Original Article

Role of Ga-68 DOTANOC Positron Emission Tomography/ Computed Tomography Scan in Clinical Management of Patients with Neuroendocrine Tumors and its Correlation with Conventional Imaging- Experience in a Tertiary Care Center in India

Deepa Singh, Amitabh Arya[1], Amit Agarwal[2], Gaurav Agarwal[2], Mudalsha Ravina[3], Sanjay Gambhir[1]

Department of Nuclear Medicine, AIIMS, Bhopal, Madhya Pradesh, Departments of [1]Nuclear Medicine and [2]Endocrine Surgery, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, [3]Department of Nuclear Medicine, AIIMS, Raipur, Chhattisgarh, India

Abstract

Purpose of Study: Aim of the study was to evaluate the role of ^{68}Gallium-DOTANOC positron emission tomography/computed tomography (^{68}Ga-DOTANOC PET/CT), a pan somatostatin receptor (SSTR) analog in the clinical management of patients with neuroendocrine tumors (NETs) and its correlation with conventional imaging. **Materials and Methods:** We retrospectively evaluated 69 patients of known/suspected NETs who underwent ^{68}Ga-DOTANOC PET/CT scan for tumor localization (n = 15), stage modification (primary staging, n = 26 and restaging, n = 25) and therapy monitoring (n = 3). We also compared PET scan with conventional imaging as reference standard and evaluated the impact of PET/CT in the clinical management of patients. **Results:** The concordant findings on ^{68}Ga-DOTANOC PET/CT and conventional imaging seen in 33 and discordant in 36 patients. Among discordant group, disease was upstaged in 32 patients; down staged in 3 patients; no stage change in one patient. PET/CT localized primary tumor in 4 patients. Among patients with raised tumor markers (39/69), PET was positive in 29 and negative in 10 patients. Patients were followed for mean duration of 27 months to assess management. We found strong agreement between positive PET and raised tumor markers (Kappa value = 0.8). Sensitivity and specificity of PET/CT for primary tumor localization, stage modification, and therapy monitoring was >90% (P < 0.05). **Conclusions:** Study shows that DOTANOC, a broad spectrum SSTRs binding peptide labeled with Ga-68 in PET/CT scan is an excellent modality in the management of NETs patients.

Keywords: *68Gallium-DOTANOC positron emission tomography/computed tomography, conventional imaging, management, neuroendocrine tumors, somatostatin receptors, tumor markers*

Introduction

Neuroendocrine tumors (NETs) are rare, heterogeneous, commonly well differentiated, slow-growing, hormone-secreting/or nonfunctioning tumors that originate from neuroendocrine cells. NETs account for 0.5% of malignancies with raise in incidence from 10.9–52.4 per million populations in the USA between 1973 and 2004 with a prevalence of 350 per million in 2004. Although NET can arise anywhere in the body, the most common locations of primary NET are the gastroenteropancreatic (GEP) tract (approximately 67%, mostly in the small intestine) and lungs (approx. 25%). Other less frequent sites are skin, adrenal, thyroid, and genital tract.[1,2] According to proliferation activity, NETs are classified as G1 with Ki67 index <2%, G2 with Ki67 index 2%–20% and G3 with Ki67 index >20%.[3]

To approach a patient of clinically suspected NET, first step should be the execution of biochemical tests including tumor markers followed by localization of primary tumor and evaluation of the extent of disease with conventional and/or molecular imaging. The second step should be histopathological confirmation (wherever possible). The conventional imaging modalities are computed tomography (CT), magnetic resonance imaging (MRI), and somatostatin receptor scintigraphy (SRS) with ^{111}In-octreotide. The positron emission tomography (PET)/CT imaging is better as compared to regional conventional

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Address for correspondence:
Dr. Amitabh Arya, Department of Nuclear Medicine, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow - 226 014, Uttar Pradesh, India.
E-mail: dramitabharya@yahoo.com

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imaging with CT and MRI to screen the whole body in single study. As compared to SRS, 68Ga-DOTA-peptide synthesis is economical and easy. PET/CT imaging is less time-consuming with better resolution as compared to SRS imaging. PET imaging also provides the possibility of quantification of tracer and thus helpful in peptide receptor radionuclide therapy (PRRNT) planning and response evaluation.[4,5]

