Chronic spontaneous urticaria associated with colon adenocarcinoma: A paraneoplastic manifestation? A case report and review of literature

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Key words: chronic urticaria; colon adenocarcinoma; malignancy urticaria.

INTRODUCTION
Chronic urticaria (CU) is a relatively common condition that is predominantly idiopathic in nature. A variety of etiologies has been established, yet most cases have no identifiable cause.\textsuperscript{1} The relationship between chronic urticaria and malignancy is controversial, with different studies showing varying results regarding whether a true association exists or if it is just a temporal coincidence.\textsuperscript{1,2} We describe the case of a 52-year-old female patient with colon adenocarcinoma with recurrent urticarial lesions and complete resolution upon removal of colon adenocarcinoma. To our knowledge, there have only been 5 cases reported that show an association between CU and colon adenocarcinoma.\textsuperscript{3-6}

CASE REPORT
A 48-year-old Hispanic female patient with no medical history presented to our dermatology clinic for evaluation of pruritic lesions on different body areas that had been present for 4 months. On physical examination, urticarial papules and plaques were observed on the trunk and extremities. The lesions appeared spontaneously and with scratching. The patient had chronic urticaria diagnosed and started on loratadine, 10 mg/d, with some improvement. Workup for chronic urticaria included: complete blood count, erythrocyte sedimentation rate, comprehensive metabolic panel, thyroid function tests, urinalysis, antinuclear antibody test, stool for ova and parasites, and stool for occult blood. All laboratory findings were unremarkable except for fecal occult blood test, which was positive. The patient was referred to a gastroenterologist who performed a colonoscopy, which found a large polyp-like lesion of 4.5 cm in the sigmoid colon that, upon biopsy, a foci of well-differentiated adenocarcinoma with high-grade dysplasia of 1.5 cm was diagnosed (Fig 1). The patient underwent a laparoscopic low anterior sigmoid resection with splenic flexure mobilization and lymphadenectomy. Several months after surgery, the patient was reevaluated at our clinic. She reported complete resolution of urticarial lesions immediately after surgery and discontinued the loratadine. On follow-up 2 years after surgery, the patient has not reported any recurrence of urticarial lesions.

Fig 1. Colonoscopic view of 4.5-cm polyp-like mass located in the sigmoid colon.
DISCUSSION

Urticaria has been associated with various causes including drugs, infections, foods, and multiple other factors. However, the cause of CU remains unknown in more than 80% of cases.1 Recently, an association between malignancy and chronic idiopathic urticaria has been suggested, but this association is controversial, and malignancy is only rarely considered the cause.7 Current guidelines do not recommend malignancy screening in patients with chronic urticaria unless indicated by specific clinical history, given insufficient evidence that supports a casual relationship.8

Because CU and malignant diseases are commonly encountered, it is not clear their concurrent occurrence suggests a causal relationship or just a mere coincidence. Malignancy has been suggested as the etiology of urticaria in a few cases. In a systematic review, Larenas-Linnemann et al9 described a total of 26 cases of urticaria caused by malignancy. With the addition of our case and one other case found,3 the number of cases increases to 28. Most cases (77%) had a CU duration of 2 to 8 months before detection of the malignancy. Most malignancies were carcinomas (68%), with 24% being hematologic and 24% papillary carcinomas of the thyroid gland. One case was seminoma, and one was astrocytoma.9 In most cases, thorough workup in search of the cause of chronic urticaria led to detection of malignancy in an early stage, improving the survival outcome of patients. Supporting the relationship between malignancy and urticaria, 6 of these cases report complete resolution of lesions after tumor removal.9 Additionally, 3 cases report the recurrence of urticarial lesions suggesting underlying cancer relapses. These findings suggest a possible shared etiology and CU manifesting as a paraneoplastic syndrome.

We describe a case of chronic spontaneous urticaria concomitant with colon adenocarcinoma in which removal of tumor led to complete resolution of lesions. To our knowledge, complete resolution of CU upon removal of colon adenocarcinoma has only been reported in 5 cases (Table I).3-6 Campanelli et al5 describes a 42-year-old female patient with CU of 9 weeks that was unresponsive to antihistamines. Upon review of systems, the patient reported heartburn, abdominal pains, and blood in the feces, which were attributed to known hemorrhoids. However, further evaluation found an adenocarcinoma of the colon for which the patient had a left hemicolectomy with 5 weeks of adjuvant chemotherapy. Information regarding the other cases is limited with further details outlined in Table I. One of the cases did not provide enough information to determine if removal of the tumor led to resolution of lesions. Although our patient did not have any gastrointestinal complaints, she did have a family history of colon cancer. Our case is relevant because it supports the finding that in certain patients, CU and malignancy may share a causal etiology; thus, urticarial lesions can be considered a paraneoplastic phenomenon. In addition, recurrence of urticarial lesions can alert physicians of possible cancer recurrence. This finding supports that along with the standard workup of CU, age-related screening tests may be incorporated to rule out malignancy. Physicians treating CU should be aware of this association, as it may aid in the prompt diagnosis and treatment of underlying malignancy in a select population of patients with chronic urticaria.

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**Table I. Summary of cases of chronic spontaneous urticaria associated with underlying colon adenocarcinoma**

| Study                        | Age (y) | Sex | Associated malignancy                                                                 | Time of duration of urticaria before diagnosis of malignancy | Resolution with removal of tumor |
|------------------------------|---------|-----|--------------------------------------------------------------------------------------|-------------------------------------------------------------|----------------------------------|
| Campanelli et al, 2005³      | 42      | F   | High-grade infiltrating adenocarcinoma of the descending colon                        | 9 wk                                                        | Yes                              |
| Lindelof et al,1990⁴         | 67      | M   | Colon (unspecified)                                                                  | 4 y                                                         | Unknown                          |
| Anderson et al, 1991⁵        | 68      | M   | Colon (unspecified)                                                                  | 12 mo                                                       | Yes                              |
| Sheldon et al., 1954⁶        | NS      | NS  | Carcinoma of the colon with central necrotic tissue                                  | NS                                                         | Yes                              |
| Current case                 | 52      | F   | Colon adenocarcinoma                                                                 | 3 mo                                                        | Yes                              |

NS, not specified.
*Two cases.
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