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Hematologic Effects of Splenectomy in Patients with Pancreatic Neuroendocrine Tumors who Receive ^{177}Lu-DOTATATE PRRT

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BACKGROUND

Peptide receptor radionuclide therapy (PRRT) can cause hematologic toxicity, but its longitudinal pattern and the impact of prior splenectomy remain poorly defined. In pancreatic neuroendocrine tumors (pNET), distal pancreatectomy with splenectomy is common and usually leads to elevated baseline platelet and leukocyte counts. We characterized PRRT-associated hematologic changes and evaluated how splenectomy modifies absolute and proportional cytopenias, using non-PRRT treated patients as controls.

METHODS

We retrospectively analyzed 227 patients with pNET across four groups: PRRT with splenectomy (n=30), PRRT without splenectomy (n=54), non-PRRT treated with splenectomy (n=55), and non-PRRT treated without splenectomy (n=88). Approximately 55,000 serial hemoglobin, platelet, WBC, MCV, and RDW values were modeled longitudinally. Outcomes included per-patient percent change from baseline, worst CTCAE grade, and multivariable logistic regression of any-grade cytopenia adjusted for baseline count and follow-up duration.

RESULTS

Groups were similar in age, sex, and race. Within treatment arms, splenectomy was not associated with disease characteristics; PRRT patients had higher-grade tumors and more metastatic disease. Splenectomy was associated with higher baseline platelets (median 280 vs 194×10^9/L; p<0.001) and WBC (7.6 vs 5.3×10^9/L; p<0.001). After PRRT, platelets and WBC declined to a 6–12-month nadir with partial recovery. Proportional platelet decline was identical with and without splenectomy (−28.5% vs −28.6%; p=0.55), as was WBC decline. Hemoglobin decreased progressively by approximately 1 g/dL over 1–2 years, with parallel MCV increase (~3–4 fL) and stable RDW, consistent with a macrocytic pattern. Non-PRRT-treated patients were frequently anemic (~94%) but lacked progressive decline or count nadirs. By CTCAE thresholds, splenectomized PRRT patients had fewer cytopenias, including leukopenia (41% vs 78%; p=0.001). For thrombocytopenia, this effect was largely baseline driven, although three splenectomized patients developed

late grade ≥3 thrombocytopenia up to 7 years post-PRRT despite normal counts at treatment. Splenectomy remained independently protective against leukopenia after adjustment (OR 0.31; p=0.009), but was not associated with anemia-related outcomes. Splenectomized PRRT patients had longer overall survival (57.6 vs 30.5 months; p=0.022), likely reflecting selection for resectable disease; splenectomy was not associated with survival in non-PRRT patients.

CONCLUSIONS

PRRT produces a reproducible hematologic signature in pNET: reversible thrombocytopenia and leukopenia with progressive macrocytic anemia, a pattern absent in non–PRRT-treated controls. Splenectomy does not attenuate proportional marrow suppression but reduces absolute-threshold cytopenias through higher baseline hematologic reserve, with additional baseline-independent protection against leukopenia. Absolute CTCAE grading may therefore underestimate PRRT marrow effects in splenectomized patients, suggesting relative-decline monitoring warrants prospective evaluation.

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