Intraindividual tumor heterogeneity in NET – Further insight by C-X-C motif chemokine receptor 4-directed imaging

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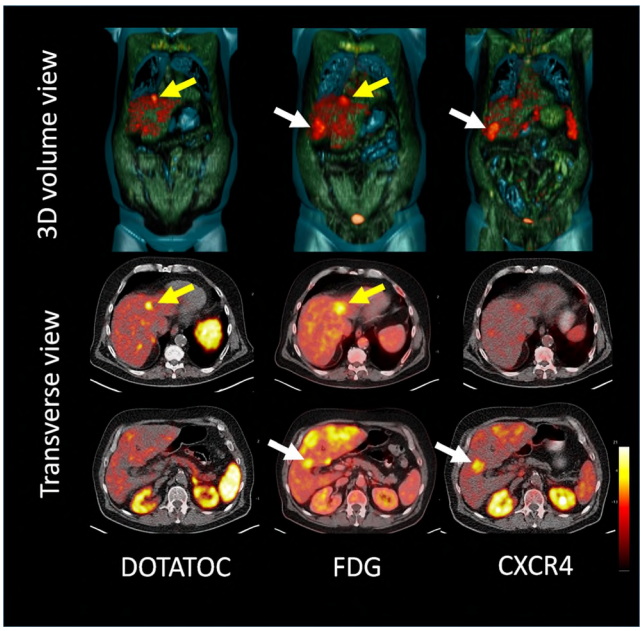

A 67-year-old man with a history of a G3 (Ki67: 80 %) neuroendocrine tumor (NET) of the stomach was referred for restaging with [^{18}F]-fluorodeoxy-glucose ([^{18}F]FDG) and somatostatin receptor (SSTR) positron emission tomography/computed tomography (PET/CT) using [^{68}Ga]-DOTA-D-Phe-Tyr^{3}-octreotide ([^{68}Ga]DOTATOC). Additionally, C-X-C motif chemokine receptor 4- (CXCR4-) directed imaging with [^{68}Ga]Pentixafor PET/CT for endoradiotherapy evaluation was performed. Imaging revealed multiple hepatic metastases. Of note, marked heterogeneity, including SSTR+/FDG+/CXCR4- (yellow arrows), exclusively FDG+ as well as FDG+/CXCR4+ lesions (white arrows) could be recorded. SSTR and CXCR4 expression did not demonstrate a significant coincidence.

Whereas different patterns of [^{18}F]FDG and [^{68}Ga]DOTATOC positivity are well-known and have been described in a number of studies [1–3], this is the first report demonstrating valuable complementary insight into the complexity of tumor heterogeneity by investigation of the CXCR4 expression profile in NET in which receptor overexpression has been described with more aggressive histology [4]. This observation might be especially interesting for G2 NET patients in whom CXCR4 positivity might denote more aggressive disease or in G3 NET in which high receptor expression might represent a new therapy option [5] , in particular in advanced disease stages. Further research is warranted to elucidate the underlying mechanisms or prognostic implications.

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