Hyperplastic polyps are often found in the rectum and are considered to be the most common type of nonmalignant colonic polyp. Hyperplastic polyposis syndrome is a specific entity in which hyperplastic polyps are found in abundance throughout the colon in the absence of gastric or small bowel involvement. Diagnostic criteria for hyperplastic polyposis syndrome include: 5 or more hyperplastic polyps proximal to the sigmoid colon, 2 of which are larger than 1 cm; any number of hyperplastic polyps proximal to the sigmoid colon in a patient who has a first-degree relative with hyperplastic polyposis; or, more than 30 hyperplastic polyps throughout the colon.[13,19] This syndrome has a male predominance and is more common in patients over 40 years of age. Usually, the polyps are large, flat, and found along haustral folds. Polyps located in the proximal colon are usually sessile, serrated adenomas, which lead to an increased risk of right-sided colon cancer.[19,20] CCS polyps have been described and interpreted as hyperplastic in appearance, but they are most appropriately characterized as hamartomatous and are distinct from hyperplastic polyps.

When encountering an unusual number or distribution of polyps during an endoscopy, clinicians can find it helpful to examine the entire gastrointestinal tract for additional involvement and to scrutinize the histopathology of the polyps. Recognition of extraintestinal manifestations also facilitates accurate identification of polyposis syndromes.

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Review

Cronkhite-Canada Syndrome: An Acquired Condition of Gastrointestinal Polyposis and Dermatologic Abnormalities

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Cronkhite-Canada syndrome (CCS) is a noninherited condition associated with high morbidity and characterized by gastrointestinal hamartomatous polyposis,

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alopecia, onychodystrophy, hyperpigmentation, and diarrhea. Seshadri and colleagues present a typical case of CSS and provide a succinct review of the syndrome's diagnosis and management.[1]

The case report by Seshadri and colleagues describes an elderly Asian man who presented with weight loss, diarrhea, dysgeusia, and the dermatologic triad of hyperpigmentation, alopecia, and dystrophic nails.[1] Subsequent endoscopic and radiologic evaluation revealed sessile polyps in the stomach, small bowel, and colorectum. Histopathologic review of biopsies obtained from these polyps showed cystically dilated and distorted glands with inflammatory infiltration and edematous changes of the lamina propria; these findings are consistent with juvenile or inflammatory polyps. Based on clinical features, endoscopic and radiologic findings, and histopathology, a diagnosis of CCS was correctly made.

Despite being first described over 50 years ago, CCS has an obscure etiopathogenesis.[2] Given increased immunoglobulin (Ig)G4 mononuclear cell staining in CCS polyps, an autoimmune mechanism may be involved.[3] CCS can develop in all ethnic groups, and symptomatic disease onset occurs at a mean age of 59 years. Diarrhea and dysgeusia are the most common initial symptoms, with the dermatologic symptoms of alopecia, hyperpigmentation, and onychodystrophy often occurring later.[4] Most CCS patients exhibit all of the cardinal manifestations of the syndrome.[3] Polyps in CCS patients can develop throughout the gastrointestinal tract (except for the esophagus) and are non-neoplastic hamartomas.[3,4] Nevertheless, there is concern that CCS polyps may possess malignant potential, as evidenced by the dysplastic intestinal changes noted by Seshadri and coworkers and by reports of gastric, colon, and rectal cancers in patients with CCS.[1,5-11]

As demonstrated in the report by Seshadri and colleagues, CCS is a clinicopathologic diagnosis based on features of malabsorption in the setting of characteristic clinical, endoscopic, radiologic, and histologic findings.[1] Although CCS often has characteristic features, the differential diagnosis includes a number of polyposis syndromes, including familial adenomatous polyposis, Peutz-Jeghers syndrome, Cowden disease, and juvenile polyposis. Usually, it is not difficult to distinguish CCS from these polyposis syndromes, as each exhibits its own characteristic clinicopathologic features.[12] However, the endoscopic and histologic features of CCS polyps and juvenile polyps overlap and may appear identical.[13] A useful distinction between these 2 types of polyps is that the mucosa among CCS polyps is histologically abnormal, revealing edema, congestion, and inflammation of the lamina propria; in contrast, the mucosa among juvenile polyps is histologically normal.[13] In addition, IgG4 plasma cell infiltration occurs in CCS polyps, and IgG4 staining of hamartomatous intestinal polyps may provide additional information when evaluating polyposis syndromes.[3,14] The considerable overlap among the endoscopic and histologic features of CCS polyps and polyps in other polyposis syndromes makes CCS a clinicopathologic diagnosis that cannot be made solely based on polyp histology.

