel diagnostics and permitted anonymized publication of related medical data. The ethical committee of Heidelberg University approved this retrospective evaluation to be in accordance with the Helsinki declaration. For case reports from clinical practice, no trial registration is required.

Conflict of interest UH, CK, and FLG have a patent application for quinolone-based FAP-targeting agents for imaging and therapy in nuclear medicine. UH, CK, and FLG have shares of iTheranostics.

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References

1. Hamson EJ, Keane FM, Tholen S, Schilling O, Gorrell MD. Understanding fibroblast activation protein (FAP): substrates, activities, expression and targeting for cancer therapy. *Proteomics Clin Appl*. 2014;8(5-6):454–63.
2. Rettig WJ, Garin-Chesa P, Beresford HR, Oettgen HF, Melamed MR, Old LJ. Cell-surface glycoproteins of human sarcomas: differential expression in normal and malignant tissues and cultured cells. *Proc Natl Acad Sci USA*. 1988;85:3110–4.

3. Mizukami Y, Michigishi T, Hashimoto T, Nakamura S, Tonami N, Takazakura E. Postpartum thyroiditis. A clinical, histologic, and immunopathologic study of 15 cases. *Am J Clin Pathol*. 1993 Sep;100(3):200–5.
4. Costa A, Kieffer Y, Scholer-Dahirel A, Pelon F, Bourachot B, Cardon M, et al. Fibroblast heterogeneity and immunosuppressive environment in human breast cancer. *Cancer Cell*. .
5. Gao MQ, Kim BG, Kang S, Choi YP, Park H, Kang KS, et al. Stromal fibroblasts from the interface zone of human breast carcinomas induce an epithelial-mesenchymal transition-like state in breast cancer cells in vitro. *J Cell Sci*. 2010;123:3507–14.
6. Heller SL, Young Lin LL, Melsaether AN, Moy L, Gao Y. Hormonal effects on breast density, fibroglandular tissue, and background parenchymal enhancement. *Radiographics*. 2018;38:983–96.
7. Sabate JM, Clotet M, Torrubia S et al. Radiologic evaluation of breast disorders related to pregnancy and lactation

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