Detection of unsuspected primary neuroendocrine tumours presenting as liver mass using $^{68}$Ga-DOTA-peptide PET/CT: A report of 2 cases

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Introduction

Neuroendocrine tumours (NETs) arises commonly from the gastrointestinal and respiratory tracts. 1 NETs frequently metastasize to liver which can be commonly misdiagnosed as hepatocellular carcinoma (HCC). Identifying the primary tumour origin is important as complete surgical resection of metastases and primary NET can be curative and may improve survival. $^{68}$Ga-DOTA-peptide PET/CT is an advanced functional imaging with superior uptake compared to conventional imaging for initial workup of NETs and localization of unknown primary tumours. It uses somatostatin analogs (DOTATATE, DOTANOC and DOTATOC) radiolabeled with 68-Gallium which bind to somatostatin receptors that are usually overexpressed by NETs. 1 We present 2 cases of NETs initially presenting as liver mass. In both cases, primary tumour origin in lung and duodenum respectively were detected and characterised on PET/CT using $^{68}$Ga-DOTA-peptide, to which conventional imaging failed to identify.

Case 1

A 37 years old gentleman with no medical illness presented with loss of appetite and lethargy. He was recently diagnosed as HCC with Child-Pugh Class A. Liver CT scan and MRI showed a 2cm liver mass at segment IV/VIII. 2 and MRI Liver (Figure 2) show multiple liver lesions likely correspond to multicentric HCC.

He was started on Sorafenib for about 1.5 years before undergoing transarterial chemoembolisation and Yttrium-90 radioembolisation.

Figure 1: CT Liver 3 phase: Segment IV/VIII liver mass (arrow) with enhancement on arterial phase and washout on portal venous phase

Figure 2: MRI Liver showed significant reduction in size of the liver mass (arrow) post-embolisation

Figure 3: Whole body Gallium-DOTATATE PET/CT shows focal Ga-DOTATATE avid lesion at the ileocecal segment of duodenum (black arrow) and at segment V/VIII (white arrow) consistent with Ga-DOTATATE avid NET of duodenum with liver metastases.

Subtotal gastrectomy, Roux-en-Y anastomosis and segment IV hepatectomy done. Intra-operatively, D1 duodenal tumour seen and resected. Duodenal and liver tumour specimens consistent with NET.

Discussion

NET with liver metastases can mimic primary HCC on imaging and histopathology. It can be diagnostically challenging especially in cases presenting only with liver manifestation. Neuroendocrine liver metastasis have variable features on conventional imaging such as CT which look similar to HCC, as illustrated in the first case. Surgical resection of primary NET and associated lymph nodes irrespective of liver metastases is the treatment of choice. The first case highlights that $^{68}$Ga-DOTA-peptide PET/CT is highly accurate in detecting unknown primary tumour in the duodenum. $^{68}$Ga-DOTATATE PET/CT has 93% sensitivity and 91% specificity to detect primary NETs compared to CT with 73% sensitivity. Various studies reported detection rates of unknown primary NET using Ga-DOTANOC are between 48-59% compared to CT with 20-38%. $^{68}$Ga-DOTATATE PET/CT has useful therapeutic application by determining somatostatin receptor status (SDR). 1 In our case, Ga-DOTATATE determined SSTR avidity in the liver and duodenum which changed the patient’s treatment plan. He was started on somatostatin analogues and was a good candidate for peptide receptor radionucide therapy (PRRT).

The second case highlights the non-DOTA avid and FDG avid features consistent with atypical carcinoid further highlighting that not all NETs show $^{68}$Ga-DOTATOC-peptide avidity. $^{68}$Ga-DOTA-peptide PET is useful to detect well-differentiated NETs and typical carcinoids with good expression of somatostatin receptors. High grade NETs and atypical carcinoids show less $^{68}$Ga-DOTA-peptide avidity but are $^{18}$F-FDG avid. FDG uptake is increased in high grade tumours due to high metabolic activity and proliferating index. 1 Hence, combined FDG/Ga-DOTA-peptide PET can be useful to differentiate typical from atypical lung carcinoid. Although the role of combined FDG/Ga-DOTA-peptide PET has yet to be established, it provides information on tumour grading and heterogeneity. It can be useful for precise staging of metastatic NETs and identify suitable patients for PRRT. 3 In our case this patient will likely not benefit from PRRT due to its non-DOTA avid feature and may benefit from other treatment option.

Conclusion

• NET with liver metastasis can mimic primary HCC on imaging and histopathology which can be diagnostically challenging.

• It is imperative to be aware of such pitfalls during evaluation of liver mass and to consider $^{68}$Ga-DOTA-peptide PET/CT for such cases.

• $^{68}$Ga-DOTA-peptide PET/CT is highly accurate in localizing primary tumour origin of grade 1 and 2 well-differentiated NETs presenting as metastatic liver disease during initial disease onset especially with negative findings on conventional imaging.

• Combined FDG/Ga-DOTA-peptide PET/CT is shown to be useful to differentiate between high grade from low grade NETs, allows tumour characterisation and grading which are significant in clinical management and prognosis.

References