Risk factors for sporadic pancreatic neuroendocrine tumors (PNETs): A single-center case control study

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BACKGROUND
- PNETs are uncommon tumors
- The annual incidence per 100,000 of PNETs in the US is 0.1 in females and 0.2 in males
- The clinical behavior of PNETs is variable, ranging from indolent to very aggressive tumors
- Little is known about risk factors for PNETs
- We evaluated smoking, alcohol use, family history of PNET and other cancers, and personal history of diabetes as potential risk factors

RESULTS: CHARACTERISTICS OF CASES AND CONTROLS

- 111 patients with PNET were evaluated
- Patients with MEN1 were excluded from the case control analysis
- The distribution of BMI, sex and race were similar among the two groups
- Fifty percent of the patients and controls came from Minnesota or the adjacent states but more controls than cases were from Minnesota
- Patients with insulinoma and high-grade PNETs were excluded
- Primary care patients seen for a general medical evaluation served as controls and were frequency matched (4:1 ratio) to patients with PNETs on age, sex and residence
- Patients and controls completed the same questionnaires at the time of their enrollment into the study
- Chi-square test or Fisher’s exact test was used for comparing categorical variables; continuous variables were compared using a two-sample t test.

RESULTS: PATIENT CHARACTERISTICS

- 178 patients with PNET were evaluated
- The mean age of patients was 59.2 years
- 50.6% were females
- The annual incidence per 100,000 of PNETs in the US is 0.1 in females and 0.2 in males
- Most tumors were either not graded or well differentiated
- 90.4% of tumors were clinically nonfunctional (defined as the absence of symptoms secondary to hormone overproduction)
- Six patients (5%) had a diagnosis of MEN
- 60% were symptomatic at diagnosis, most commonly with abdominal pain
- Cases were more likely to report a first degree family member with cancer, particularly sarcoma (p=0.001), PNET (p=0.033) and cancer of unknown primary (p=0.05), though numbers are small.
- There was no association of PNET with other cancers in first degree relatives

RESULTS: ANALYSIS OF RISK FACTORS

- Personal smoking history was not associated with PNETs (p=0.22)
- Environmental tobacco exposure was more common among cases than controls (p=0.001)
- Alcohol use was less common among cases than controls (p=0.001)
- Cases were more likely to have a diagnosis of diabetes than controls (p=0.001)
- Cases were more likely to report a first degree family member with sarcoma (p=0.001), PNET (p=0.033) and cancer of unknown primary (p=0.05), though numbers are small.

CONCLUSIONS
- The majority of patients had nonfunctional tumors with only 7% having clinically functional tumors
- Sporadic PNETs were metastatic in the majority of patients at the time of diagnosis
- There may be an association between smoking and exposure to environmental smoke and PNETs but this needs to be confirmed using a larger sample of patients
- Other studies have reported an association between smoking and carcinoid tumors of the small bowel but a recent case-control study using a large sample of GI neuroendocrine tumors did not observe such an association
- Although patients with PNET were more likely than controls to report a personal history of cancer, there was no association with any particular type of cancer
- The potential association of cancer in first degree relatives, particularly sarcoma, PNET and cancer of unknown primary needs to be explored using larger datasets

METHODS
- Patients with PNETs seen for the first time at the Mayo Clinic Rochester between 2000 and 2005 were included
- Patients with insulinoma and high-grade PNETs were excluded
- Primary care patients seen for a general medical evaluation served as controls and were frequency matched (4:1 ratio) to patients with PNETs on age, sex and residence
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