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Gastrointestinal polyposis and PTEN mutations: an under-acknowledged diagnostic criterion

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Background

The International Cowden Consortium (ICC) created operational diagnostic criteria that specify gastrointestinal (GI) hamartomas as a minor criterion. Previous review of reported case studies found that 35-85% of Cowden syndrome (CS) patients had GI hamartomas. Our goal is to describe the GI phenotype of our PTEN mutation positive (+) series.

Methods

Blood was collected for PTEN mutation analysis and medical records were requested to document diagnoses. Patients who are PTEN+ with ≥5 GI polyps, ≥1 of which is hyperplastic (hyp) or hamartomatous (ham, n=4) or who met relaxed ICC criteria (n=118) were analyzed. Upper and lower GI endoscopy and pathology reports were reviewed and findings are reported descriptively. Fisher's 2-tailed exact test and unpaired T-tests were utilized for comparison of PTEN+ patients with and without polyps.

Results

Out of 122 PTEN+ patients, 64 underwent ≥1 endoscopy, and 60(50%) had polyps or colorectal cancer (CRC). Average age at first colonoscopy and upper endoscopy was 37yrs (range: 2-73) and 40 (2-73) respectively. Number of polyps ranged from 1-innumerable. Polyps were found in the colorectum, ileum, duodenum, stomach, and esophagus. Pathology includes serrated adenomas; ham, hyp, adenomatous (ade), and inflammatory polyps; lymphoid aggregates; neuromas; lipomas; and ganglioneuromas. 16 patients had a hyp or ham polyposis mixed with other types of polyps, 13 had purely hyp or ham polyposis, and 6 had ganglioneuromatosis. 8 patients (6.6%) had CRC, 1 of whom did not have colorectal polyposis. One patient had gastric signet ring cell carcinoma in the setting of diffuse mixed hyp and ade polyposis. Polyposis patients were older at the time of study enrollment (mean=41.6yrs) compared to non-polyposis patients (26.7yrs, p=0.0001). The most common CS feature in polyposis patients was macrocephaly (70%). When compared to patients without polyps, those with polyps were more likely to have goiter/thyroid nodules (p=0.0001), trichilemmomas (p=0.0018), and papillomatous papules (p=0.0001), but less likely to have breast cancer (p=0.0412) and mental retardation/developmental delay (p=0.0062).

Conclusions

GI polyposis is the second most common CS feature in our series. Inclusion of this manifestation as a major criterion would result in an additional 19 patients (16%) meeting ICC criteria. We propose that the ICC revise their guidelines to include GI polyposis (defined as ganglioneuromatosis, mixed hyp or ham polyposis, ham or hyp polyposis) as a major criterion.

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