Imaging of chemokine receptor 4 expression in neuroendocrine tumors in comparison to DOTATOC and FDG PET/CT

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Introduction: Diagnostic imaging of neuroendocrine tumors (NETs) is the domain of somatostatin receptor (SSTR) agonists as well as FDG PET/CT in dedifferentiated tumors. SSTR also serves as target for receptor directed peptide therapy. More recently, specific ligands targeting the chemokine receptor 4 (CXCR4) for diagnostic and therapeutic purposes were introduced potentially offering an additional theranostic option in NETs. Here we evaluated the CXCR4 expression using 68Ga-Pentixafor PET/CT in NET patients in comparison to 68Ga-DOTATOC and 18F-FDG PET/CT.

Material and Methods: 8 consecutive patients with histologically proven advanced NETs were retrospectively analyzed (2 female, 6 male; mean age, 65 ± 11 years; Ki67 39 ± 36%). 4/8 (50%) patients suffered from pancreatic NETs, 2/8 (25%) from ileum NETs and 1/8 (12.5%) from gastric NETs. 1/8 (12.5%) was classified as cancer of unknown primary. DOTATOC, FDG and Pentixafor PET/CT were performed in all patients within 4 weeks to confirm target expression of SSTR, CXCR4 and to detect dedifferentiated tumor lesions. Visual image analysis was performed visually.

Results: On visual analysis, Pentixafor was positive in 3/8 (37.5%), FDG in 6/8 (75%) and DOTATOC in 5/8 (62.5%) patients, respectively. Of the five SSTR positive patients three and two were also FDG- and CXCR4-positive. Three DOTATOC negative patients were FDG positive and one of them also Pentixafor positive. One patient was positive on all three PET/CT scans. Interestingly, the patients with a Ki67 > 90% were CXCR4-positive.

Conclusions: In this pilot study, only one third of NET patients were CXCR4 positive. However, one NET patient without SSTR expression was Pentixafor positive. Interestingly all Pentixafor positive Tumors were located in the Pankreas. Hence, CXCR4-directed radionuclide therapy can be envisioned for patients with SSTR-negative tumors. Our results warrant further evaluation of CXCR4 expression as potential therapeutic target in SSTR-negative NET patients.

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