Can injection of pentagastrin stimulate the identification of metastases of medullary thyroid carcinoma by ^{18}F-FDG PET/CT?

To the Editor: Pentagastrin, an analog of gastrin has been used for provocative testing in patients with medullary thyroid carcinoma (MTC) [1]. After the approval of the Ethics Committee of Ankara University we studied three patients who had undergone total thyroidectomy for sporadic MTC and had elevated basal levels, >100pg/mL of calcitonin (Ayerst, USA) (Table 1), normal range 0-10pg/mL. We performed two consecutive fluorine-18-fluoro desoxyglucose positron emission tomography/computed tomography (^{18}F-FDG-PET/CT) scans with and without pentagastrin stimulation. Pentagastrin in a dose of 0.5μg/kg was injected intravenously (i.v.) over 5sec, 15 days apart. We examined the sera for serum calcitonin (SCT) with radioimmunoassay (RIA, Diagnostic System Laboratories, Texas, USA). The patients were then operated for excision of all detected lesions. In patients 1 and 3 the detected lesions were metastatic while in patient 2 were reactive.

We used Discovery ST PET/CT scanner (General Electric, Milwaukee, Wisconsin, USA) with ^{18}F-FDG. Images were obtained approximately 1h after the i.v. injection of 555MBq of ^{H8}F-FDG.

Many authors report that ^{18}F-FDG PET rarely detects MTC disease in patients with SCT levels below 500pg/mL [2]. On the contrary, a study reported a ^{18}F-FDG PET sensitivity of 67% for lesions detected in patients with SCT levels below 500pg/mL [3]. Others report that the overall sensitivity using a cutoff level of below 1.000pg/mL is about 21% and a clinically meaningful sensitivity of 73%-78% can be achieved only for SCT levels above 1000pg/mL [2-10]. In our study, all baseline SCT levels were less than 500pg/mL (127.7pg/mL, 331.4pg/mL and 293.1pg/mL). Two of our patients after pentagastrin stimulation showed an increase above 500pg/mL of SCT but not above 1000pg/mL (Table 1). In our study, the mean SUVmax of ^{18}F-FDG avid MTC metastatic lesions were 5.3 and 4.4, which is relatively low and may reflect the more indolent nature of these lesions after the relatively low levels of SCT. Others have found SUVmax of 5.3±3.2 and 3.9±1.6 for the detection of metastases from MCT postoperatively, with median SCT of 16,600pg/mL (range 514,000–541,000pg/mL) [2, 11].

Gastrin stimulates the formation of cAMP by the activation of adenylate cyclase (AC). Not only secretion, but also synthesis of SCT is regulated by cAMP and cAMP binding to the regulatory unit of protein kinase A [12, 13]. Pentagastrin is supposed to act in the same way [12, 13]. It may increase the metabolic rate of "C" cells of the thyroid and also the consumption of glucose, so that we could expect to have better retention of ^{18}F-FDG after stimulation by pentagastrin, although we found no better retention of ^{18}F-FDG up to the SCT level of 990.9pg/mL.

Gastrin stimulation, as in the case of the omeprazole-CT stimulation test [14], with omeprazole 20mg b.i.d. given for 3 days, increases SCT levels. By this test, in patients with MTC, baseline mean SCL of 647±919ng/mL significantly increased by day 3 of the test reaching to a mean value of 1351±1257ng/L, which may indicate a prolonged stimulation [14] and may increase the retention of ^{18}F-FDG and the sensitivity of imaging.

In conclusion, 3 patients operated for MTC were examined by ^{18}F-FDG PET/CT before and after pentagastrin stimulation. Although SCT increased up to 990.9pg/mL, the PET/CT scans after pentagastrin did not better identify MTC metastases.

Table 1. *Postoperative basal and after stimulation serum calcitonin, ^{18}F-FDG PET/CT and histopathology findings of the three patients*

	Patient 1	Patient 2	Patient 3
Postop. SCT pg/mL (0-10)	124.7	331.4	293.1
Stimulated peak SCT pg/mL	243.8	990.9	578.1
Baseline ^{18}F-FDG-PET, lesions and (SUVmax early, late)	Right deep cervical LAP (4.8, 5.71) Left sup. jugular and deep cervical LAP (4.7, 4.3)	Bilateral paramandibular and submental LAP (3.9, 4.6) Left ant-cervical LAP (2.5, 4.5)	Right apical region behind clavicle pathological retention (3.77, 5.1)
Stimulated ^{18}F-FDG-PET lesions, (SUVmax early, late)	Right deep cervical LAP (5.3, 5.3) Left sup. jugular and deep cervical LAP (4.2, 4.7)	Bilateral paramandibular - submental LAP (2.47, 4.64) Left ant-cervical LAP (3.72, 3.85)	Right apical region behind clavicle pathological retention (3.35)
Histopathology	MTC metastasis right and left cervical LAP	Reactive LAP left ant-cervical LAP	MTC metastasis on the right apical region behind clavicle

LAP: Lymphadenopathy; sup: superior; ant: anterior; MTC: medullary thyroid carcinoma; Postop: postoperative, Normal post oper. SCT: 0-10pg/mL, Normal CEA: 0-3.4ng/mL

The authors declare that they have no conflicts of interest.

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Hell J Nucl Med 2012; 15(2): 155-156

Published on line: 27 June 2012
Epub ahead of print: 27 June 2012