First line treatment with 177Lu-Dotatate in a patient with miliary liver metastases and carcinoid syndrome from a midgut neuroendocrine tumor

A. Diamantopoulos[a], V. Antonopoulou[a], G. Kyriakopoulos[b], M. Papachristou[c], SE. Papadimitriou[c] , P. Stavrou[c], I. Datseris[c], DA. Vassiliadi[a], S. Tsagarakis[a]*

[a] Department of Endocrinology, Diabetes and Metabolism, National Expertise Center for Rare Endocrine Disorders and member of the Endo-ERN, "Evangelismos" General Hospital of Athens, Athens, GREECE ; [b] Pathology Department, "Evangelismos" General Hospital of Athens, Athens, GREECE ; [c] Nuclear Medicine and PET/CT Department, "Evangelismos" General Hospital of Athens, Athens, GREECE

Introduction

Surgery is the only curable treatment for neuroendocrine tumors (NETs). However, many patients are diagnosed at an advanced, inoperative stage, aggravating their prognosis. Endocrine syndromes may impair both quality of life and survival. The NETTER-1 study established ^{177}Lu-Dotatate as an effective therapeutic tool for patients with well-differentiated, metastatic midgut NETs. Herein we present the outcome of ^{177}Lu-Dotatate as first-line treatment in a 21-year-old male patient with a clinically and structurally advanced metastatic midgut NET.

Observation

A 21-year-old male presented with:

- Multiple liver metastases (>30 lesions, affecting c.75% of the liver) and splenomegaly *(Figure 1A)*
- Carcinoid heart disease (affecting both tricuspid and pulmonary valves as well)
- Carcinoid syndrome (flushing up to 10 times daily and diarrheas)
- Excessively high serotonin (8,1xULN) and 5-HIAA levels (48xULN)

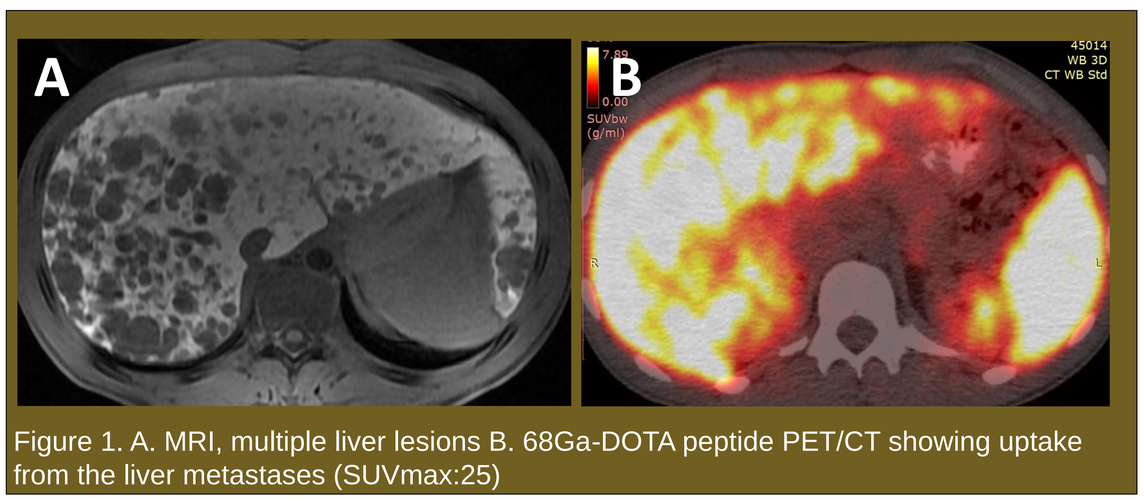

Figure 1. A. MRI, multiple liver lesions B. 68Ga-DOTA peptide PET/CT showing uptake from the liver metastases (SUVmax:25)

Liver biopsy: metastasis from well-differentiated neuroendocrine tumor (NET), Grade-2, ki67%: 8%, 0,6 mitosis per 10HPF, SSTR2a: +++ , Serotonin (+,100%), Chromogranin(+), Synaptophysin(+), CK8.18(+,100%), NKX2.2(+), CDX-2(+)

68Ga-DOTApeptide PET/CT *(Figure 1B):* uptake from the liver metastases and other abdominal lesions (Krenning3).

Therapeutic approach:

- Lanreotide and Telotristat, resulted clinical improvement and partial biochemical control.
- Lutetium-177(177Lu)-Dotatate at a dose of 7355MBq every 8 weeks. Lanreotide and Telotristat were continued.

Results

PRRT was very well tolerated with **mild adverse effects**, mainly during the infusion of the amino-acid solution. After completion of treatment, we noted grade 1-2 myelosuppression, which improved 1 year after the last infusion.

With regards to response,

- the patient is biochemically controlled *(Table 1)* and reports significantly reduced frequency of flushing and complete recession of diarrhea (note: he continues on SSA and telotristat)
- Carcinoid heart disease improved and pro-BNP levels returned to normal
- According to RECIST criteria both the size and number of liver metastases were reduced. Liver involvement reduced from 70% to 55% *(Figure 2*). A 20% reduction in metabolic activity was noted, as estimated by SUVmax *(Figure 3).*

Due to gall bladder stones, a consequence of lanreotide treatment, he underwent an uneventful cholecystectomy and resection of primary tumor, located in the small intestine.

