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Case Report

Changing Amino Acid Infusion Rate Did Not Alter Renal Function, the Biodistribution and Subsequent Outcome of Lutathera Therapy: Report of an Experience Resulted by an Accidental Broken Lutathera Vial

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A Case Report

Background

The use of peptide-receptor radionuclide therapy (PRRT) with Lutathera for metastatic neuroendocrine tumors (NETs) has demonstrated an increased progression free survival [1]. High concentration of Lutathera in the kidneys requires amino acid infusion pre and post administration of Lutathera to protect the kidneys from radiation effects. The ACR–ACNM–ASTRO–SNMMI practice guidelines and the IAEA, EANM, and SNMMI guidelines describe that the amino acid infusion should be started 30 minutes prior to 177-Lu Dotatate therapy and continued for 3 hours post 177 Lu-Dotatate. The rate of amino acid infusion should be 250ml/hour [2].

The literature on the effect of different infusion rates of amino acids on the biodistribution of Lutathera and subsequent outcome of therapy is limited. Here we report our experience of the effect of a slower infusion rate of amino acids on the biodistribution of lutathera and outcome of therapy.

38 year old male patient diagnosed with grade 2 small bowel well differentiated NET status post resection of the primary in 2018 came to the nuclear medicine department on December 12th 2019, 11:30 am for his first cycle of Lutathera, 177-Lu Dotatate.

The pretreatment lab work showed a serum creatinine of 0.93 mg/dl, hemoglobin of 14.1 gm/dl and a normal platelet count. The technologist picked up the lead pig not realizing the cap was not tight. The pig and vial fell to the floor. The vial of Lutathera broke and the survey done by the Radiation Safety team showed contamination on the floor in the hot lab. The readings were over 200mR/hr at 1 meter. The patient had already started receiving the amino acid infusion at 250ml/hour.

Two patients were scheduled for Lutatthera treatment for that day and it was decided to proceed with treatment with this first patient who had already started the amino acids infusion using the Lutathera dose for the second patient (200 mCi) which arrived after two hours of starting the amino acids. The second patient was rescheduled. The amino acid infusion had to be adjusted appropriately due to the broken vial of Lutathera and resultant delay in administration of the lutathera.

Since this patient had already started the amino acid infusion, and since the plan was to administer the radiopharmaceutical 30 minutes into the infusion, now we had to modify the administration rate of the amino acids and/or total volume. We communicated with the clinical representative of the makers of Lutathera who offered two options in such a scenario. The first option would be to slow the infusion rate of amino acids so that it would still infuse for 3 hours after the Lutathera was given. The second option was to hang another bag of amino acids still at 250 ml/hr until 3 hours have been completed. Here even though you keep the rate the same a larger volume of amino acids will get infused. As the lutathera administration got delayed by one hour for example, this meant that there is only (1000 mL - 2hr × 250 mL/hr) = (1000 mL- 500 mL) = 500 mL left in the bag.

We opted for the first option and divided the remaining 500 mL over 3 hours to get 167 mL/hr. Thus, to infuse the remaining amino acids over 3 hours, we slowed the rate to 167 mL/hr.

The biodistribution of the radiotracer, such as renal uptake, on the 7 day post therapy scan after the first cycle with a lower infusion rate didn't look much different from the baseline Ga-68-Dotatate scan. The patient returned for a second dose of Lutathera therapy and the lab work showed serum creatinine of 0.91 mg/dl, hemoglobin of 12 g/dl, and a normal platelet count.

The 7 day post therapy scan after the second cycle using the standardized infusion rate of 250 ml/hr showed some improvement. The patient completed four cycles of PRRT, and subsequently a MRI abdomen the following year demonstrated improvement of multiple known metastatic liver lesions with stable mesenteric lymphadenopathy. A post 177-Lu dotatate scan after the fourth cycle of PRRT was not obtained as the patient completed his fourth cycle amidst the ongoing pandemic.

