

# The Use of $^{99m}\text{Tc}$ -HYNIC-TOC and $^{18}\text{F}$ -FDG PET/CT in the Evaluation of Duodenal Neuroendocrine Tumor with Atypical and Extensive Metastasis Responding Dramatically to a Single Fraction of PRRT with $^{177}\text{Lu}$ -DOTATATE

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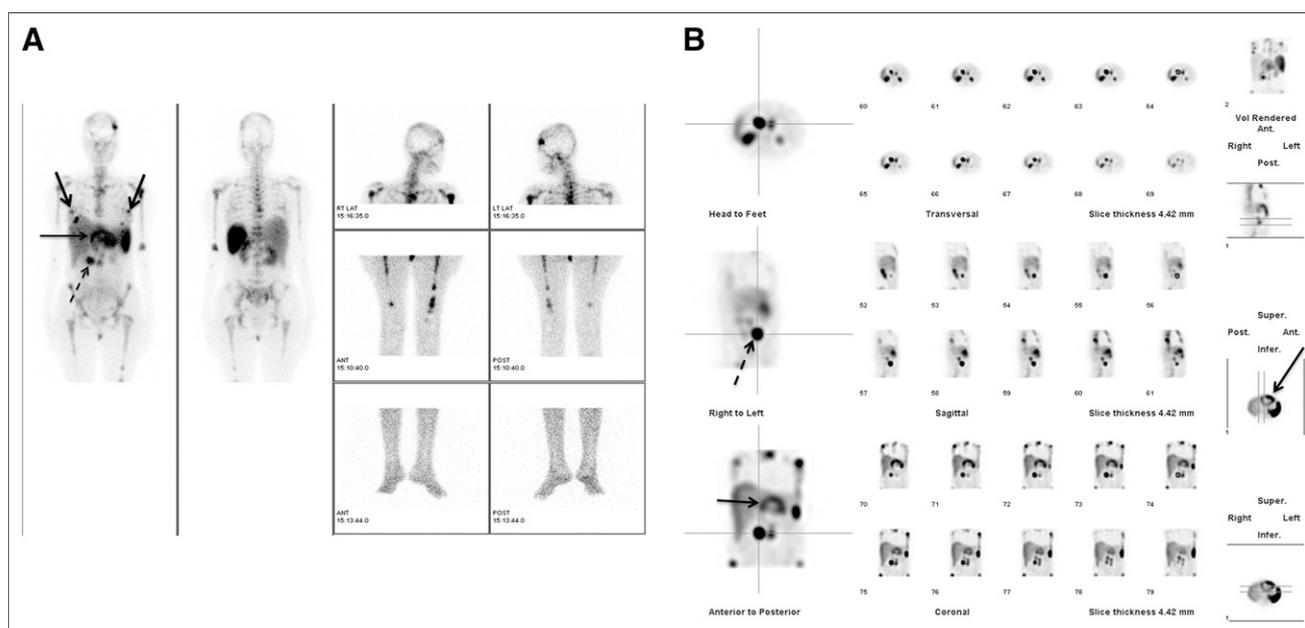
This report describes a case of extensive diffuse bone marrow involvement with bilateral breast metastases from duodenal neuroendocrine tumor giving rise to a superscan-like appearance on somatostatin receptor-targeted  $^{99m}\text{Tc}$ -hydrazinonicotinamide-TOC scintigraphy. The metastatic lesions demonstrated partial concordance with  $^{18}\text{F}$ -FDG PET/CT findings, signifying varying tumor biology and heterogeneity among metastatic lesions in the same individual, as illustrated with a dual-tracer approach.

There was a dramatic symptomatic and biochemical response and better health-related quality of life with a single fraction of peptide receptor radionuclide therapy with  $^{177}\text{Lu}$ -DOTATATE, and radiologically there was stable disease at that point.

