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CCK_2 Receptor–Targeted PET/CT in Medullary Thyroid Cancer Using [^{68}Ga]Ga-DOTA-CCK-66

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Medullary thyroid cancer (MTC), a neuroendocrine tumor arising from the parafollicular cells of the thyroid gland, accounts for approximately 1%–2% of all thyroid cancers (*1*). Only recently was cholecystokinin-2 receptor (CCK_2R) identified as a suitable target for PET/CT imaging of MTC (*2,3*).

We report on a 74-y-old man with a history of locally advanced MTC who had undergone tumor debulking including a hemithyroidectomy and lymph node dissection on the right side. Informed consent was obtained from the patient, and the project was approved by the institutional ethics committee of Ludwig-Maximilians-Universität München, Munich, Germany (permit 23-0627).

Postoperative [^{18}F]F-3,4-dihydroxyphenylalanine (DOPA) PET/CT detected residual local tumor as well as cervical and upper mediastinal lymph node metastases, prompting additional external-beam radiotherapy. After treatment, serum calcitonin levels decreased (from 5,300 to 720 pg/mL) but remained significantly elevated. Thus, another restaging with [^{18}F]F-DOPA PET/CT (201 MBq) was performed.

To assess the possibility of CCK_2R-directed radioligand therapy, the patient additionally underwent PET/CT with [^{68}Ga]Ga-DOTA-CCK-66 (150 MBq; time interval between scans, 16 d), a novel CCK_2R-directed tracer. It was well tolerated and demonstrated a favorable biodistribution with only physiologic uptake in the stomach and renal tracer excretion. In concordance with [^{18}F]F-DOPA, [^{68}Ga]Ga-DOTA-CCK-66 detected an identical number of MTC lesions composing the still viable local tumor (SUV_{max} of 7.4, vs. 7.0 for [^{18}F]F-DOPA), as well as multiple

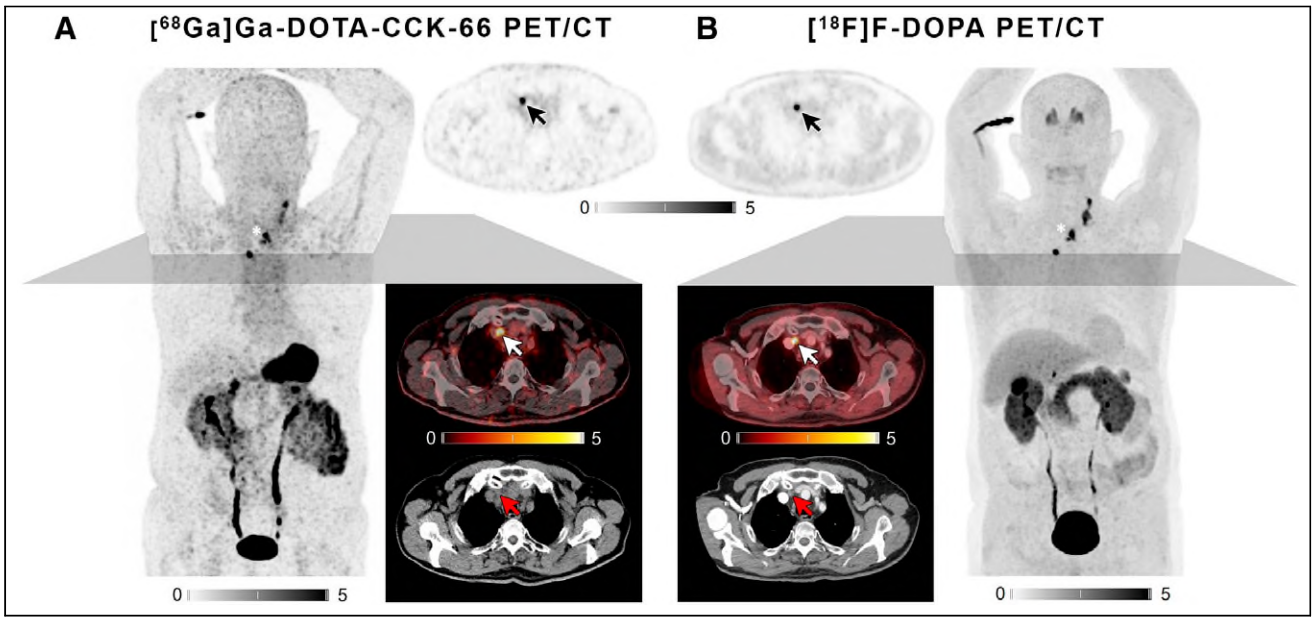

FIGURE 1. Maximum-intensity projections and axial sections of [^{68}Ga]Ga-DOTA-CCK-66 (A) and [^{18}F]F-DOPA (B) PET/CT. White stars indicate local tumor in left thyroid bed. Arrows indicate lymph node metastasis in right upper mediastinum. Intensity scale bars are SUV.

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cervical and mediastinal lymph node metastases (SUV_{max} of 9.5, vs. 8.7 for [^{18}F]F-DOPA) (Fig. 1).

CCK_2R-directed PET imaging with [^{68}Ga]Ga-DOTA-CCK-66 is feasible. Given the possibility of receptor-directed radioligand therapy using its ^{177}Lu- or ^{225}Ac-labeled analog, this new compound might prove a valuable addition to the theranostic armamentarium in MTC. Further research with a special focus on kidney doses, which have been a relevant issue for therapeutic CCK_2R ligands regarding the amount of administered activity, is warranted.

DISCLOSURE

A patent application on CCK_2R-targeted compounds was filed by Thomas Günther, Nadine Holzleitner, Hans-Jürgen Wester, and Constantin Lapa. No other potential conflict of interest relevant to this article was reported.

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