The neuroendocrine cells belong to the amine precursor uptake and decarboxylation system and characterized by the expression of different types of hepta-helical G-protein–coupled glycoprotein trans-membrane somatostatin receptors (SSTRs), which forms the basis of molecular imaging.[6,7] The introduction of SST analogs labeled with Gallium-68 using 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) as conjugate has revolutionized the traditional diagnostic approach of NETs from conventional to molecular imaging with PET/CT. ^{68}Ga-DOTANOC PET/CT scan being a wide spectrum SSTR imaging is helpful in the detection of the occult primary tumor, localization of unsuspected metastatic disease or local relapse, primary staging or restaging, PRRNT planning by confirmation or exclusion of SSTRs expression to modify therapeutic approach and also helpful in monitoring of ongoing therapy. However NETs with high Ki67 index and high cellular proliferation show less SSTRs expression and poor localization with 68Ga-DOTA-peptide PET/CT scan. These NETs show better localization with ^{18}FFluorodeoxyglucose (18F-FDG) PERT/CT scan.[8]

The aim of this study was to assess the role of ^{68}Ga-DOTANOC PET/CT in the clinical management of NET patients and its correlation with conventional imaging.

Materials and Methods

We evaluated known or suspected patients of NETs in the Department of Nuclear Medicine, in university hospital setting from May 2013 through September 2014. The data were collected retrospectively, and all patients were followed for a mean period of 27 months to see the change in clinical management based on PET and disease status of patients.

Study design and patient characteristics

A total of 69 patients were evaluated in the study with known/suspected NETs based on clinical evaluation, previous imaging, biochemical markers, and/or The histopathology include reports of sample following surgery (as definitive treatment), biopsy or FNAC (as diagnostic procedure). Wreports. The cold octreotide therapy (if taken) was discontinued to avoid possible SSTR blockade: one day before test for short-acting and 3–4 weeks for long-acting SST analogs. The detailed informed consent was obtained from all the patients before the scans. Pregnant or lactating females and patients not giving consent were not included. Patient's characteristics are summarized in Table 1.

^{68}Ga-DOTANOC positron emission tomography/computed tomography acquisition

Gallium-68 was eluted with 0.1N HCI from "The Eckert and Ziegler Germanium-68/Gallium-68" in house generator and labeled with DOTANOC peptide using fully automatic synthesizer.[9]

The study was acquired 45 ± 15 min after intravenous injection of approximately 111–148MBq (3–4 mCi) of ^{68}Ga-DOTANOC in dedicated Siemens mCT biograph 64 slices PET/CT scanner. Oral contrast was given 30 min before imaging in most of the patients and iodinated intravenous contrast during the CT part of PET/CT was given in only few patients. The CT acquisition was performed with 64 multi-detector CT using care dose four-dimensional techniques. PET emission images were acquired with acquisition parameter of 3 min per bed position in three-dimensional modes from vertex to mid-thigh or whole body (if required). PET images were reconstructed with iterative reconstruction algorithm using Gaussian filter.

Image interpretation

Images were interpreted qualitatively as well as semi-quantitatively by two experienced nuclear medicine physicians at the Syngo Multimodality Workplace VE40A workstation equipped with fusion software to display PET, CT, and fused PET/CT images. The maximum standardized uptake values (SUVmax) were calculated by body weight. The positive 68Ga-DOTANOC uptake was decided with liver SUVmax as reference standard. Any discrepancy between nuclear medicine physicians was resolved by a third physician who was not related to the study. Scan findings were compared with conventional imaging (CT, MRI, Ultrasonography, SRS), available ^{18}F-FDG PET/CT, and correlated with tumor markers. All the patients were followed and clinical management following PET/CT was recorded.

Statistics

Data were analyzed using SPSS, version 21 (SPSS, Chicago, IL, USA). The normality of quantitative data was analyzed with the Shapiro-Wilk test along with visual inspection of the histogram, Q-Q plot, and box plot. Descriptive statistics such as mean ± standard deviation, range, and numbers were used to describe the demographics and clinical profile of patients. The Chi-square test was used for sensitivity and specificity calculation. Statistical significance was referred at $P < 0.05$. The level of agreement between PET scan and tumor markers was assessed with Cohen's kappa value.

