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Bowel Obstruction as a Complication of Peptide Receptor Radionuclide Therapy (PRRT)

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To the Editor:

With great interest, we recently read Strosberg et al.'s publication regarding the risk of bowel obstruction in patients with mesenteric/peritoneal disease who receive peptide receptor radionuclide therapy (PRRT).[1] At their institution, they reported that five patients experienced a bowel obstruction within three months of treatment. The authors hypothesized the mechanism of the bowel obstruction was inflammation induced by PRRT; this was supported by surgical findings of a "frozen abdomen" in two of those patients. Prior to their publication, there had been no known reports highlighting intestinal obstruction as a complication of PRRT.

Based on our institution's experience with the use of PRRT (^{177}Lu-dotatate) for gastroenteropancreatic neuroendocrine tumors (GEPNET), we would like to provide further evidence supporting Strosberg et al.'s hypothesis by reporting additional cases of bowel obstruction after PRRT. After witnessing several patients presenting with abdominal pain in the days shortly after treatment, we reviewed 80 patients who received PRRT prior to December 2018 at our institution. We found that sixteen patients went to the emergency department or were admitted to the hospital within the first fourteen days after a PRRT cycle, four of which were ultimately diagnosed with a bowel obstruction.

Our findings are in contrast with the clinical trial data in NETTER-1. In that trial's supplemental appendix, of patients who received PRRT there were only two hospitalizations in a much larger cohort of patients (n=116).[2] This could be explained by significant differences in the study population compared to our real-world cohorts. In the NETTER-1 trial, only 17 (15%) and 7 (6%) of the patients in the PRRT arm had metastases to the mesentery and peritoneum,

respectively. On the other hand, all four of our patients that had a bowel obstruction had known peritoneal disease, and in Strosberg et al.'s report, 81/159 (51%) of their patients had peritoneal/mesenteric disease, including all five who had an obstruction.[1]

Although peritoneal disease itself is a risk factor for intestinal obstruction, the fact that the patients at our institution developed obstructive complications within 14 days of PRRT treatment suggests an even stronger temporal cause-effect relationship. The hypothesized inflammation mechanism is even further supported by the radiographic finding of "pseudoprogression" with NETs which has already been commonly observed in other reports[3].

Existing literature regarding safety of PRRT has previously focused primarily on long-term complications and laboratory abnormalities, such as hematologic or renal toxicity. For example, the rare but serious complication of secondary myeloid neoplasms has been well-documented[4]. There are fewer reports of immediate toxicity or short-term complication, but in one retrospective review of patients who received PRRT in Grade 3 NETs (n=69) the authors reported that "PRRT was well tolerated by all patients"[5].

Unfortunately, our real-world experience provides additional examples that support Strosberg et al.'s observation that bowel obstruction is a short-term complication of PRRT treatment in patients with baseline peritoneal and mesenteric disease. To our knowledge, ours is the only other report that highlights this specific complication of PRRT. Clinicians should remain cognizant of the potential for intestinal obstruction when weighing risks and benefits of treatment options until we have more definitive evidence and experience.

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