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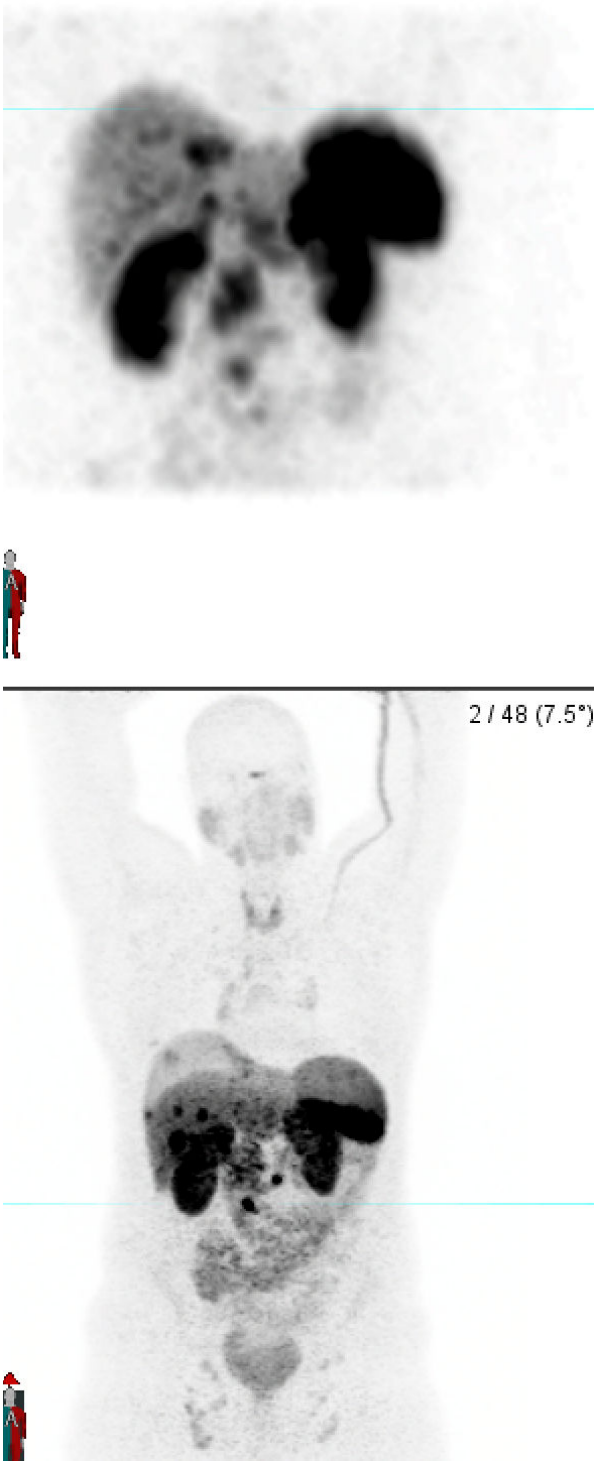

Image1: Pretherapy MIP image of Ga68- Dotatate PET demonstrating multiple liver lesions, scattered upper abdominal radiotracer avid lymphadenopathy.

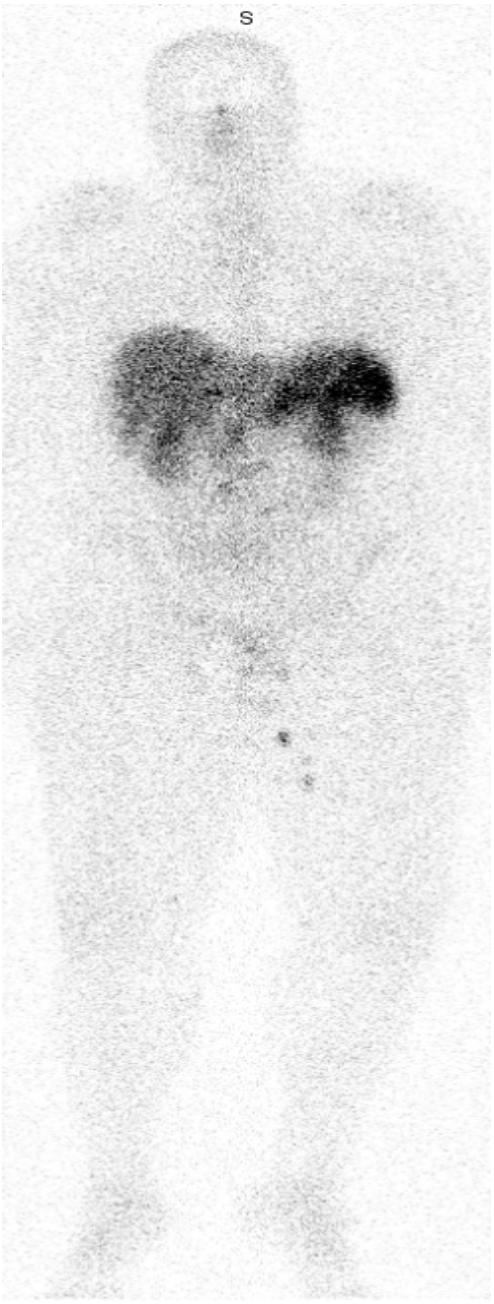

Image2: Post first cycle of therapy (177-Lu Dotatate) whole body planar images acquired 7 days after the infusion. These images were acquired after a slower infusion rate of the amino acid solution of 167 ml/hr for reasons as described above. The image demonstrates scattered regions of abnormally increased uptake within the liver and upper abdominal regions compatible with known sites of somatostatin avid disease. The additional region of uptake in the left thigh is urinary contamination.