Results

We detected SSTRs expressing lesions in 52/69 patients

Table 1: Patient's characteristics

Variable	Number of patients (*n*=69)
Age (years): mean±SD (range)	38.7±20.4 (0.7-71 years)
Sex	44 male & 25 female
Type of known/suspected NET	GEP-18 (included 1-esophageal, 5-duodenal, 2-stomach, 4-jejunum/ileum, 3-pancreatic, 1-colon, 2-rectal); Thyroid-8 (included 1-hurthle, 7-MCT); Lung- 0; Pheochromocytoma-7; Paraganglioma-7; Neuroblastoma-11; ACTH dependent Cushing syndrome-8; Occult-2; Others-4 (kidney, breast, spine & RP, one each); MEN1-1; Von Hippel-Lindau syndrome-1
Ki67 availability	11 patients (≤2% in 10 patients & 20% in 1 patient with occult NET, diagnosed by CT guided biopsy from metastatic mediastinal lymph node).
Tumor markers availability	48 patients (raised in 39 and within ranged in 9 patients) (S chromogranin raised in 16 patients)
S. Chromogranin: mean±SD (range)	505±267.4ng/ml (90.3-815)
Indication of ^{68}Ga-DOTANOC PET/CT	To localize primary tumor site & extent of disease-15; primary staging-26; restaging-25; therapy monitoring-3
Histopathology	54 patients: abnormal in 49 patients (previous surgery-23 & biopsy/FNAC-26) & normal in 5 HPE
Conventional imaging availability	69 patients
Previous ^{18}F-FDG PET/CT scan availability	11 patients

n - number of patients; SD - standard deviation; NET - neuroendocrine tumor; GEP - gastroenteropancreatic; MCT - medullary carcinoma thyroid; ACTH - adrenocorticotrophic hormone; RP - retroperitoneal; MEN - multiple endocrine neoplasia; PET/CT - positron emission tomography/computed tomography; HPE - histopathology

on ^{68}Ga-DOTANOC PET scan and PET was negative for SSTRs expressing lesions in the remaining 17/69 patients.

The lesions on PET/CT scans were at: primary tumor site in 12 patients; primary tumor with regional lymph nodes in 3 patients; primary tumor with distant metastasis in 21 patients; only regional lymph nodes in 1 patient; only metastatic disease in 10 patients; significant tracer avid lesions other than the primary disease in 8 patients and normal PET scan in 14 patients.

Primary lesions detected on PET/CT in 36/69 patients were tracer avid in 33/36 patients with maximum standardized uptake values (SUVmax) of 14.8 ± 26.6 (range 2.7–165) and nontracer avid in 3/36 patients. Distant metastatic lesions on PET/CT scans were detected in 31/69 patients. The mean value of SUVmax of lymph nodal metastatic lesions was 22.0 ± 14.2 (range 0.8–67.4) and distant metastatic lesions were of 8.3 ± 3.9 (range 2.2–18.2).

As mentioned earlier tumor markers were available in 48/69 patients. In the patients with raised tumor markers (39/48 patients), PET scan was positive in 29 and negative in 10 patients. These were 9 patients out of 48 patients, in whom tumor markers were evaluated but makers were not raised. Among these 9 patients, PET was positive in 5 patients and negative in 4 patients. PET was positive in 5 patients and negative in 4 patients. The study showed a strong agreement between positive PET and raised tumor markers (kappa value = 0.8).

According to the referral indication of localization of primary tumor with the extent of disease (n = 15), we localized primary tumor site in 4 patients (2-ACTH dependent ectopic Cushing syndrome, 1-paraganglioma, 1-neuroblastoma). Only metastatic lesions without localization of primary tumor site in 1 patient of occult NET. We have not localized primary tumor site or metastatic lesion in 6/15 patients. The referral diagnosis in these patients were occult NET (1 patient), pheochromocytoma (1 patient) and ACTH dependent cushing syndrome (4 patinets). We found suspicious tracer avid lesions in these patients, but these suspicious lesions were not primary or metastatic lesions and appears to be non significant benign lesions.

PET/CT was done in 3 patients of neuroblastoma for therapy monitoring and all showed disease upstaged in comparison to conventional imaging.

As compared to previously done ^{18}F-FDG PET/CT (available in 11/69 patients), present ^{68}Ga-DOTANOC PET/CT scan upstaged the disease in 7 patients, down staged in 3 patients and no change in disease stage in 1 patient.

The mean duration of follow-up after ^{68}Ga-DOTANOC PET/CT was 27 months (range 5–37 months).

Among 13 patients who underwent surgery (included 1 patient who further received chemotherapy and another who received PRRNT), HPE was positive in 10 and negative in 3 patients.

We did PET scan in 4/69 patients of indeterminate adrenal tumors (incidentaloma) and detected tracer avid suprarenal lesions in 3 patients (2 patients were operated subsequently and verified pheochromocytoma on HPE; 1 patient was loss to follow-up). One patient who showed nontracer avid masses in bilateral adrenal glands was clinically diagnosed as malignant pheochromocytoma with inferior vena cava and hepatic vein thrombus. However, this patient died on subsequent follow-up and not verified on HPE.

