

Treatment with somatostatin analogues and PRRT uptake in Bones

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Abstract

Introduction: Somatostatin analogues is a routinely used and a standard investigation for screening and diagnosing neuroendocrine tumours. It has become a standard of care for assessment of response to chemotherapy and radiation as well as for follow up of these malignant conditions. It is an also a highly valued imaging modality in detecting small mesenchymal tumours associated with hypophosphatemic oncogenic osteomalacia. Some of these scans showed ^{68Ga} Ga-DOTATATE PET/CT avid lesions in bones which were not explained by tumour load. A retrospective study was done to evaluate these areas of uptake.

Methodology: A total of 252 patients referred for ^{68Ga} Ga-DOTATATE PET/CT scan from June 2013 to May 2016 were screened to look for abnormal uptake in the bones in the PET/CT scan study. It was correlated with the CT findings. Any bone damages / abnormality in the corresponding CT images were taken into account.

These were classified as under metastatic lesions and as benign conditions (healing, mixed, non-healing, old fractures) with the SUV of the most avid lesion taken into consideration. A statistical analysis comparing the abnormal uptake against CT findings was done to assess the significance of these findings.

Results: Malignant and metastatic lesions (n = 25) showed higher uptake. The SUV ranged from 6.30 to 93.75 (Mean:27.47 with SD =30.89). Benign bony abnormality which included healing, mixed, non-healing and old fractures (n = 15) showed much lower intensity of the lesions. The SUV ranged from 2.03 to 7.78 (Mean:5.05 with SD =2.02).

Conclusion: Malignant and metastatic neuroendocrine tumours are DOTA avid with higher uptake as seen on standardized uptake value (SUV) as compared with the bone lesions with benign disease which had lower uptake values on [^{68Ga} Ga-DOTATATE PET/CT. Regions devoid of tumour with increased uptake on

correlation with CT was found to be fracture sites in various stages of healing. SUV values can be used to differentiate between malignant and benign osseous lesions.

Keywords: CT-based, Fractures, Neuroendocrine, Hypophosphatemic

Introduction

Neuroendocrine tumours (NET) are characterized by the fact that they express somatostatin peptide receptors. The standard imaging modality for this currently is [68Ga] Ga-DOTATATE PET/CT study and has become increasingly used recently. Many centres use Ga-68 DOTANOC PET/CT or [68Ga] Ga-DOTA-TOC PET/CT for the same. Physiologically increased uptake in [68Ga] Ga-DOTATATE PET/CT study has been described in the intestine, liver, and head of pancreas, spleen, bowel, bladder and both kidneys. Also, tumour uptake in the areas of primary and metastatic lesions has been investigated. These uptakes are highly variable ranging from lack of visual uptake to quite intense and diffuse distribution. Depending on the site and pattern of uptake noted in the scan, they are interpreted as physiological or of pathological significance. It is well described in the literature that metastatic lesions in the bones from neuroendocrine primary tumours elsewhere can be [68Ga] Ga-DOTATATE PET/CT avid., Published data in the literature focusing on [68Ga] Ga-DOTATATE avid findings in bone which are not due to tumours is scanty. This study was conducted to investigate these uptakes and an attempt to explain it.

Methodology

Patient population

A total of 252 [68Ga] Ga-DOTATATE PET/CT studies were done from June 2013 to May 2016 in our institute. These were mostly whole-body scan with a small percentage of them being regional studies. A

retrospective study was done to select all those patients whose CT scan showed any abnormality or area of bone damage showing an uptake in the scan.

Statistical analysis

IBM SPSS Analytics 16.0 software (Chicago, IL, USA) and SAS/STAT software, version 7.3 (Copyright © SAS Institute Inc., Cary, NC, USA) were used for statistical analysis. The relationship of bone lesion uptake and CT abnormalities was studied using Chi square test.

Results

Overall, 40 patients (34 whole body and 6 regional) were found to be eligible to be included in this study. Analysed data for 40 patients (14 females and 26 males) showed that most of the patients were middle aged (mean age of 45.69 years with a standard deviation of 15.12 years) with a slight preponderance to the males.

Table 1: Diagnosis distribution

Carcinoma / Carcinoid	7
MTC	5
NEN /NET/NEC	11
HPO	12
Cushing's Syndrome / Insulinoma / Paraganglioma / Pheochromocytoma / Schwannoma	5

Legend: HPO - Hypophosphatemia oncogenic osteomalacia

MTC - Medullary Thyroid Carcinoma

NEC - Neuroendocrine Carcinoma

NEN - Neuroendocrine Neoplasm

NET - Neuroendocrine Tumour

SUV- Standardized Uptake Value (Max)

About a third of the patients were evaluated for HPO. The remaining was mostly comprised of malignant disease conditions.

