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Characterization of early-onset gastroenteropancreatic neuroendocrine neoplasms at UCSF

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BACKGROUND

Incidence rates of early-onset (age<50) neuroendocrine neoplasms (EO-NENs) in California are rising significantly across multiple organ sites. Recognizing the limitations of population-based registries (e.g. lack of detail regarding Ki67, grade progression, treatment sequence, functional status, germline findings), this study seeks to understand the incidence, clinicopathologic (CP), and demographic features of EO-NENs at UCSF.

METHODS

For this retrospective IRB-approved cohort study we identified 439 patients diagnosed with pancreatic NENs (panNENs) and 514 patients with gastrointestinal NENs (GI-NENs) between 2011 and 2023 (any stage, age, grade, or differentiation). Eligible patients are restricted to age < 50 at diagnosis. Chi-squared tests and Wilcoxon rank sum tests were used to test associations for categorical and continuous variables, respectively.

RESULTS

The study population consists of 132 with EO-panNENs and 120 with EO-GI-NENs. Preliminary results are available for EO-panNENs. (median follow-up 7.1 yr), which account for 30.1% of panNENs at UCSF: 50% female, 54.8% locoregional disease, and 70.8% White, 18.4% non-White, and 10.8 % “other”. The majority of EO-panNENs occur in the tail (54.5%) and 95.8% are well differentiated. Additional CP characteristics are summarized in **Table 1**:

Characteristic	Total (<50 yrs old) (n= 132, 100%)	18-39 yrs old (n=47, 35.6%)	40 - 49 yrs old (n=85, 64.4%)	P value
Grade at Diagnosis:				
G1/G2 NET	103 (91.2)	37 (94.9)	66 (89.2)	
G3 NET	6 (5.3)	0 (0.0)	6 (8.1)	
G3 NEC	4 (3.5)	2 (5.1)	2 (2.7)	0.299
Grade Progression	15 (12.7)	5 (12.5)	10 (12.8)	1.000
Functional Tumor	29 (24.0)	16 (35.6)	13 (17.1)	0.039

Demographic and CP variables associated with EO-panNENs are similar in very young (18-39) and young (40-49) patients (including tumor size, initial Ki67, and metastases or grade progression at any point), with the exception of functional tumors being more prevalent in the very young. N=59/132 (44.7%) underwent germline testing: 22/59 (37.3%) tested positive (the most common mutations being in MEN1, BRCA1, CHEK2, MSH2, and MUTYH2).

CONCLUSIONS

EO-panNENs represent a growing subset of patients that warrants special attention. EO-panNENs account for 30% of cases at UCSF and are predominantly low-grade, well-differentiated, and locoregional at diagnosis. Of note, 37% of tested patients harbor a pathogenic/likely pathogenic mutation. Further analyses of treatment patterns and survival according to CP variables are pending, as is an analysis of EO-GI-NENs (which will be reported at the meeting). Advances in our understanding of EO-NENs should lead to clues regarding etiology, detection, and optimal treatment.

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