During follow-up, repeat ^{68}Ga-DOTANOC PET/CT was done in 7/69 patients and we found the progression of disease in 3 patients (of pancreatic, duodenal, and lung NETs) and regression of disease in 4 patients of neuroblastoma, suggested favorable response to chemotherapy.

We had mixed population of NET patients with various indications and we have the limitation of the availability of HPE in all the patients. However, after consideration of combined results of PET/CT findings, clinical and imaging follow-up as well as HPE (wherever available) as reference standard, we found sensitivity and specificity of ^{68}Ga-DOTANOC PET/CT scan of >90%, significant statistically ($P < 0.05$) in all subgroups.

Discussion

The diagnosis of NETs is often delayed because of nonspecific or infrequent manifestation of symptoms and difficulty in localization of primary tumor site due to small size. However, expression of SSTRs is a special feature of most NETs, making functional imaging possible. In our study, we used DOTANOC peptide to label with Ga-68 for PET/CT rather than DOTATATE and DOTATOC peptide used in most of the previously published studies.[4,10-12] The DOTANOC has the advantage of having a good affinity for SSTR3 along with 3–4 time higher affinity to SSTRs 2 and 5, thus labeled as pan-somatostatin analog.[5,13,14] The widespread SSTRs affinity of DOTANOC peptide is helpful in localization of more number of lesions as compared to the other peptides which may be important in stage modification of disease as compared to conventional imaging modalities and to see the response of ongoing therapy during the follow-up periods. Thus, PET scan may change the management of patients in the form of surgical intervention to systemic therapy.

We found the superiority of PET/CT over conventional imaging in stage modification of disease as reported in the literature.[15-18] One of our patients, a 24-year-old man operated for paraganglioma in the paraaortic region within the abdomen, underwent ^{68}Ga-DOTANOC PET/CT for restaging. PET scan localized tracer avid lesions along the course of bilateral carotid arteries in the cervical regions. He was operated again and verified as synchronous bilateral carotid body paraganglioma on HPE [Figure 1]. Thus, whole-body PET scan showed the advantage over conventional imaging to define the exact stage of disease before surgery or initiation of any other therapy. Among patients referred for initial staging and showed downstaged disease in PET scan, a 44-year-old male diagnosed with stomach NET on biopsy. Later conventional imaging showed suspicious lesion in the stomach but PET scan showed no abnormal tracer avid lesion. Subsequently, he underwent total gastrectomy and HPE was gastritis, thus showed that PET staged the disease

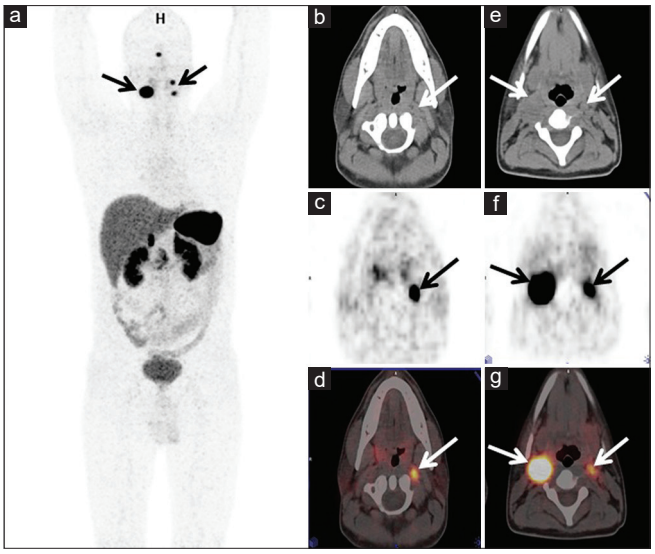

Figure 1: A 24-year-old man operated and histpathologically proven case of paraganglioma in the paraaortic region in abdomen underwent ^{68}Ga-DOTANOC positron emission tomography/computed tomography scan for restaging. Maximum intensity projection image (a) showing intensely tracer avid foci in the bilateral neck regions (arrows). Axial computed tomography, positron emission tomography and fused positron emission tomography/computed tomography (b-d) images showing tracer avid soft tissue lesion (measuring ~ 0.7 cm × 0.9 cm × 0.7 cm, SUVmax 26.8) in the left cervical region along the course of carotid artery (arrows). Axial computed tomography, positron emission tomography and fused positron emission tomography/computed tomography (e-g) images showing tracer avid soft tissue lesions along the course of bilateral carotid arteries (right cervical region: measuring ~ 2.0cm × 2.2 cm × 2.8 cm, SUVmax 152.6; left cervical region: measuring ~ 0.6 cm × 1.0 cm × 0.8 cm, SUVmax 35.3) (arrows). He was operated again and verified as right & left synchronous carotid body paraganglioma on HPE

accurately. No further investigation or treatment was done in this patient and he is doing well. Naswa *et al*.[17] did a study with ^{68}Ga-DOTANOC PET/CT scan in NET patients and showed its superiority over conventional imaging in the detection of both primary tumor ($P < 0.001$) and metastases ($P < 0.0001$).