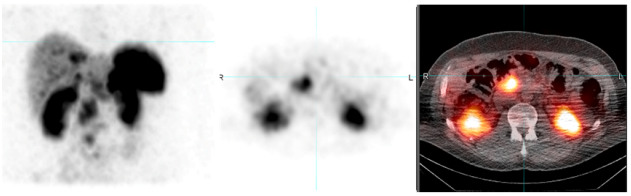

Image3: Snapshot of whole body planar, SPECT, SPECT/CT fused images acquired after first cycle of 177-Lu Dotatate therapy

better illustrating the radiotracer avid foci within the liver and upper abdomen.

Image4: Post second cycle of therapy (177-Lu Dotatate) whole body planar images acquired 7 days after the infusion. These images were acquired after a recommended infusion rate of the amino acid solution of 250ml/hr. The image again demonstrates scattered regions of abnormally increased uptake within the liver and upper abdominal regions in a similar pattern to prior study.

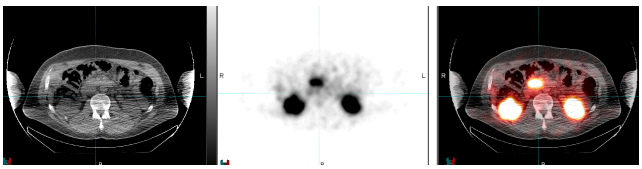

Image5: Snapshot image after the second cycle of therapy redemonstrating radiotracer avid upper abdominal lymphadenopathy in a similar pattern.

DISCUSSION

Our institution has performed around 80 cases of Lutathera (80x4 infusions) treatment. This is the first case where we had decreased the amino acid infusion rate from 250ml/hour to 167ml/hour after the Lutathera administration. In our case the reason for change was a broken Lutathera vial in the hot lab and delay in obtaining the replacement Lutathera dose. One can perceive altered infusion rate due calculation error or administration error.

In this single case of the decreased amino acid infusion rate the pre and 2 month post therapy renal function was unchanged and the protection to renal function was adequate.

This report highlights how to manage the amino acid infusion rate in case the delivery of Lutathera is delayed. We also are highlighting that the biodistribution of the tracer and renal protection is not significantly changed with changes in infusion rate.

It is known that coadministration of these amino acids leads to a significant reduction in the renal absorbed dose, which ranges from 9 % to 53 %. [3]. Renal absorbed dose is further reduced by up to 39 % by extending the infusion time of the amino acid solution over 10 h, and up to 65 % by extending the protection over 2 days following radiopeptide administration, thereby covering the renal elimination phase more efficiently [4,5]. A second study did not identify any difference in kidney dose for different amino acid protocols including 4 – 5 h before injection, 2 h before injection + 2 – 3 h after injection, 1 h before injection + 2 h after injection [8].

The original Bad Berka approach by Baum et al. iterated the infusion rate of amino acids to be 250 cc/hr and to be completed over 4 hours.[6].

The European Neuroendocrine Tumour Society (ENETS) consensus guidelines recommend intravenous administration of 2.5 % lysine, 2.5 % arginine in 1 L of normal saline over 4 h, starting 30 min before administration of the radiopharmaceutical [7].

Results of a study done by Bodei et al suggest that after a median follow-up period of 30 months, none of the patients treated with LuTate PRRT without chemotherapy showed renal toxicity [10].

Nausea and vomiting are common during the administration of commercial amino acid solutions when infusion rates are above 250 mL/hr. The NANETS/SNMMI procedure standard for somatostatin receptor based peptide radionuclide therapy with 177Lu Dotatate in 2019 recommends up to a 320 ml/hr infusion rat [11]. They recommend adding an antiemetic with infusions above 250ml/hr. However, of note is that most institutions across the United States follow the European guidelines [7]. And this seems to be a typically well accepted standard. Our case is an example where for unexpected reasons the infusion rate of amino acids had to be reduced to 167 ml/hr from 250 ml/hr but there was no significant change in biodistribution of the radiotracer with the post therapy scan being similar in appearance to the scan post another subsequent therapy [12].

The purpose of this paper is to highlight that a reduction in amino acid infusion rate did not change the biodistribution of the tracer, and the infusion rates can be customized to the patient needs. Thus a hypothesis is that we can customize the infusion rate in patients who will benefit from a slower infusion rate such as underlying heart and renal failure.

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