Most of the patients had more than ten lesions and SUV was taken of the lesion with maximum intensity.

The patients with benign diseases were found to have much lower intensity in the lesions. The SUV ranged from 2.03 to 7.78 (Mean SUV:4.91 with SD =1.66).

Those patients with malignant diseases were found to have much higher uptake in the lesions. The SUV ranged from 6.30 to 93.75 (Mean SUV:23.58 with SD =28.99).

Table 2: Treatment received

Chemotherapy	9
Surgery	21
External Radiotherapy	5
Radionuclide therapy *	11
Combinations	27

* Lutetium-177 (¹⁷⁷Lu)-Dotatate therapy and MIBG therapy

About 70% (n=27) of all the patients who had malignancy received multimodality treatment prior to the scan. Out of the 40 patients, 21 of them had surgical intervention while 9 had received chemotherapy and another 11 had treatment with "radionuclide therapy. Only a few (5) had received prior external radiotherapy.

Table 3: CT findings of DOTA avid lesions.

CT finding	DOTA avid
Metastases	25
Healing fracture	7
Mixed fracture	3
Old fracture	2
Non-healing fracture	1
Non-specific	2
Total	40

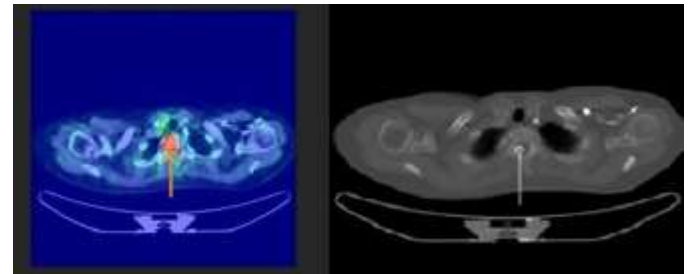
More than half of the DOTA positive patients (25) were due to metastatic lesions.

CT characteristics of the bony pathology as of benign or malignant nature was found to be correlating with the intensity of the uptake in these lesions.

The patients with benign diseases were found to have much lower intensity of the lesions. The SUV ranged from 2.03 to 7.78 (Mean SUV:5.05 with SD =2.02).

Those patients with malignant diseases were found to have much higher uptake in the lesions. The SUV ranged from 6.30 to 93.75 (Mean SUV:27.47 with SD =30.89).

Figure 1: Scan showing intense uptake (coloured arrow) in metastatic lesion in thoracic vertebra in a patient with Neuroendocrine carcinoma. Corresponding CT scan showing lytic changes (white arrow).



Discussion

It has been widely accepted standard to do evaluation and staging of neuroendocrine tumours. It has been reported that increased uptake is noted in non-malignant conditions. An evaluation of increased uptake in the bones revealed many areas which were not due to tumour. Comparing with the CT scan which is co-registered it was found to have areas of damage to the bones. This was classified by the radiologist. Many areas in the bones showed uptake but showed no significant abnormality in the corresponding CT images. Previous authors have identified the difficulty in the interpretation of the abnormal focal uptake without corresponding anatomic abnormality on the CT imaging which poses a dilemma in whole-body Fluoro-deoxy glucose PET/CT imaging diagnosis. This is a possible basis for actively

healing fractures to show increased uptake. This has lot of practical applications in traumatic Orthopaedics.

Limitations of the study

- The analysed groups of patients are very inhomogeneous and it is one of the main limitations of this study.
- The scans were done for the screening of the neuroendocrine tumours and for finding the location of mesenchymal tumour as a cause of HPO. These selective indications imply a selection bias. The selection bias maybe skewing the trend noted in the study.
- The number of patients who qualified for the inclusion criteria was found to be small. This small number can limit the power of this study. Although all the scans which were for damage to bone structure were reviewed by one Nuclear Medicine physician and one Radiologist for verification of the findings, those scans which were not reported as having an uptake were not seen again thus contributing to the loss in the number of patients included in the study.
- Since there was only a single physician from either of the specialties reviewing the images, errors due to individual variation in the interpretation and classification can occur.

Conclusion

Malignant and metastatic neuroendocrine tumours are DOTA avid with higher uptake as seen on SUV as compared with the bone lesions with benign disease (healing, mixed, non-healing, old fractures) which had lower uptake values on PET/CT. Regions devoid of tumour with increased uptake on correlation with CT was found to be fracture sites in various stages of healing.

The present study is however limited by the small sample size. Further study with increased samples size and wider sampling criteria can confirm this observation.

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