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Baseline grade discordance in patients with pancreatic neuroendocrine tumors (PanNETs)

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BACKGROUND

Pancreatic neuroendocrine tumors (panNETs) are heterogeneous, with grade (G) defined by Ki67 proliferation index (<3% G1, 3-20% G2, and >20% G3) or mitotic rate. Previous studies suggest that baseline Ki67 index may be confounded by biopsy site (primary or metastasis), biopsy technique and primary tumor size. Ki67 differences leading to grade discordance in PanNETs at baseline is relatively understudied. Our study aims to evaluate grade discordance in synchronous biopsy samples.

METHODS

N=59 patients with two biopsies taken within 3 months of diagnosis between 2010 and 2021 were identified from an IRB approved database. Retrospective chart review was conducted to collect demographic and pathological data. Grade discordance proportion was estimated with Wald 95% CI. Comparison of biopsy characteristics and demographics were made using Pearson chi-square and Kruskal-Wallis test.

RESULTS

Among 59 initial biopsy samples (B1), 95% were from FNA/Core biopsy and 5% from surgical resection; 90% (n=53/59) from primary tumor, 10% (n=6/59) from a metastatic site. Median initial Ki67 index 2% (range 0-47.6%) and 83% had locoregional disease. Median follow-up 3.8 years. The second biopsy (B2) was taken a median of 46 days (range 0-91) later, mostly in the context of surgical samples (84.6%); 16% collected as FNA/core biopsy. Only 8% (n=5/59) B2 was performed in the setting of suspicious clinical behavior. In 84.7% of cases, both B1 and B2 taken from primary site. Grade discordance was observed in 22% (n=13/59, 95%CI: 11-32%); with 18.6% (n=11/59) revealing higher grade in B2 (G1 to G2 = 9, G2 to G3=2) and 3.3% (n=2/59) lower grade (G2 to G1). Median Ki67 index in B2 5.2% (range: 1-57%). Grade discordance (higher grade in B2) was more common in Black patients (75%, n=3/4) compared to non-Hispanic White patients (15%, n=6/33) [OR: 16.5, 95% CI: 1.5-186, p-value=0.01]. In this cohort, there is no evidence that grade discordance at baseline is associated with differences in biopsy sites, (p=0.73), diagnostic stage (p=0.86) and biopsy acquisition type (p=0.87).

CONCLUSIONS

Our study suggests baseline grade discordance is present in 22% of panNETs, regardless of type of biopsy or initial tumor stage. The higher prevalence in Black patients warrants additional study. Ongoing work is focused on assessing the relationship between tumor size, grade discordance, and overall survival. Further research is needed to determine the significance of and mechanisms underlying baseline grade discordance, particularly in larger and more diverse cohorts and those with metastatic disease at diagnosis (underrepresented in this cohort).

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