NET with unknown primary site is a less common although important entity which shows better role of ^{68}Ga-DOTANOC PET/VT as compared to conventional imaging with low sensitivity. In our study, among patients referred for primary tumor localization (*n*-15) in suspected/proved NETs, we localized primary tumors in 4 patients. A 46-year-old man presented with high suspicion of ectopic ACTH producing Cushing syndrome on the basis of the clinical and biochemical parameters. Previously done CT showed two small-sized ill-defined lesions, one in the upper lobe and another in the lower lobe of the left lung. However, ^{68}Ga-DOTANOC PET scan showed intense tracer avid lesion in the lower lung and identified as culprit lesion, operated and HPE verified as well-differentiated neuroendocrine carcinoma. The upper lung lesion was a benign finding. The patient is doing well during the follow-up period [Figure 2]. A 43-year-old hypertensive woman presented with clinical suspicion of ACTH-dependent ectopic Cushing syndrome showed

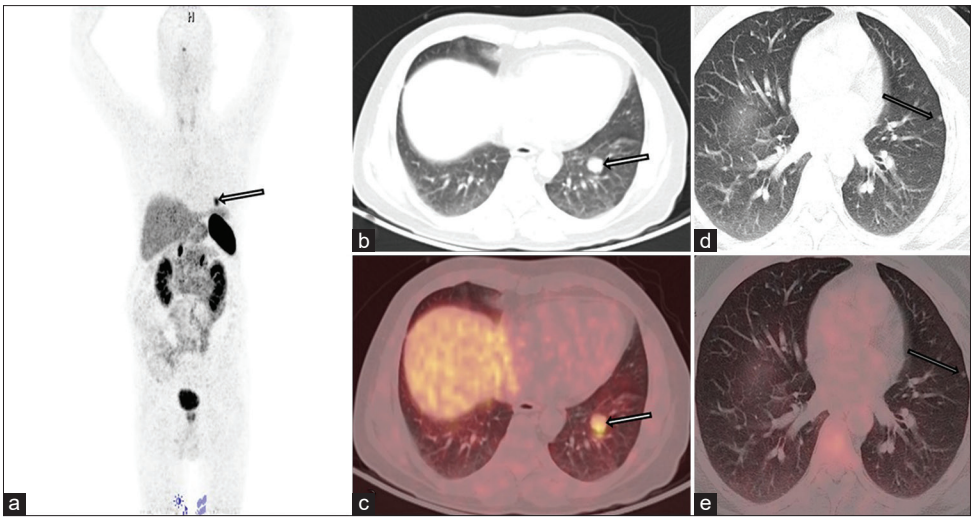

Figure 2: A 46-year-old man with history of hypertension presented with complaints of hyper-pigmentation, recurrent episodes of flushing and skin infection for one year. On evaluation, his serum ACTH was raised (118 pg/ml) and computed tomography scan showed small sized nodules in the anterior segment of upper lobe and anterior basal segment of lower lobe of left lung, suspicious for ectopic ACTH producing tumor. ^{68}Ga-DOTANOC positron emission tomography/computed tomography scan was done to characterize the lesions, revealed: Maximum intensity projection (a) image showing focal intense tracer uptake in the left lower lung (arrow). Axial computed tomography (b), and fused positron emission tomography/computed tomography (c) images showing intensely tracer avid (SUVmax 14.6) soft tissue lesion (measuring ~ 1.4 cm × 1.3 cm) in the anterior basal segment of lower lobe of left lung (arrows). Axial computed tomography (d) and fused positron emission tomography/computed tomography (e) images showing non tracer avid small sized nodule in the upper lobe of left lung (arrow). The tracer avid lesion in the lower lobe of lung was excised following positron emission tomography and histopathologically verified as well differentiated neuroendocrine carcinoma

subcentimetric lesion in the right lung on CT. However, ^{68}Ga-DOTANOC PET scan showed nontracer avid lung nodule and considered as benign. Following PET, the same conservative treatment was continued and the patient is doing well. A similar kind of study done by Prasad and Baum[19] to evaluate ^{68}Ga-DOTANOC PET/CT in the localization of primary tumor with an assessment of molecular behavior in 59 patients of carcinoma of unknown primary NETs. They found PET/CT identified primary tumor site in 59% of patients in comparison to CT alone which identified the primary site in only 20% of patients.