**Key Words:** duodenal neuroendocrine tumor;  $^{99m}\text{Tc}$ -HYNIC-TOC scintigraphy;  $^{18}\text{F}$ -FDG PET/CT;  $^{177}\text{Lu}$ -DOTATATE

**J Nucl Med Technol 2014; 42:296–298**

DOI: 10.2967/jnmt.114.139238



**FIGURE 1.**  $^{99m}\text{Tc}$ -HYNIC-TOC planar (A) and SPECT (B) images demonstrating tracer uptake in residual primary tumor in duodenum (dotted arrow) and liver lesion (thin solid arrow) with fairly large area of photopenia suggesting necrosis. Diffuse uptake over axial and appendicular skeleton (with interspersed areas of focal uptake, particularly in left parietal bone) and intense bilateral uptake in breast nodules (thick solid arrows) indicate metastases from NET.

Received Feb. 18, 2014; revision accepted Apr. 14, 2014.

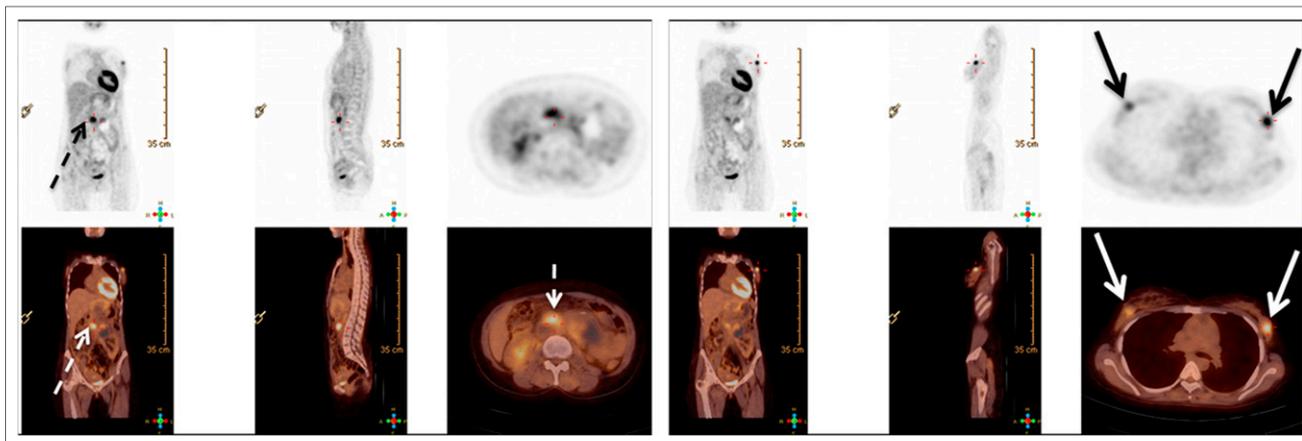
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Published online Sep. 4, 2014.

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**W**e present an unusual case of atypical metastatic disease from gastroenteropancreatic neuroendocrine tumor (NET) in bone marrow and breast, diagnosed using  $^{99m}\text{Tc}$ -hydrazinonicotinamide (HYNIC)-TOC scintigraphy. Varying biology and



**FIGURE 2.**  $^{18}\text{F}$ -FDG PET/CT demonstrating relatively intense uptake in duodenal primary tumor (dotted arrow), intense uptake bilaterally in metastatic breast nodules (solid arrows), low-grade  $^{18}\text{F}$ -FDG uptake in liver lesion, and no uptake in bone marrow.

heterogeneity among metastatic lesions in the same individual was demonstrated by a dual-tracer approach. Substantial symptomatic improvement with better health-related quality of life was documented with a single fraction of peptide receptor radionuclide therapy (PRRT) with  $^{177}\text{Lu}$ -DOTA-trocatate.

