Further Defining the Polyposis Phenotype Associated with *PTEN* Mutations

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Background

PTEN hamartoma tumor syndrome (PHTS) is associated with an increased risk for colonic polyposis, particularly hamartomatous polyps. With the advent of multi-gene panel testing, *PTEN* mutations have been identified in patients with other polyp histologies, potentially widening the spectrum of gastrointestinal disease burden in these patients. We sought to define the polyp spectrum amongst *PTEN* mutation carriers identified by multi-gene panels.

Methods

In a review of over 14,000 results of five multi-gene panels (*BRCA*plus, BreastNext, ColoNext, OvaNext, and CancerNext) that include full gene sequencing and gross deletion/duplication analyses of *PTEN* resulted between March 2012 and March 2014, 23 (0.15%) *PTEN* positive cases were identified. Clinical histories provided by ordering clinicians were reviewed, and clinicians were contacted to confirm history. Family history of polyposis was not assessed.

Results

Of the *PTEN* positive cases, 11/23 (47.8%) had a reported personal history of colonic polyps of varying type and quantity. Four patients met criteria for attenuated or classic familial adenomatous polyposis, with one having 20-99 adenomas, one having 20-99 adenomas and 20-99 hamartomas, and two having greater than 100 adenomas. Two patients presented with less than 10 adenomas, but had other polyp types including mucosal, inflammatory, hyperplastic, and a rectal lipoma. One patient presented with 10-19 hamartomas. In 4 individuals polyps were reported without further information.

Conclusions

These results reveal that the polyp burden in *PTEN*-positive patients expands beyond hamartomatous polyps. However, our study was limited to information reported by ordering providers, which may be influenced by patient recall, inability to access prior medical records, or lack of prior screening colonoscopy. Furthermore, subjective pathological review of polyps may complicate the characterization of CS-associated gastrointestinal manifestations. Additional studies focused on polyp histologies of *PTEN* mutation carriers would help further delineate the gastrointestinal disease burden in these individuals. Our findings suggest that *PTEN* mutations should be part of the differential diagnosis for individuals with adenomatous and mixed polyposis and support the use of multi-gene panel testing in patients with colonic polyposis.