The baseline ^{68}Ga-DOTANOC PET scan is helpful in decision making for the type and magnitude of systemic therapy as chemotherapy or PRRNT and most importantly to see the response of therapy during the follow-up period. In our study, we identified distant metastatic lesions in 31/69 patients. Most of these were skeletal metastasis in patients of neuroblastoma (with bone marrow involvement) and medullary carcinoma thyroid (MCT) (with high serum Calcitonin and carcinoembryonic antigen [CEA]), followed by GEP and lung NET. Among the pediatric patients of neuroblastoma in our study (n = 11), we found skeletal metastasis in 9 patients on PET as compared to only 3 patients on CT. During follow-up, repeat PET scans were done in 4 patients showed regression of disease in all patients of neuroblastoma, thus showed favorable response to chemotherapy. Ambrosini *et al*.[15] did a retrospective study to evaluate the sensitivity, specificity, and accuracy of ^{68}Ga-DOTANOC PET/CT and CT alone for the evaluation of bone metastasis in patients with NET. They found that ^{68}Ga-DOTANOC PET was more accurate than CT for identification of bone lesions and led to a change in clinical management with higher sensitivity (100% vs. 80%), specificity (100% vs. 98%), positive predictive value (100% vs. 92%), and negative predictive value (100% vs. 95%).

NETs have a wide range of cellular differentiation from poorly to well differentiated. ^{18}F-FDG PET/CT scan demonstrates increased metabolic activity with high glucose utilization within poorly differentiated neuroendocrine carcinomas, which lose their receptors (dedifferentiation). Previously published literature showed the superiority of ^{68}Ga-DOTA peptide PET over ^{18}F-FDG PET in NET patients.[12,20] Furthermore, Ki67, a nuclear protein is a very good marker for the assessment of the degree of differentiation of tumors. In our study, we found superiority of ^{68}Ga-DOTANOC PET over ^{18}F-FDG PET (available in 11 patients) in well-differentiated NET. However, we had a limitation of nonavailability of detailed HPE with Ki67 in all the patients to better characterize the degree of differentiation.[15,17] Higher value of SUVmax is suggestive of higher expression of SSTRs and thus provide high detection rate even in very small sized lesion and shows better prognosis with targeted radionuclide therapies in metastatic disease.[19,21] The mean SUVmax of 14.8 in the primary tumor in 33 of our patients is suggestive of well-differentiated nature of lesions. A study done by Kroiss *et al*.[22] found the significant differences in SUVmax between nonmalignant and malignant tissue in patients with bone and liver metastases and pancreatic NET ($P < 0.0001$).

In our upstaged patients on ^{68}Ga-DOTANOC PET/CT as compared to ^{18}F-FDG PET/CT, a 25-year-old operated woman of MCT (total thyroidectomy + central compartment lymph node dissection) presented with raised serum calcitonin and CEA level. ^{68}Ga-DOTANOC PET showed SSTR expressing nodular lesion in the left paraspinal region at D6 vertebral level. However, ^{18}F-FDG PET scan did not show tracer uptake in the lesion. Subsequently, she underwent PET-guided biopsy and found to have metastatic MCT with positive immunohistochemistry (calcitonin, chromogranin, and CEA) [Figure 3].

Among downstaged patients, one patient was an operated case of MCT referred for restaging, ^{18}F-FDG PET/CT scan showed hypermetabolic lung lesions with cervical lymph nodes and ^{68}Ga-DOTANOC PET/CT scan showed non-SSTRs expressing lesions at the same sites. However, management following PET/CT scan was not changed. In an another patient a suspected case of pheochromocytoma referred for diagnosis, ^{18}F-FDG PET/CT showed suspicious uptake in the left adrenal gland. However, ^{68}Ga-DOTANOC PET/CT was normal. During follow-up, the patient was found asymptomatic and no further investigation or any specific treatment was given.