### CASE REPORT

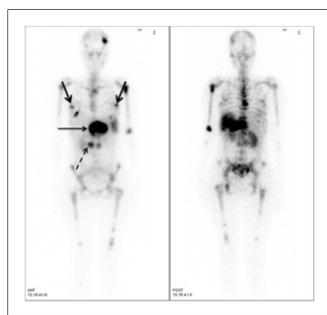
A 35-y-old woman diagnosed with duodenal NET (MiB-1 labeling index, 20%) with liver metastasis (involving the left lobe), and a history of radiofrequency ablation of the liver metastasis and external radiotherapy 6 mo previously, had progressively worsening symptoms of dyspnea on mild exertion, along with skeletal pain and weight loss. She was referred to determine her eligibility for PRRT. A  $^{99\text{m}}\text{Tc}$ -HYNIC-TOC planar study (Fig. 1A) and SPECT study (Fig. 1B) demonstrated tracer uptake in the liver lesion, with a large area of photopenia (suggesting necrosis) at the residual primary in the duodenum. In addition, diffuse bone marrow involvement (over the axial and appendicular skeleton, with interspersed focal areas of uptake, particularly in the left parietal bone) and bilateral breast metastases were observed. Both had been unknown before scintigraphy. Comparative  $^{18}\text{F}$ -FDG PET/CT showed partial concordance, demonstrating relatively intense uptake in the duodenal

primary tumor and bilateral metastatic breast nodules, with low-grade uptake in the liver lesion and absence of uptake in the bone marrow (Fig. 2). To summarize, the  $^{99\text{m}}\text{Tc}$ -HYNIC-TOC study demonstrated the duodenal primary tumor and 4 metastatic lesions (liver, both breasts, and bone marrow);  $^{18}\text{F}$ -FDG PET was positive for the primary tumor, breast disease, and only low grade uptake in the liver; and previous CT was positive only for the liver lesion, with the other metastatic lesions being unknown previous to the functional imaging.

The patient was treated with 7,104 MBq (192 mCi) of  $^{177}\text{Lu}$ -DOTATATE, and the posttherapy scan (Fig. 3) demonstrated an uptake pattern similar to that observed on the diagnostic  $^{99\text{m}}\text{Tc}$ -HYNIC-TOC scintigraphy. At the 3-mo posttherapy assessment, symptoms were substantially improved, health-related quality of life was better, and disease was radiologically stable. The serum chromogranin A level decreased from 1,135 to 786.70 ng/mL;  $^{99\text{m}}\text{Tc}$ -HYNIC-TOC scintigraphy demonstrated stable disease. The patient was prepared for a second cycle of PRRT.

### DISCUSSION

In recent years, PRRT has evolved as an effective therapeutic option for metastatic NET. Somatostatin receptor-targeted imaging (with  $^{99\text{m}}\text{Tc}$ -HYNIC-TOC,  $^{111}\text{In}$ -octreotide scintigraphy, or  $^{68}\text{Ga}$ -DOTANOC/TATE PET/CT) is integral for evaluating whether metastatic NET patients are eligible for PRRT.  $^{18}\text{F}$ -FDG PET/CT in NET can be regarded to be of more value for prognosis than for diagnostic staging (1–3) and can be positive, negative, or (interestingly) mixed positive/negative (as observed in this patient), thus depicting heterogeneity among different metastatic lesions in the same individual. The prognosis for NET with the dual-tracer approach is a subject of current research, and it is expected that the lesions with somatostatin receptor positivity and  $^{18}\text{F}$ -FDG negativity will demonstrate the most favorable behavior, followed by



**FIGURE 3.** Scan after  $^{177}\text{Lu}$ -DOTATATE therapy showing uptake pattern similar to that on pretreatment diagnostic  $^{99\text{m}}\text{Tc}$ -HYNIC-TOC scintigraphy.

those that are both somatostatin receptor–positive and  $^{18}\text{F}$ -FDG–positive, whereas the least favorable prognosis will be for those who are somatostatin receptor–negative and  $^{18}\text{F}$ -FDG–positive. However, this expectation needs further validation in prospective trials. A dramatic symptomatic response is one of the gratifying experiences with PRRT in this setting.

## CONCLUSION

An atypical metastatic pattern and differing tumor biology among the various lesions within the same individual was demonstrated in this report. Irrespective of the behavior, a dramatic symptomatic response and better quality of life were documented with PRRT with  $^{177}\text{Lu}$ -DOTA-octreotate.

## DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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