Table 1	At diagnosis	21 months after Lutathera completion	Normal Values
CgA - (nmol/L)	625	70	*< 4*
5HIAA urine (mg/24h)	394	8.2	*0.7-8.2*
Serotonine (ng/ml)	2446	484	*70-300*

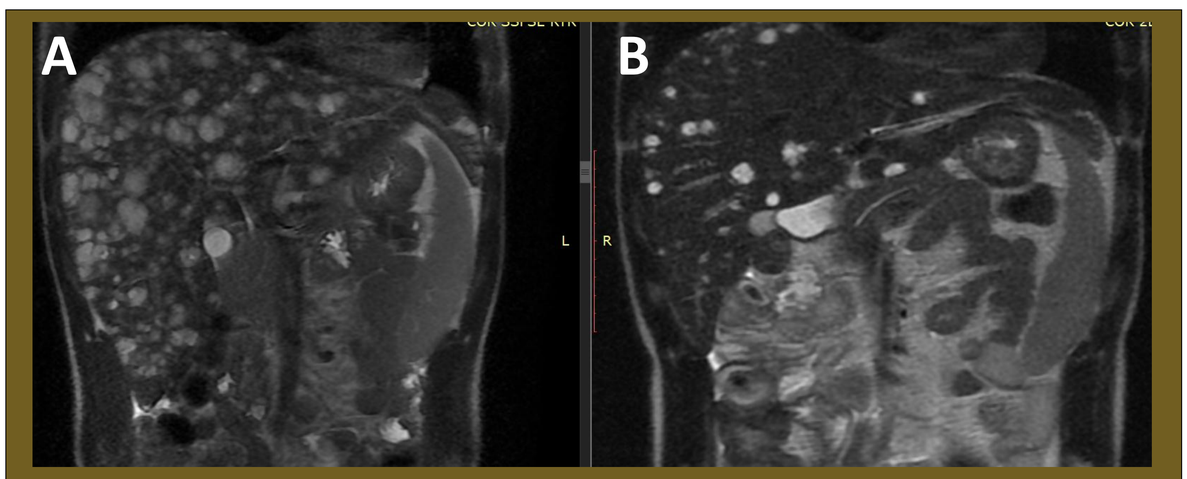

Figure 2. A. MRI liver lesions at diagnosis B. liver lesions 16 months post ^{177}Lu-Dotatate completion

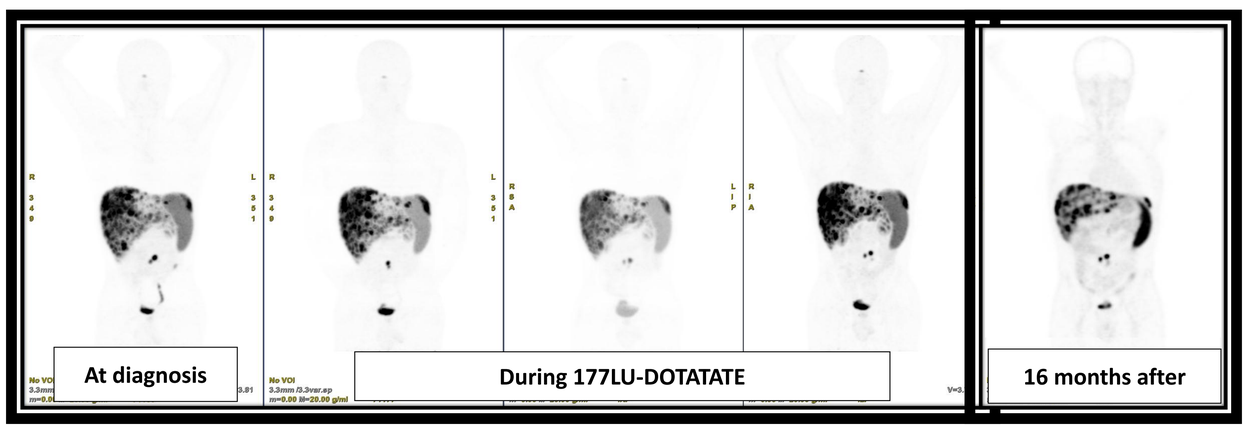

Figure 3: 68Ga-DOTA peptide PET/CT from diagnosis up to 16 months after ^{177}Lu-Dotatate completion
*The first 3 scans were performed in GE DISCOVERY ST and the last 2 scans in GE DISCOVERY MI DR

Discussion

Among other conventional therapies, PRRT has recently been shown to be effective, with regards to improved PFS and quality of life rate, significantly higher response, and a relative safe option when surgery is not feasible. In our case, treatment with 177Lu-Dotatate and somatostatin analogue was well-tolerated and resulted to PR that is sustained during a 21-month period, with biochemical normalization, clinical improvement and improvement of parameters of carcinoid heart disease.

Conflicts of Interest

No conflict of interest