Fibroblastic Polyps: A Novel Polyp Subtype in Cowden Syndrome

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ABSTRACT

Cowden syndrome (CS) represents one possible phenotype of the PTEN gene mutation, and it can cause hamartomas throughout the gastrointestinal tract, with a predisposition for malignancy. Fibroblastic polyps have not been associated with CS. A 45-year-old woman with CS presenting for colonoscopic surveillance was found to have multiple sessile polyps throughout the transverse, descending, and sigmoid colon, all 2–5 mm in diameter. Based on the morphologic features and the immunohistochemical profile, these lesions were classified as fibroblastic polyps. This polyp subtype is recognized as a benign process of the colonic mucosa but is a novel histologic observation in the setting of CS.

INTRODUCTION

Phosphatase and tensin homolog (PTEN) hamartoma tumor syndrome represents a phenotypic spectrum resulting from mutations in the PTEN gene. Among the autosomal dominant conditions associated with such mutations, the most common is Cowden syndrome (CS), with an estimated incidence of 1 in 200,000–250,000 individuals based on prior population studies.¹⁻⁴ While a variety of clinical manifestations results from this condition, the increased risk of malignancy is principal among those affecting the gastrointestinal (GI) system. In parallel, the appreciation of the various endoscopic features of CS also continues to expand.

CASE REPORT

An asymptomatic 45-year-old woman with CS presented for routine endoscopic surveillance. The patient’s CS diagnosis had been substantiated on the basis of a remote history of pathology-confirmed minimally invasive follicular thyroid carcinoma status-post subtotal thyroidectomy, dermatologist-diagnosed oral papillomas of the tongue, multiple biopsy-proven trichilemmomas, macrocephaly (head circumference measuring 60 cm), and genetically confirmed heterozygous L108P PTEN mutation. She also had a history of Schwann cell hamartoma in the colon. Her father had also been diagnosed with genetically confirmed CS several years prior to her own diagnosis. On esophagogastroduodenoscopy (EGD), glycogenic acanthosis was observed in the esophagus (Figure 1). On colonoscopy, 12 sessile polyps measuring 2–5 mm in diameter were seen in the transverse, descending, and sigmoid colon (Figure 1). Histologic review following endoscopic removal and retrieval revealed that all 12 colon polyps featured replacement of the mucosa by bland spindle cells without an architectural pattern. Entrapped crypts demonstrated slight reactive change, distinct from the inflammation typically observed with inflammatory fibroid polyps, and also showed no evidence of hyperplasia or dysplasia (Figure 2). On immunohistochemical staining, the spindle cells were negative for S-100, epithelial membrane antigen, claudin-1, and CD34 (Figure 3). Based on these features, these lesions were classified as benign fibroblastic polyps. On a follow-up colonoscopy performed 2 years later, multiple small sessile polyps were again observed in the descending colon; histologic review with immunohistochemical staining was consistent with the prior findings and diagnosis.
DISCUSSION

Colonic fibroblastic polyps have only recently been identified as distinct histological entities amidst a variety of mucosal polyps. In 2004, Eslami-Varzaneh et al. initially described the cytologically bland spindled cells with fibroblastic features now characteristic of this polyp subtype. Since its initial description, studies have approximated the incidence of this mucosal lesion to range between 0.1–1.46% of all colon polyps, although others suggest this may be an underestimation. Some serrated polyps are associated with fibroblastic changes in the lamina propria, but the pathogenesis of fibroblastic polyps remains undefined.

In the clinical setting, benign fibroblastic polyps have largely been described in asymptomatic patients during routine screening endoscopy and may appear as mucosal lesions throughout the colorectum. The differential diagnosis includes ganglioneuroma, Schwann cell hamartoma, and perineurioma. Ganglioneuroma will have ganglion cells, and the spindle cell component will be at least focally positive for S100. Schwann cell hamartoma is strongly and diffusely S100-positive. Perineurioma is positive for epithelial membrane antigen and claudin-1. Fibroblastic polyps should not be mistaken for leiomyoma, which forms a well-circumscribed nodule arising from the muscularis mucosa and extending into submucosa, or for GI stroma tumor, which arises in the muscularis propria and is populated by plump spindle cells or epithelioid cells.

CS is categorized as a hamartomatous polyposis syndrome, given its propensity for the development of hamartomas, which are defined by non-malignant and disorganized proliferation of native tissue specific to the affected organ. Although hamartomatous polyps are considered to be the predominant lesion in this condition, a number of other polyp subtypes have also been observed, including ganglioneuromas, adenomas, serrated polyps, inflammatory polyps, lymphoid polyps, and leiomyomas. The diagnostic criteria for CS have recently been revised following a systematic review of the medical literature to include major and minor criteria based on the known clinical features of CS across multiple affected organ systems.

The variation in CS-associated polyp histology is reflected throughout the GI tract as associated findings include esophageal glycogenic acanthosis and a broad assortment of gastric, duodenal, and colon polyps. Despite a higher prevalence of GI polyps and an increased risk for breast, thyroid, and endometrial cancers, the predisposition for upper GI and colon cancers in CS is less clear. A recent study of 10 PTEN mutation carriers enrolled in a GI surveillance program concluded that adenomas and cancers may be more prevalent than presently estimated. In a larger study of PTEN mutation carriers, Heald et al. found 9 patients (13% of study group), all younger than 50 years of age, with colorectal cancer. Although the recommendations for GI surveillance are currently outlined in the National Comprehensive Cancer Network Guidelines, they remain missing from other major societal guidelines.

We hypothesize that the fibroblastic polyps observed in this case may have manifested as a part of the hamartomatous process associated with CS. While it is acknowledged that the discovery of fibroblastic polyps as illustrated in this case may also be an incidental finding without a pathophysiologic link to CS, an association between these conditions is strengthened by the observation of multiple fibroblastic polyps on subsequent endoscopic evaluations. As fibroblastic polyps have only recently been distinguished from other polyp subtypes, retrospective review of prior polypectomy specimens in the setting of CS may result in the identification of other cases. While this is an initial description of this association, the rarity of both conditions may account for the absence of interim reports. Regardless, the now-recognized association between these entities may lead to a better understanding of the pathogenesis for each condition with further study. As fibroblastic polyps have not been associated
with malignant potential, the interval for ongoing endoscopic surveillance interval as used by our individual practice was not altered by these findings.

DISCLOSURES

Author contributions: B. Anderson wrote the manuscript and is the article guarantor. T. Smyrk and S. Sweetser wrote and revised the manuscript.

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