To assess the impact of ^{68}Ga-DOTANOC PET/CT scan on the clinical management, Ambrosini *et al*.[23] did a study in patients of pathologically confirmed NET with a follow-up of 1 year and they found that ^{68}Ga-DOTANOC PET/CT scan either affected stage or caused a therapy modification in more than half of patients. In the present study, we followed the patients for the longest period of 37 months and also found the usefulness of ^{68}Ga-DOTANOC PET/CT in stage modification followed by the change in clinical management. In the present study, a 26 years man presented with complaint of recurrent abdominal pain, increased bowel frequency and exertional palpitation for 1 year. On evaluation, serum Chromogranin A was found to be raised and CT showed suspicious lesion in the mid jejunum. The patient was diagnosed as carcinoid tumor, planned for surgery and ^{68}Ga-DOTANOC PET/CT was done for initial staging. PET scan showed intensely tracer avid lesion in the mid jejunum along with metastatic abdominal lymph nodes and liver lesions. In view of active metastatic lesions, surgery was deferred and SST analog was started [Figure 4].

^{68}Ga-DOTANOC PET scan has a role in the evaluation of indeterminate adrenal tumors, incidentally discovered on conventional imaging.[24] We also did PET scan in the patients referred with adrenal incidentaloma and detected tracer uptake in some of them.

PRRNT with radiolabeled SSAs is among the promising newly developed targeted tools in well-differentiated NET treatment with either ^{90}Y-DOTA-TOC or ^{177}Lu-DOTATATE, allowing the delivery of high-absorbed radiation doses to SSTR expressing tumors with partial

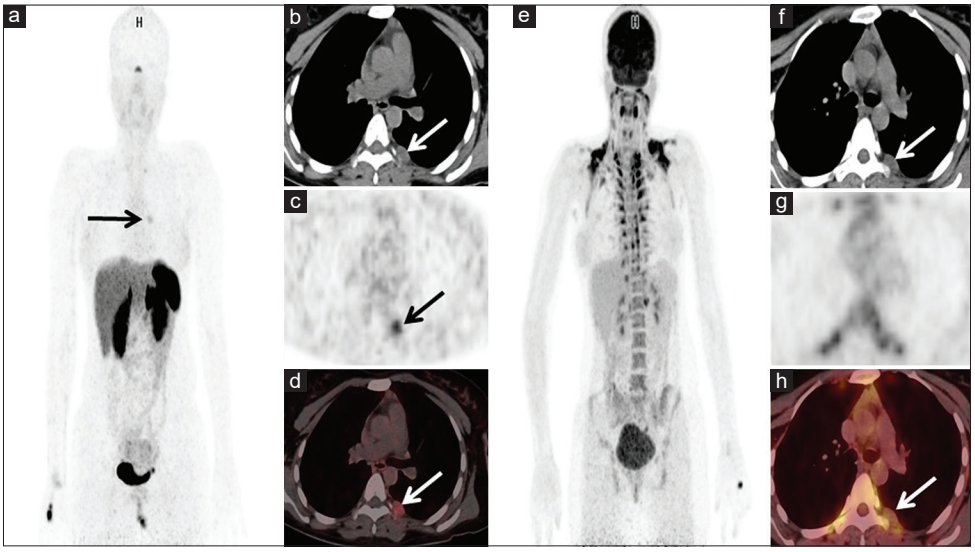

Figure 3: A 25-year-old woman of medullary carcinoma thyroid, post total thyroidectomy with central compartment lymph nodes dissection underwent positron emission tomography/computed tomography scans (^{18}F- Fluorodeoxyglucose and ^{68}Ga-DOTANOC) for restaging in view of raised serum calcitonin (1651 pg/ml) and carcinoembryonic antigen (63.15 ng/ml) levels. ^{18}F- Fluorodeoxyglucose positron emission tomography/computed tomography scan revealed: Maximum intensity projection (a) image showing increased physiological Fluorodeoxyglucose uptake in the brown fat (cervical, supraclavicular, axillary, mediastinal and paraspinal regions). Axial computed tomography, positron emission tomography and fused positron emission tomography/computed tomography (b-d) images showing nodular lesion in the left paraspinal region at D6 vertebral level (arrows). However the pathological Fluorodeoxyglucose avidity of the lesion was not differing from the physiological Fluorodeoxyglucose uptake of the brown fat and considered as benign. Further ^{68}Ga-DOTANOC positron emission tomography/computed tomography scan done: Maximum intensity projection image (e) showing focal area of SSTR expression in the thoracic region (arrow). Axial computed tomography, positron emission tomography and fused positron emission tomography/computed tomography (f-h) images showing SSTR expressing (SUVmax 3.4) nodular lesion in the left paraspinal region at the level of D6 vertebra (arrows). She underwent positron emission tomography guided biopsy from SSTR expressing lesion in the left paraspinal region and histopathology verified as metastatic medullary carcinoma thyroid with positive immunohistochemistry (calcitonin, chromogranin and carcinoembryonic antigen)

