**Dual tracer functional characterization of metastatic gastric carcinoid**

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**ABSTRACT**

Because of the increasing clinical importance of gastric carcinoids and the difficulty in diagnosing them, the need for non-invasive diagnostic methods is growing. Currently, the only reliable method is upper gastrointestinal endoscopy with biopsy. We report the case of a 32-year-old male where a combination of functional imaging studies (¹⁸F-fluorodeoxyglucose-positron emission tomography/computed tomography [PET/CT] and ⁶⁸Ga-DOTA-NOC PET/CT) not only helped in the correct staging, but also highlighted certain important biological aspects of these tumors, which are important from the management point of view and can prognosticate the patients.

**Keywords:** ¹⁸F-fluorodeoxyglucose, ⁶⁸Ga-DOTA-NOC, carcinoid, positron emission tomography/computed tomography, stomach

**INTRODUCTION**

Gastric carcinoids are of increasing clinical importance. Whereas, in older studies these composed only 2-3.8% of all carcinoids, more recently investigators have suggested that the incidence may be significantly higher-11-30% of all carcinoids. In addition, to the increased frequency of gastric carcinoids, they are receiving more attention because of recognition that they occur not only sporadically (type-III), but also with increased frequency in chronic hypergastrinemic states (atrophic gastritis type-I) and Zollinger-Ellison syndrome, type-II. Recognition of gastric carcinoids is important because each type can, on occasion, become malignant and metastasize to lymph nodes or the liver (type-I, 5%; type-II, 30%; and type III, 71%). In particular the type-III carcinoid tumors are sporadic, large solitary tumors not associated with a hypergastrinemic state, are highly proliferating due to intense over expression of a mutated p53 gene, have a high propensity to ulcerate and are more likely to be invasive with metastasis. They appear with striking predominance in men; 80% patients diagnosed with type-III carcinoids are men. Accurate pre-therapy staging with other non-invasive imaging modalities is therefore mandatory to select the appropriate mode of therapy.

In this context, we report a case of a patient having gastric carcinoid with liver metastases (type-III) with classic textbook description except that the tumor was non-functional and the patient did not have any of the clinical syndromes. Accurate pre-therapy localization was carried out by positron emission tomography using two different radiotracers. The diagnosis was confirmed by fine needle aspiration cytology (FNAC) from a liver space occupying lesion (SOL) and a gastric biopsy.

**CASE REPORT**

A 32-year-old man presented with features of abdominal pain and enlargement of 6 months duration. Clinical examination revealed a massively enlarged liver reaching up to the umbilicus with no other positive clinical findings. Biochemical examination, liver function tests, and viral markers were within normal limits except for an elevation of serum alkaline phosphatase. A preliminary high-resolution dual phase computed tomography (CT) revealed a grossly enlarged liver with multiple enhancing hypodense lesions suggestive of hypervascular secondaries and thickening of the greater curvature of the stomach [Figure 1]. An upper gastrointestinal (UGI) endoscopy done during the same time revealed a 3 cm × 2 cm ulcer with rolled up edges along the greater curvature of the stomach. FNAC from one of the liver SOL revealed features of neuroendocrine tumor (NET) with positive immunohistochemistry and a Ki-67 index of 40-50%, following which the patient underwent positron emission...
had recurrence later on and despite aggressive treatment even including a bone marrow transplant, he succumbed to his disease.

DISCUSSION

Among the gastrointestinal carcinoids, small intestine is the most frequent site (28%), followed by rectum (19%) and colon (8%). The incidence of gastric carcinoids is 6%. The average age at diagnosis of patients with gastric carcinoids is 62 years with an equal male to female distribution. Patients are often asymptomatic; carcinoids being found incidentally at the time of UGI endoscopy. When symptomatology occurs they are usually dyspeptic. It has been reported that almost all patients with gastric carcinoids have elevations of plasma chromogranin-A, a peptide secreted by all neuroendocrine cells, although prospective studies for its use as a tumor marker for carcinoids have not yet been proposed.

The management of gastric carcinoids is controversial; sporadic carcinoids have a higher rate of regional lymph node involvement and thus surgical resection with lymph node sampling is generally recommended. Liver is a common site of metastasis. The CT appearance of these lesions is similar to other hepatic metastasis:

18F-FDG PET/CT revealed multiple hypodense lesions in liver with focally increased radiotracer uptake, suggestive of poorly differentiated secondaries with high metabolic activity, which was earlier proven on FNAC from a liver SOL [Figure 2a] while foci of increased tracer uptake in a soft-tissue mass at the greater curvature of the stomach was seen on a 68Ga-DOTA-NOC PET/CT scan suggesting a well-differentiated primary somatostatin receptor expressing tumor seeking tracer.

A gastric biopsy later confirmed this finding (well-differentiated NET; Ki-67 index-2%) [Figure 3]. Based on a combination of these findings the patient was deferred from surgery and instead underwent chemotherapy protocol with etoposide and cisplatin, following which he went into a near total clinical and radiological remission [Figure 4]. The patient however had recurrence later on and despite aggressive treatment even including a bone marrow transplant, he succumbed to his disease.
Multiple, low-density lesions that are rarely calcified and with variable density after intravenous contrast enhancement.

Gastric carcinoids, similar to other carcinoids have a high density of somatostatin receptors (SSTR). With recent studies showing that somatostatin receptor scintigraphy (SRS) are highly sensitive and specific in localizing carcinoids in other locations, the possibility exists that SRS can be used to localize gastric carcinoids. Recently labeled octreotide (DOTA-NOC) showing the presence of somatostatin receptors (SSTR) have been used as radiotracers for SRS PET imaging because they exhibit better tumor-to-background ratio. However, because NETs are mostly well-differentiated tumors, they have a low metabolic activity and cannot be visualized efficiently with 18F-FDG, which is more useful in less differentiated NETs without expressing SSTR. Our results also demonstrate similar findings as described with 68Ga coupled to Octreotide via a bifunctional chelate DOTA (1, 4, 7, 10 tetraazacyclododecane-1, 4,7,10 tetra acetic acid) have been used as radiotracer for SRS PET imaging showing increased uptake on 68Ga-DOTA-NOC imaging. It therefore represents a unique example of combining two functional imaging modalities, which are complementary to each other for accurately functional mapping of tumor lesions and predicting response to therapy. Furthermore, the positivity of liver lesions on 18F-FDG imaging meant that this patient had a poor prognosis despite the primary showing increased uptake on 68Ga-DOTA-NOC imaging.

In conclusion, our observations suggest that these functional imaging findings are characteristic of neuroendocrine cellular differentiation and are very useful in the pre-therapy localization/staging of tumors, predicting, and monitoring response to therapy and follow-up of the patient for future recurrences/relapse and also for prognostication.

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