The question of whether polyps in CCS patients possess malignant potential is controversial. As seen in the report by Seshadri and colleagues, the risk of colorectal neoplasia appears to be increased in CCS patients.[1] There are case reports suggesting that both typical and serrated adenomatous polyp pathways may be involved, and the overall risk of colorectal cancer has been suggested to be as high as 25%.[6-11,15] In the largest single-center case series conducted in CCS patients to date, the incidence of colorectal neoplasia within the follow-up period was high (adenomas, 71%; cancer, 14%).[3] It is unknown whether the duration and/or extent of polyp formation accelerate the risk of neoplasia in CCS patients. One possibility is that the chronic generalized mucosal inflammation in CCS may increase neoplastic transformation similar to the inflammation-induced mutagenesis of idiopathic inflammatory bowel disease.

The risk of colorectal cancer may warrant aggressive screening in CCS patients. It may be extremely difficult—in fact, nearly impossible—to endoscopically detect background malignant polyps or concurrent adenocarcinoma, given the myriad of inflammatory-type polyps in CCS patients.[16] A recommended solution to this dilemma is to perform a repeat endoscopy after successful treatment, as treatment causes remission of most CCS polyps that are potentially inflammatory and non-neoplastic. The remaining large polyps (>1 cm) should then be electrosurgically removed, as they are more likely to contain an adenomatous component than smaller polyps.[16] However, despite prolonged treatment with corticosteroids, inflammatory CCS polyps may not regress. If repeat biopsy samples of persistent polyps in CCS patients show any degree of dysplasia, intestinal resection (eg, subtotal colectomy) should be considered. Therefore, endoscopic surveillance may be practical only after diffuse inflammatory polyposis responds to therapy, at which time otherwise obscured adenomas or cancer may be revealed.

Given the rarity of CCS, there are no evidence-based therapies, and no systematic investigations of medical or surgical interventions have been conducted to guide management. Numerous treatments have been attempted in CCS patients, with varying degrees of success. These treatments include hyperalimentation, corticosteroids, H_2-receptor antagonists, antibiotics, acid suppression, cromolyn sodium, anabolic steroids, surgery, and combinations of these therapies.[17] Corticosteroids are considered the mainstay of medical treatment for CCS. The typical steroid treatment regimen is 40 mg of prednisone for

1 week, with a 5-mg decrease every week until the patient is tapered off. In one study, a symptomatic response was seen within 3 months in 10 of 11 CCS patients treated with this regimen.[3] However, relapse of symptoms is common during the taper of corticosteroids; therefore, a steroid-sparing strategy has been employed with the immunomodulatory agent azathioprine in the previously mentioned study.[3] Five CCS patients who responded to corticosteroid treatment were placed on immunomodulatory therapy in the form of azathioprine (2 mg/kg/day); these patients achieved maintenance of clinical remission and no relapse after approximately 5 years of follow-up.[3]

Summary

The report by Seshadri and colleagues describes a patient diagnosed with the rare gastrointestinal polyposis syndrome of CCS based on a combination of clinical, endoscopic, and pathologic findings.[1] The diagnosis of CCS should be considered in patients with gastrointestinal hamartomatous polyps, diarrhea, and the dermatologic triad of alopecia, hyperpigmentation, and onychodystrophy. Malignant transformation of CCS polyps may occur, and the risk of colorectal cancer may warrant aggressive screening in CCS patients. Immunosuppression with corticosteroids or long-term azathioprine therapy may eradicate or lessen manifestations of CCS.

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