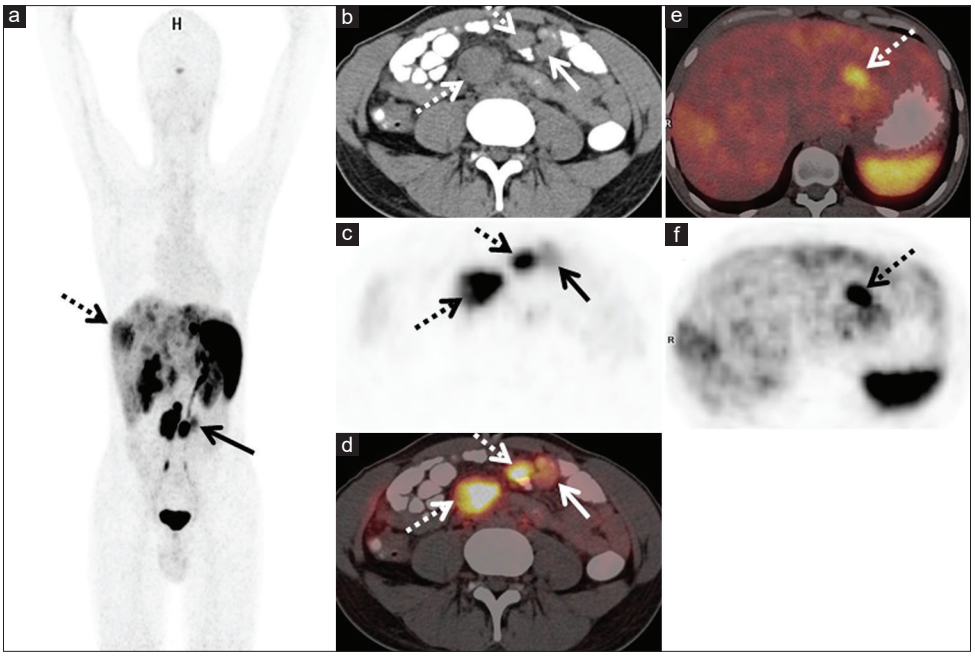

Figure 4: A 26-year-old man with history of bronchial asthma presented with complaint of recurrent episodes of flushing since 2004 along with recurrent abdominal pain, increased bowel frequency, exertional palpitation and dyspnoea for one year. On evaluation serum Chromogranin A was raised (424 ng/ml) and computed tomography showed suspicious lesion in the mid jejunum. Patient was diagnosed as carcinoid tumor and planned for surgery. ^{68}Ga-DOTANOC positron emission tomography/computed tomography scan was done for initial staging, revealed: Maximum intensity projection (a) image showing multiple intensely tracer avid lesions in the abdomen (solid arrow) and liver (broken arrow). Axial computed tomography (b), positron emission tomography (c) and fused positron emission tomography/computed tomography (d) images show tracer avid (SUVmax 11.9) primary lesion in the mid jejunum (solid arrows) and multiple mesenteric lymph nodes (largest measuring ~ 2.7 cm × 3.9 cm, SUVmax 42.2) (broken arrows). Axial fused positron emission tomography/computed tomography and positron emission tomography (e and f) images showing tracer avid multiple liver lesions with no definite morphological abnormalities (SUVmax 21.5 in the left lobe) (arrows). Following positron emission tomography, surgery was deferred in view of active lymph nodal and liver metastasis and patient was put on cold somatostatin analogue

or complete objective responses. ^{68}Ga-DOTA-peptide PET/CT is a useful modality for early prediction of time to progression and clinical outcome in the patients undergoing PRRNT.[4] In the present study, PRRNT was started in 4 patients following PET scan (among those, 1 patient underwent surgery for primary tumor followed by PRRNT).

The limitation of the study was small patient population with mixed subgroups of NET, nonavailability of conventional imaging, HPE and Ki67 values in all the patients. In future, we will try to overcome these limitations along with the enrolment of large number of patients in all the subgroups, so that we can define the role of ^{68}Ga-DOTANOC PET/CT in each subgroup individually.

Conclusions

Our study showed that DOTANOC, a broad-spectrum SSTRs binding peptide labeled with Ga-68 in PET/CT scan is an excellent modality and should be used as primary imaging investigation in the localization and characterization of tumor, staging, re-staging, treatment planning, and monitoring and in the regular follow-up of NETs patients.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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